Treatise on the pathology of the urine, including a complete guide to its analysis.

Contributors

Thudichum, J. L. W. 1829-1901.
Royal College of Physicians of London

Publication/Creation

London : John Churchill, 1858.

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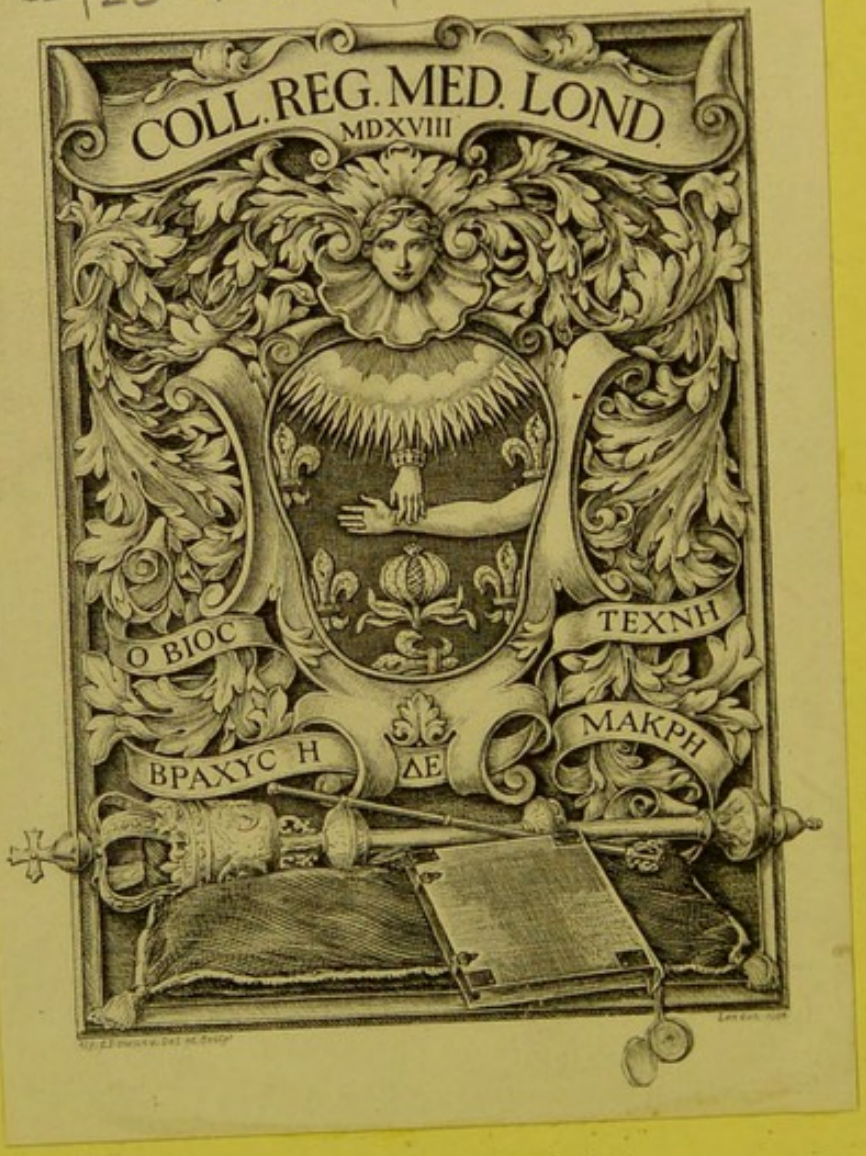
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A TREATISE

ON THE

PATHOLOGY OF THE URINE.

A TREATISE

ON THE

PATHOLOGY OF THE URINE,

INCLUDING

A COMPLETE GUIDE

TO

ITS ANALYSIS.

BY

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WITH SEVEN PLATES.



LONDON:
JOHN CHURCHILL, NEW BURLINGTON STREET.
MDCCCLVIII.

ROYAL COLLEGE OF PHYSICIANS
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PRINTED BY J. E. ADLARD,
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LIST OF CHAPTERS.

CHAPTER I.

GENERAL CHARACTERS OF URINE.

CHAPTER II.

QUANTITY OF URINE AND INGREDIENTS.

CHAPTER III.

UREA.

CHAPTER IV.

URIC ACID.

CHAPTER V.

CREATINE AND CREATININE.

CHAPTER VI.

COLOURING MATTER. URÆMATINE.

CHAPTER VII.

HIPPURIC ACID.

CHAPTER VIII.

CHLORINE AND CHLORIDES.

CHAPTER IX.

SULPHURIC ACID AND SULPHATES.

CHAPTER X.

PHOSPHORIC ACID AND PHOSPHATES.

CHAPTER XI.

FREE ACID OF THE URINE.

CHAPTER XII.

POTASH AND SODA.

CHAPTER XIII.

LIME AND MAGNESIA.

CHAPTER XIV.

IRON.

CHAPTER XV.

AMMONIA.

CHAPTER XVI.

CARBONIC ACID.

CHAPTER XVII.

BLOOD AND ITS ANATOMICAL ELEMENTS.

CHAPTER XVIII.

HÆMATINE OR HÆMATO-GLOBULINE.

CHAPTER XIX.

FIBRINE. CHYLOUS URINE.

CHAPTER XX.

CASTS OF URINIFEROUS TUBULES.

CHAPTER XXI.

ALBUMEN.

CHAPTER XXII.

PUS.

CHAPTER XXIII.

MUCUS.

CHAPTER XXIV.

FAT AND OIL.

CHAPTER XXV.

CANCER-CELLS AND TUBERCULAR MATTER.

CHAPTER XXVI.

ECHINOCOCCUS HOMINIS.

CHAPTER XXVII.

SPERMATIC FILAMENTS, OR SPERMATOZOA.

CHAPTER XXVIII.

BILE AND BILIARY MATTERS.

CHAPTER XXIX.

LEUCINE AND TYROSINE.

CHAPTER XXX.

XANTHINE.

CHAPTER XXXI.

HYPOXANTHINE.

CHAPTER XXXII.

SARCINE (CARNINE).

CHAPTER XXXIII.

CYSTINE.

CHAPTER XXXIV.

ALLANTOINE.

CHAPTER XXXV.

GRAPE SUGAR.

CHAPTER XXXVI.

ACETONE.

CHAPTER XXXVII.

INOSITE.

CHAPTER XXXVIII.

URERYTHRINE OR PURPURINE

CHAPTER XXXIX.

UROXANTHINE, OR INDICAN.
UROGLAUCINE, OR INDIGO BLUE.
URRHODINE, OR INDIGO RED,

CHAPTER XL.

PHENYLIC OR CARBOLIC ACID.

CHAPTER XLI.

DAMALURIC ACID.

CHAPTER XLII.

OXALIC ACID.

CHAPTER XLIII.

LACTIC ACID.

CHAPTER XLIV.

UROPHANIC ORGANIC ACIDS.

CHAPTER XLV.

UROPHANIC ORGANIC BASES.

CHAPTER XLVI.

UROPHANIC INORGANIC SUBSTANCES.

CONTENTS.

CHAPTER I.

GENERAL CHARACTERS OF URINE

PAGE

Physical Characters of Urine 1
Clearness and Turbidity . . . . . ib.
Tints 2
Table illustrative of the Tints 6
Odour 8
Taste . . . . . ib.
Chemical Reaction of Urine . . . . . ib.
Table showing the substances which cause the Reaction of Urine expelled from the bladder 15
Changes on Cooling 16

CHAPTER II.

QUANTITY OF URINE AND INGREDIENTS.

Modes of Collecting Urine 18
Total Quantity of Urine discharged in a given time . . 20
Quantity of Urine discharged in Health 21
Observations 22
Table showing the total Quantity of Urine discharged in given times by healthy individuals 24
Quantity of Urine discharged in Disease 27
Solids and Water.—Specific Gravity 30
Table for reducing the Indications at a Higher Temperature of a Glass Gravimeter to the standard temperature . . 35

CHAPTER III.

UREA.

PAGE

Symbol, Formula, Composition, Definition . . . 43
History 44
Physical Properties 46
Decomposition 45
Combinations 47
with Protoxyde of Mercury 48
Chloride of Sodium . . . . ib.
Nitric Acid . . . . . ib.
Oxalic Acid 49
Nitric Acid and Protoxyde of Mercury . . . 50
Diagnosis of Urea in Urine and other Animal Fluids . . 51
Liebig's Method of ascertaining the Absolute Quantity of Urea in Urine 52
Preparation of the Solution of Mercury for precipitating Urea from Urine 54
Episode: Mode of ascertaining the Amount of Protoxyde of Mercury contained in a Solution of Nitrate of Mercury . . 55
Episode in Episode: Preparation of the Standard Solution of Chloride of Sodium to be employed in ascertaining the Amount of Mercury in Solution 56
Mode of ascertaining Amount of Protoxyde, &c. (continued) . 57
Preparation of Mercurial Solution graduated for Urea (continued) . 59
Analysis of Urea in Urine.—Special Proceedings . . . 61
Modification of this Method required by an Excess of Urea in Urine ib.
Modification required by the Urea sinking to one per cent. . 62
Modification required by the Presence in Urine of Chloride of Sodium ib.
Modification required by the Urine containing Ammonia . . 65
Modification required by the Presence in Urine of certain Nitrogenized Matters, not being Urea . . . 66
Bunsen's Method of ascertaining the Absolute Quantity of Urea in Urine 67
Dr. Davy's Method of determining the Amount of Urea in Urine . 69
Physiological Quantity of Urea 73
Pathological Indications 74

CHAPTER IV.

URIC ACID.

Symbol, composition, and history 77
Occurrence of Uric Acid, and Methods of obtaining it pure . . 78
Physical Properties 79
Crystallography 80
Metamorphoses by Different Agents 81
Uric Acid Group 82
Determination of Uric Acid in Urine 83
Volumetrical Analysis for Uric Acid 85

PAGE

Salts of Uric Acid—Urates 87
Urate of Ammonia 88
Urate of Soda 90
Urate of Lime 91
Differential Diagnosis of Urates . . . . ib.
Amount of Uric Acid discharged during Twenty-four Hours . . 93
Pathological Changes in the Quantity of Uric Acid discharged during Twenty-four Hours 95
Deposits of Uric Acid and Urates 96
Deposits of Urates occurring after Emission . . . 99
Deposits of Urates occurring in the Urinary Passages . . 101
Observation . . . . . ib.
Deposits of Uric Acid occurring after Emission . . . 104
Deposits of Uric Acid occurring in the Urinary Organs . . 105
Observation 106
Crystallized Sediments 107
Observation . . . . . ib.
Observation 108
Uric Acid Concretions 109
1. Sand or Gravel. Crystalline Sediments . . . ib.
2. Uric Acid Calculi 111
Chemical Characters of Uric Acid Concretions . . 112
Concretions of Urate of Ammonia, Soda and Lime . . 113
Layers of Uric Acid and Urates in alternating and mixed Calculi . 114

CHAPTER V.

CREATINE AND CREATININE.

History 115
Creatine . . . . . ib.
Composition—Occurrence . . . . ib.
Liebig's Method of obtaining Creatine 116
Physical Properties 117
Chemical Properties 118
Decompositions . . . . . ib.
Physiology of Creatine 119
Quantity discharged in Twenty-four hours . . . 120
Creatinine 121
Composition—Occurrence . . . . ib.
Mode of obtaining Creatinine and Creatine from Urine . . ib.
Mode of obtaining Creatinine from Putrid Urine . . . 122
Mode of obtaining Creatinine from Creatine . . . 123
Physical Properties of Creatinine . . . . ib.
Chemical Properties 124
Combinations . . . . . ib.
with Chlorine . . . . . ib.

PAGE

Combinations with Chlorine and Bichloride of Platinum . . 125
with Sulphuric Acid . . . . . ib.
with Chloride of Zinc . . . . . ib.
Observations on the Quantity of Creatinine and Creatine discharged in given times by healthy individuals 126
Tables of these Observations 130

CHAPTER VI.

COLOURING MATTER—URÆMATINE.

Chemical Properties 131
Colour determining Groups of Urine 134
First Group.—Yellowish Urines . . . . ib.
Second Group.—Reddish Urines . . . . ib.
Third Group.—Brown Urines . . . . ib.
Table showing Amount of Uræmatine in equal parts of Urine of different colours 135
Physiology of Uræmatine 137
Quantity of Uræmatine in Disease.—Pathological Indications . . 138

CHAPTER VII.

HIPPURIC ACID.

Composition, History, and Literature 139
Occurrence and Methods of obtaining it pure . . . 140
Physical Properties, Chemical Properties, Decompositions . . 143
Compounds 145
with Nitric Acid . . . . . ib.
Hippuric Acid Salts—Hippurates 146
Hippurate of Baryta . . . . . ib.
Hippurate of Lime . . . . . ib.
Hippurate of Lead 147
Hippurate of Iron . . . . . ib.
Deposits of Hippuric Acid . . . . . ib.
Quantity of Hippuric Acid secreted in Twenty-four hours . . 148
Physiology . . . . . ib.
Pathological Occurrence 151

CHAPTER VIII.

CHLORINE AND CHLORIDES.

Remarks on the Incineration of Urine 153
Chloride of Sodium 154
Composition and Occurrence . . . . . ib.
Crystallography . . . . . ib.

PAGE
Chemical Properties 155
Diagnosis in Urine . . . . . ib.
Liebig's Method of determining the Quantity of Chlorine in neutral fluids by means of Nitrate of Protoxyde of Mercury . . ib.
Preparation of Mercurial Solution graduated for Chloride of Sodium 158
The Fluid applied to the Urine.—Special Proceedings . . 161
Daily average Amount of Chlorine discharged during Health . . ib.
Chlorine of the Urine in Disease 165

CHAPTER IX.

SULPHURIC ACID AND SULPHATES.

General Remarks 169
Method of determining the Amount of Sulphuric Acid in Urine by Volumetrical Analysis 170
Preparation of Test-fluid . . . . ib.
Application of Test-fluid to Urine . . . ib.
Direct Analysis of Sulphuric Acid 171
Quantity of Sulphuric Acid discharged by Healthy Persons during twenty-four hours 172
Physiological origin of Sulphuric Acid 173
Table showing the Influence of Diet upon the Amount of Sulphuric Acid discharged in the Urine 174
Quantity of Sulphuric Acid in Disease 176
Pathological Indications 177

CHAPTER X.

PHOSPHORIC ACID AND PHOSPHATES.

Phosphoric Acid. Composition, Equivalent, Formula . . 179
Physical Properties . . . . . ib.
Chemical Properties 180
Phosphates of Alkalies . . . . . ib.
Phosphates of Alkalies and Earths . . . . ib.
Phosphates of the Alkaline Earths . . . . ib.
Method of Ascertaining the Amount of Phosphoric Acid in Urine . 183
Preparation of the Solution of Iron of known strength . . ib.
Solution of Acetate of Soda 184
Application to the Urine. Total amount of Phosphoric Acid . 185
PO_5 of Alkalies and Earths separately . . . ib.
Quantity of Phosphoric Acid discharged by Healthy Persons during twenty-four hours 186
Table showing the Amount of Phosphoric Acid in Urine of twenty-four hours . . . . . ib.

PAGE

Table showing the Amount of Phosphoric Acid secreted in single hours 187
Physiology of Phosphoric Acid in the Urine . . . ib.
Quantity of Phosphoric Acid in the Urine of Disease . . 189
Examples. Males . . . . . ib.
„ Females 190
Table of Examples 191

CHAPTER XI.

FREE ACID OF THE URINE.

Mode of determining the Amount of Free Acid in the Urine . . 192
Preparation of the Standard Solution of Caustic Soda, according to Neubauer . . . . . ib.
The Fluid applied to the Urine 193
Quantity of Free Acid discharged in a given time by Healthy Individuals . ib.
Quantity of Free Acid in Disease 194

CHAPTER XII.

POTASH AND SODA.

Symbols, Equivalents. General Remarks . . . 195
Mode of determining the Quantity of Potash and Soda in the Urine . ib.
Physiological Relations of Potash and Soda . . . 196

CHAPTER XIII.

LIME AND MAGNESIA.

Symbols, Formulæ, Equivalents, and General Remarks . . 198
Aggregation 199
Separation of Phosphate of Lime and Magnesia from Urine, and Determination of their Collective Amount . . ib.
Modes of ascertaining the separate Quantities of Lime and Magnesia in Urine . . . . . ib.
Determination of the Lime as Sulphate . . . ib.
Determination of the Magnesia as Pyrophosphate . . . 200
Hempel's Method of determining the Lime as Oxalate, by means of Permanganate of Potash . . . . ib.
Preparation of the Solution of Permanganate of Potash . . 201
Determination of the Lime by a Graduated Solution of Hydrochloric Acid 202
Preparation of the Standard Solution of Hydrochloric Acid . ib.
Preparation of the Solution of Soda to correspond to the former Solution . . . . . ib.
The Fluids applied 203

PAGE

Determination of Magnesia by means of Volumetrical Analysis of its Phosphoric Acid 203
Deposits of Earthy Phosphates . . . . . ib.
Deposits of Phosphate of Lime 205
Physical Characters . . . . . ib.
Crystallization . . . . . ib.
Chemical Diagnosis of Deposits of Phosphate of Lime . . ib.
Deposits of Ammonio-Phosphate of Magnesia . . . 206
Physical Characters . . . . . ib.
Form of Crystallization . . . . . ib.
Chemical Properties 207
Earthy Phosphates in Calculi . . . . . ib.
Physiological Quantities of Earthy Phosphates in the Urine . . 209
Observations of the Quantity of Phosphoric Acid combined with Earths in Urine . . . . . ib.
Observations of the Quantity of Lime and Magnesia discharged during twenty-four hours 210
Pathological Indications . . . . . ib.
Carbonate of Lime 213

CHAPTER XIV.

IRON.

Symbol, Equivalent, and General Remarks . . . 214
Chemical Properties . . . . . ib.
Marguerite's Method of determining the Quantity of Iron in Urine . 215
Preparation of the Standard Solution of Permanganate of Potash . ib.
Application to the Urine 216
Physiology and Pathological Indications of Iron . . . ib.

CHAPTER XV.

AMMONIA.

General Remarks 218
Symbol, Equivalent, and Chemical Properties . . . 220
Demonstration of the Presence of Ammonia in Urine . . ib.
Determination of the Quantity of Ammonia in Urine by Volumetrical Analysis . . . . . ib.
Preparation of Standard Solution of Sulphuric Acid . . 221
Preparation of Standard Solution of Caustic Soda . . ib.
Application of the Fluids 222
Quantity of Ammonia discharged in the Urine during twenty-four hours by Healthy Individuals 223
Physiological Origin of Ammonia . . . . ib.
Pathological Indications 224

CHAPTER XVI.

CARBONIC ACID

PAGE

Symbol, Equivalent, Mode of determining its Quantity . . 226

CHAPTER XVII.

BLOOD AND ITS ANATOMICAL ELEMENTS.

General Remarks. Blood, Blood-Corpuscles, and Coagula . . 227
Microscopical Appearances and Reactions of Blood-Corpuscles . 228
Chemical Diagnosis of Blood in Urine 230
Pathological Indications . . . . . ib.

CHAPTER XVIII.

HÆMATINE OR HÆMATO-GLOBULINE.

Definition. Occurrence 234
Observations 235
Pathological Indications 237

CHAPTER XIX.

FIBRINE. CHYLOUS URINE. FIBRINOUS CASTS.

General Remarks 238
Chylous Urine . . . . . ib.
Pathology of so-called Chylous Urine 240
Fibrine, the Produce of Diseased Kidneys, coagulating after Excretion . 241

CHAPTER XX.

CASTS OF URINIFEROUS TUBULES.

Casts of Small Diameter 243
Intratubular Casts . . . . . ib.
Casts of Medium Diameter . . . . . ib.
Epithelial Casts . . . . . ib.
Granular Casts . . . . . ib.
Casts containing Fatty Matter . . . . ib.
Casts of Considerable Diameter 244
Pathological Indications of Casts of Uriniferous Tubules . . ib.
Intratubular Hyaloid Casts 245
Epithelial Casts 246
Granular Casts . . . . . ib.
Fatty Casts . . . . . ib.
Large Hyaloid Casts . . . . . ib.

CHAPTER XXI.

ALBUMEN.

	PAGE
Composition and General Remarks	247
General Characters of Albumen	ib.
Diagnosis of Albumen in Urine	250
Coagulation by Heat	251
Nitric Acid Test	252
Quantity of Albumen in Urine	ib.
Pathological Indications	253

CHAPTER XXII.

PUS.

General Remarks	256
Pus-corpuscles	ib.
Pathological Indications	258

CHAPTER XXIII.

MUCUS.

Chemical Characters of Mucus	260
Physical Characters	ib.
Physiological Quantity	261
Excess of Mucus	ib.
Pathological Indications	ib.

CHAPTER XXIV.

FAT AND OIL.

Different Forms	263
Chemical Characters	ib.
Pathological Indications	264

CHAPTER XXV.

CANCER-CELLS AND TUBERCULAR MATTER.

Occurrence and Microscopical Appearances	263
Cancerous Matter	ib.
Tubercular Matter	ib.

CHAPTER XXVI.

ECHINOCOCCUS HOMINIS.

PAGE

Description of Cysts 267
Symptoms 268
Cases . . . . . ib.

CHAPTER XXVII.

SPERMATIC FILAMENTS, OR SPERMATOZOA.

Occurrence 269
Indications . . . . . ib.
Reactions for, and Motility of Spermatozoa . . . 270

CHAPTER XXVIII.

BILE AND BILIARY MATTERS IN URINE.

General Description of Bile 271
Cholic or Glycocholic Acid 272
Decompositions: Choloidinic Acid and Glycocoll . . ib.
Cholalic Acid and Glycocoll . . . 273
Cholinic, or Taurocholic Acid . . . . . ib.
Decomposition: Cholalic Acid and Taurine . . . 274
Taurine, and Isæthionate of Ammonia . . ib.
Colouring Matter of Bile 275
Biliverdine . . . . . ib.
Bilifulvine 276
Diagnosis of Biliary Matters in Urine . . . . ib.
Pathological Indications 277

CHAPTER XXIX.

LEUCINE AND TYROSINE.

Leucine 279
Elements, History, Occurrence . . . . . ib.
Production 280
Chemical and Physical Properties 283
Decompositions 284
Salts of Leucine . . . . . ib.
Hydrochlorate and Nitrate . . . . ib.
Compounds of Leucine and Metallic Oxydes . . . 285
Copper, Mercury, Lead . . . . . ib.
Mode of obtaining Leucine from Urine . . . . ib.

PAGE

Tyrosine 285
Elements and Occurrence . . . . . ib.
Physical and Chemical Properties 286

CHAPTER XXX.

XANTHINE.

History, Occurrence 287
Mode of obtaining Xanthine from Calculi . . . ib.
Chemical Properties 288

CHAPTER XXXI.

HYPOXANTHINE.

Elements and History 289
Mode of obtaining Hypoxanthine . . . . ib.
Physical and Chemical Properties 290

CHAPTER XXXII.

SARCINE (CARNINE).

Formula and Composition 291
History and Occurrence . . ; . . ib.
Mode of obtaining it pure 292
Physical and Chemical Characters . . . . ib.
Compounds . . . . . ib.
Hydrochlorate . . . . . ib.
Hydrochlorate and Bichloride of Platinum . . . 293
Nitrate and Sulphate . . . . . ib.
Carnine, with Baryta . . . . . ib.
Oxyde of Silver . . . . ib.
Nitrate of Silver . . . . ib.
Diagnosis, and Relations 294

CHAPTER XXXIII.

CYSTINE.

Elements, Composition, Literature 295
Occurrence . . . . . ib.
Decompositions and Chemical Properties. . . . 296

CHAPTER XXXIV.

ALLANTOINE.

PAGE

Elements, Composition, Literature 298
Mode of obtaining Allantoine 299
Mode of obtaining it from Uric Acid . . . ib.
Physical and Chemical Properties 300
Decomposition: Urea and Allanturic Acid . . . ib.
Pathological Indications 301

CHAPTER XXXV.

GRAPE-SUGAR.

Elements, History, and Occurrence 302
Mode of obtaining it 303
Physical and Chemical Properties 304
Combinations . . . . . ib.
with Oxydes of Metals . . . . . ib.
Chloride of Sodium . . . . . ib.
Sulphuric Acid 305
Decompositions . . . . . ib.
Vinous Fermentation 306
Lactic Acid Fermentation 307
Viscous Fermentation . . . . . ib.
Quantitative Determination of Grape Sugar by Volumetrical Analysis . ib.
Preparation of Test Fluid 308
Application of the fluid . . . . . ib.
Optical Saccharimetry 309
Use of Polarizing Apparatus 310
Pathological Indications of Sugar in Urine . . . 312

CHAPTER XXXVI.

ACETONE.

Elements, and Mode of obtaining it 314
Physical and Chemical Properties . . . . ib.
Acetone in the Urine of Diabetic Patients . . . ib.
Dr. Petter's Observation 315

CHAPTER XXXVII.

INOSITE.

Elements, Composition, and History 318
Mode of obtaining Inosite . . . . . ib.
Physical and Chemical Properties 319

CHAPTER XXXVIII.

URERYTHRINE OR PURPURINE.

PAGE

History 320
Occurrence 321
Mode of obtaining it pure . . . . . ib.
Physical and Chemical Properties 322
Diagnosis in Urine 322
Pathology of Urerythrine 323
Diseases in which Urerythrine most commonly occurs in Urine . 324

CHAPTER XXXIX.

UROXANTHINE OR INDICAN. UROGLAUCINE, OR INDIGO BLUE. URRHODINE, OR INDIGO RED.

History 326
Uroxanthine, or Indican 328
Occurrence 329
Products of Decomposition, Indigo Blue and Indigo Red . . ib.
Mode of obtaining these substances pure . . . ib.
a. From the Indigo of Commerce . . . . ib.
Crystalline Indigo Blue by Sublimation . . 330
„ „ by Reduction . . . ib.
Amorphous Indigo Blue by Reduction . . . ib.
Physical and Chemical Properties . . . 331
b. Heller's Method of obtaining Indigo Blue and Indigo Red from Pathological Urine . . . . ib.
Proofs of the Identity of Uroglaucine and Urrhodine with Indigo Blue and Indigo Red . . . 332
c. Schuncks's Method of obtaining Indigo Blue from ordinary Urine 334
Metamorphoses of Indigo Blue 336
Indigo White . . . . . ib.
Isatine . . . . . ib.
Anthranilic Acid 337
Physiology of Indican . . . . . ib.

CHAPTER XL.

PHENYLIC OR CARBOLIC ACID.

Formula, History, and Occurrence 339
Mode of obtaining it Pure . . . . . ib.
From Coal Tar . . . . . ib.
From Urine of Cows 340
From Human Urine . . . . . ib.
Observation of Phenylic Acid in Urine after Inunction of Tar . ib.
Physiology of Phenylic Acid 342

CHAPTER XLI.

DAMALURIC ACID.

PAGE

Formula, History, Physical, and Chemical Properties . . 343
Compounds . . . . . ib.
Mode of obtaining it pure . . . . . ib.

CHAPTER XLII.

OXALIC ACID.

Formula, Composition 345
History and Occurrence . . . . . ib.
Mode of producing Oxalic Acid 346
Physical and Chemical Properties . . . . ib.
Decompositions 347
Compounds . . . . . ib.
Oxalate of Lime . . . . . ib.
Physical Characters of Oxalate of Lime 348
Preparation of Objects for Microscopical Observation . . 353
Artificial Oxalate of Lime 354
Pure . . . . . ib.
From Well Water 355
From Urine 356
Oxalate of Lime occurring in Urine spontaneously . . . 358
Case of so-called Oxaluria . . . . . ib.
Oxalate of Lime in decomposing Urine 360
Crystals of Oxalate of Lime from Urinary Calculi . . . ib.
Polarization of Oxalate of Lime 361
Mode of determining the Quantity of Oxalic Acid in Urine . . 362
Pathological Indications . . . . . ib.
Experiments of Wöhler 363
Experiments of Piotrowsky and Buchheim . . . 364
Further Indications of Oxalic Acid in Urine . . . 366
Case of Albuminuria, with Oxalate of Lime in the Urine . . 368
Concretions of Oxalate of Lime 370
Sand and Gravel . . . . . ib.
Renal Concretions . . . . . ib.
Calculi. Mulberry Calculi . . . . . ib.
Layers of Oxalate of Lime in alternating and mixed Calculi . . 371
Chemical Characters of Oxalate of Lime Concretions . . ib.
Statistics of Oxalate of Lime Concretions . . . 372

CHAPTER XLIII.

LACTIC ACID.

PAGE

Formula, Composition, Occurrence 373
Mode of obtaining it pure . . . . . ib.
from Alanine . . . . . ib.
by Fermentation of Sugar . . . . . ib.
from the Juice of Flesh (Liebig's method) . . 374
Mode of ascertaining the Presence of Lactic Acid in Urine . . 375
Physical and Chemical Properties . . . 376
Compounds 377
Lactate of Lime . . . . . ib.
„ Zinc . . . . . ib.
„ Copper . . . . . ib.
„ Lime from the Juice of Flesh . . . ib.
„ Zinc from „ . . . ib.
Pathological Indications 378

CHAPTER XLIV.

UROPHANIC ORGANIC ACIDS.

General Remarks 380
1. *Succinic Acid* 381
Formula, Composition . . . . . ib.
Experiments . . . . . ib.
2. *Malic Acid* 381
Formula, Composition . . . . . ib.
Experiments . . . . . ib.
3. *Tartaric Acid* 382
Formula, Occurrence . . . . . ib.
Experiments on the Reappearance of Tartaric Acid in Urine after Ingestion into the Stomach . . . ib.
Wöhler's Experiments 382
Buchheim's Experiments 383
Free Tartaric Acid . . . . . ib.
Bitartrate of Potash 384
Neutral Tartrate of Potash 385
Tartrate of Soda and Potash . . . , ib.
Tartrate of Iron and Potash . . . . ib.
Tartrate of Suboxyde of Nickel and Potash . . ib.
Table of the Experiments 386
4. *Citric Acid* 387
Formula . . . . . ib.
Experiments of Morichini, and others . . . ib.
„ Buchheim . . . . ib.

PAGE

5. *Tannic Acid* 338
Elements . . . . . ib.
Experiments of Wöhler and Frerichs . . . ib.
Decomposition of Tannic Acid into Gallic Acid and Sugar . ib.

6. *Toluylic Acid* . . . . . ib.
Elements . . . . . ib.
Experiments of Kraut . . . . . ib.
Compound of Toluylic Acid and Glycocoll, Toluric Acid . 389

7. *Salicylic Acid* 390
Elements . . . . . ib.
Bertagnini's Experiments . . . . ib.
Compound of Salicylic Acid and Glycocoll, Salicyluric Acid . ib.

8. *Camphoric Acid* 391
Elements . . . . . ib.
Bertagnini's Experiments . . . . ib.

9. *Anisic Acid* 392
Elements . . . . . ib.
Bertagnini's Experiments . . . . ib.

10. *Cuminic Acid* . . . . . ib.
Elements . . . . . ib.
Experiments . . . . . ib.

CHAPTER XLV.

UROPHANIC ORGANIC BASES.

General Remarks 393

1. *Quinine and Quinidine* . . . . . ib.
Elements . . . . . ib.
Herapath's Test. Iodo-chinine and Sulphuric Acid . . ib
Special Proceedings 394

2. *Strychnine* 397
Elements. Diagnostic Properties . . . . ib.
Mode of obtaining Strychnine from Urine . . . ib.

3. *Santonine* 398
Elements . . . . . ib.
Red Pigment in Alkaline Urine . . . . ib.
Kletzinsky's Experiments 399
Relations between Santonine and Pyrotartaric Acid . . ib.
Compound of Santonine and Soda . . . . ib.

CHAPTER XLVI.

UROPHANIC INORGANIC SUBSTANCES.

PAGE

1. *Iodine* 401
General Remarks . . . . . ib.
Volumetrical Analysis of Iodine in the Urine. Kersting's method . 402
Preparation of Solution of Iodide of Potassium of known strength . ib.
Solution of Chloride of Suboxyde of Palladium of known strength . 403
Application to the Urine 404
2. *Arsenic and Antimony* 405
General Remarks . . . . . ib.
Reinsch's Method of obtaining Arsenic and Antimony from Urine . ib.
Diagnosis of Arsenic and Antimony 406
3. *Lead* . . . . . ib.
Kletzinsky's Method of obtaining Lead from the Urine of Patients labouring under Lead-Poisoning . . . ib.
Dr. Sieveking's Case 407
4. *Mercury* 408
Demonstration of Mercury in Urine . . . ib.
5. *Copper* . . . . . ib.
Kletzinsky's proceeding for demonstrating the Presence of Copper in Urine . . . . . ib.
Various Inorganic Substances 409

ADDENDA.

1. *Trimethylamine* 411
Dessaigne's Mode of obtaining it from Human Urine . . ib.
2. *Sarkine* . . . . . ib.
Remarks on Synonyms . . . . . ib.
Mode of obtaining Sarkine from Human Urine . . ib.
3. *Sarcina Ventriculi* 413
Synonym, Description, Cases . . . . ib.
4. *Urostealith* 414
Heller's Case . . . . . ib.
Chemical Properties 415

TABLE I.—Table showing the Constituents of the Normal Urine of Twenty-four Hours 416

" II.—Table for discovering the Nature of Urinary Deposits by Chemical reagents 417

PAGE

TABLE III.—Table for the Microscopical Chemical Examination of Urinary Deposits 418

„ IV.—Table for the Conversion of the Centigrade Thermometer Scale into that of Fahrenheit, and *vice versa* . . . 419

„ V.—Tables for the Conversion of French Weights and Measures into English Weights and Measures 420

„ VI.—Table for the Conversion of the Millimètre Barometer Scale into the Scale of English Inches 421

ALPHABETICAL INDEX 423

EXPLANATION OF PLATES.

PLATE I.

Fig. 1. Urea. Quadratic prisms, and their combinations. The lower, more perfect crystals, are obtained by the addition of absolute alcohol to a saturated solution of urea in spirits of wine. The upper half of the circular field exhibits prisms and needles obtained by the rapid evaporation of a solution of urea in methyl-alcohol. (See p. 45.)

„ 2. Nitrate of urea. Rhombic prisms and plates, representing the type of a precipitate obtained by adding to a concentrated watery solution of urea, colourless nitric acid. Much more perfect crystals, radiary groups of needles, are obtained by the slow evaporation of a solution of this salt in water. (See p. 48.)

„ 3. Oxalate of urea. Rhombic prisms and plates, representing the type of a precipitate, by adding oxalic acid to a solution of urea. (See p. 49.)

„ 4. Nitrate of urea and mercury; the salt obtained by permitting the precipitate of Liebig's quantitative test to crystallize in the acid fluid. (See pp. 50, 53.)

„ 5. Uric acid, pure, in delicate rhombic prisms and plates. They polarize in beautiful colours between crossed Nicholl prisms. (See p. 80.)

„ 6. Uric acid, in rhombic prisms and plates, crystallized from concentrated hydrochloric acid. (See p. 80.)

Plate I.

Fig. 1.



Fig. 2.

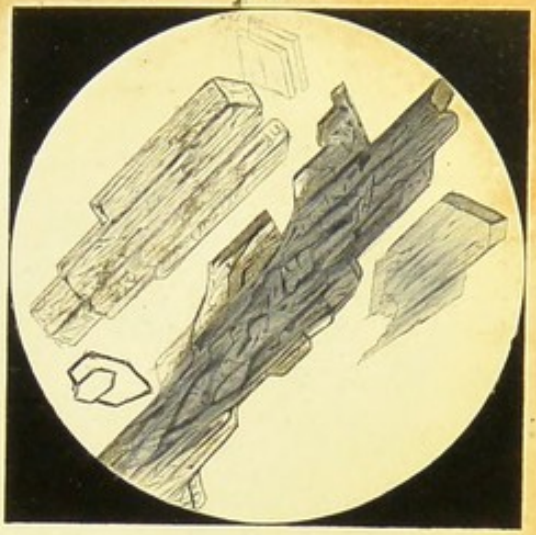


Fig. 3.



Fig. 4.

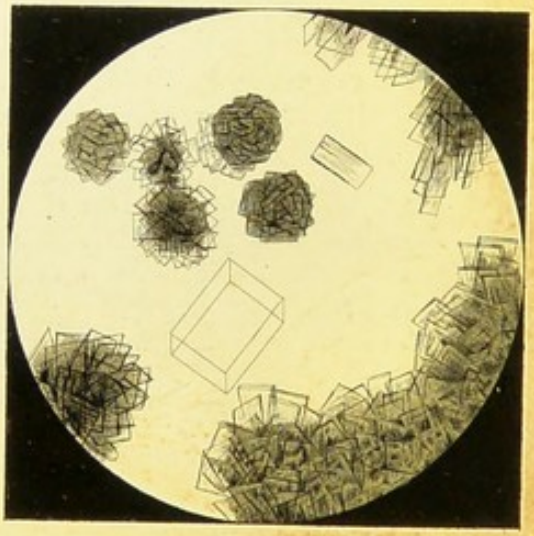


Fig. 5.

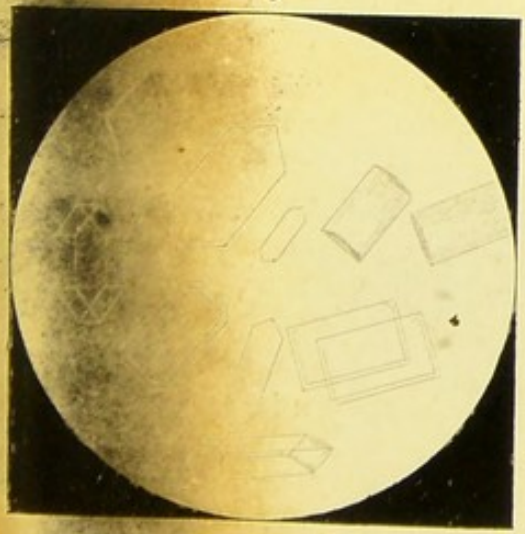


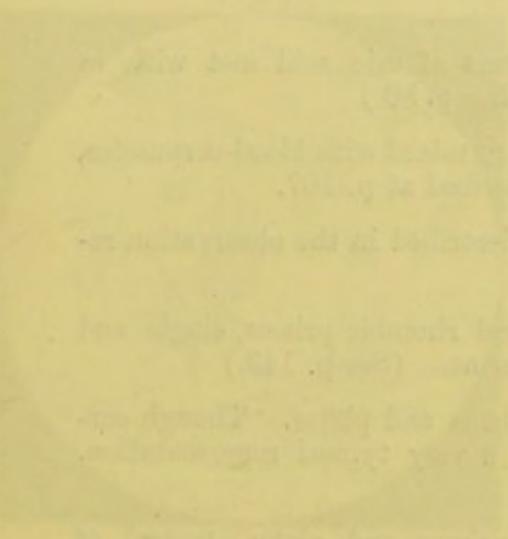
Fig. 6.



Lith. Anst. v. Adolph Werl in Leipzig.







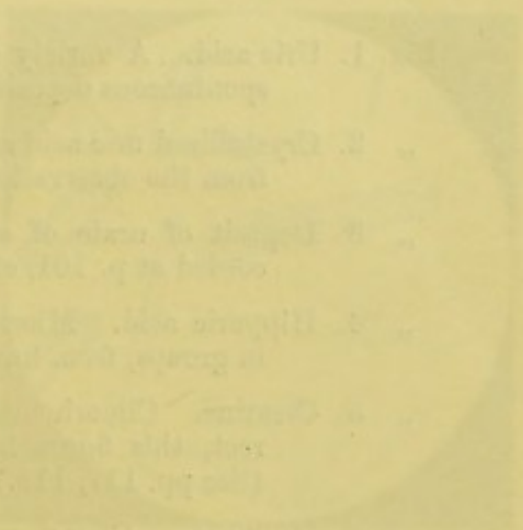






PLATE II.

Fig. 1. Uric acid. A variety of forms of uric acid met with in spontaneous deposits. (See p. 80.)

„ 2. Crystallized uric acid sediment mixed with blood-corpuscles, from the observation described at p. 107.

„ 3. Deposit of urate of soda, described in the observation recorded at p. 101, et seq.

„ 4. Hippuric acid. Microscopical rhombic prisms, single and in groups, from human urine. (See p. 143.)

„ 5. Creatine. Clinorhombic prisms and plates. Though correct, this figure is not a very typical representation. (See pp. 117, 118.)

„ 6. Creatinine. Clinorhombic prisms and plates, typical of a good specimen, crystallized from alcohol. (See p. 123.)

Plate II.

Fig. 1.



Fig. 2.



Fig. 3.

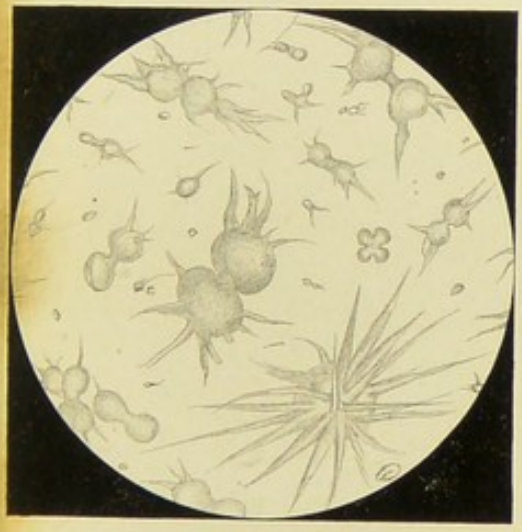


Fig. 4.

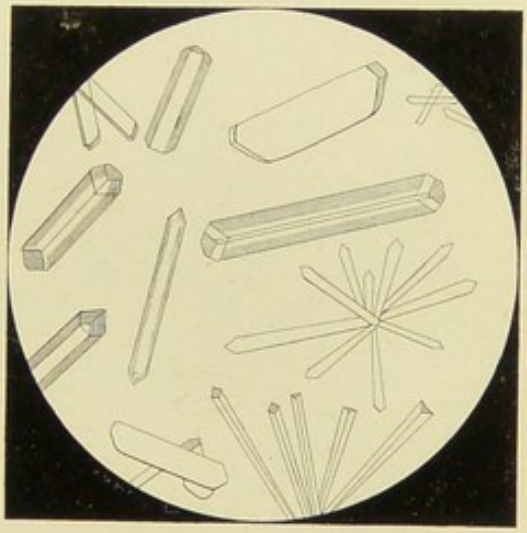


Fig. 5.

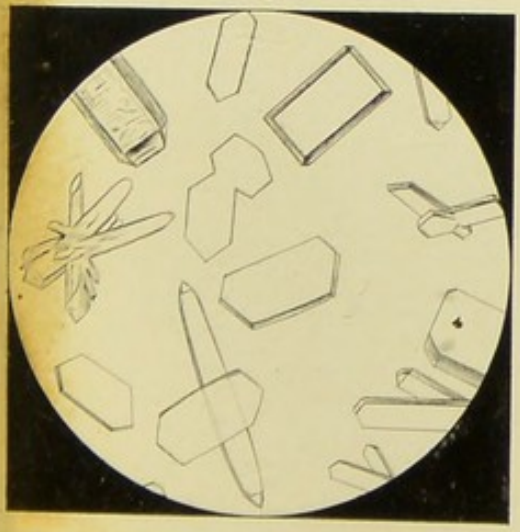
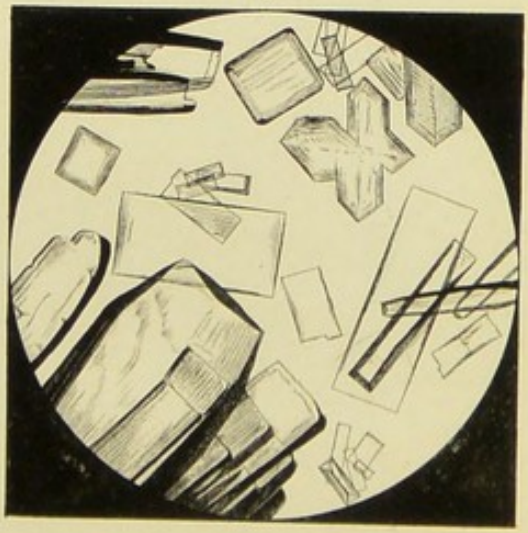


Fig. 6.



Lith. Anst. v. Adolph. Werl in Leipzig

PLATE III.

Fig. 1. Chloride of zinc-creatinine, free of creatine. Delicate needles in brushes and zeolithic arrangement. (See pp. 124, 125.)

„ 2. Ammonio-phosphate of magnesia in the form of rhombic crystals, mixed with amorphous granules, phosphate of lime, and granular urates. From the urine of a paraplegic patient. (See pp. 205, 206.)

„ 3. Epithelial fibrinous casts, with some loose epithelial cells and blood-corpuscles, typical of a deposit in the urine of a child suffering from acute desquamative nephritis. (See p. 241.)

„ 4. Epithelial casts of the uriniferous tubules, and loose epithelial cells, characteristic of a deposit in the urine of a patient labouring under jaundice. The cells are deeply impregnated with biliary colouring matter.

„ 5. The various appearances of blood-corpuscles under the circumstances described at pp. 228 to 230.

„ 6. Blood-casts and blood-corpuscles, somewhat changed by preserving. From the urine of a patient, who had taken half an ounce of turpentine. The characteristic hourglass shape of blood-corpuscles seen from the side, diagnostic of fresh blood-casts, could not be represented in this specimen. (See p. 231.)

Plate III.

Fig. 1.



Fig. 2.



Fig. 3.



Fig. 4.



Fig. 5.



Fig. 6.



Lith. Anst. v. Adolph Werl in Leipzig.

PLATE IV.

Fig. 1. Intra-epithelial small pus-casts, from the urine of a case of suppurative nephritis. The drawing is made after a specimen kindly lent to me by Dr. Johnson. (See p. 258.)

„ 2. Intramembranous large pus-casts, with casts, perhaps fibrinous, containing pus-corpuscles. There are some loose pus-corpuscles at the margin. After a specimen from Dr. Johnson. (See p. 258.)

„ 3. Granular casts, and disintegrated granular matter, and degenerated epithelial cells. From the urine of a man with gibbus, hypertrophy of the heart, and anasarca. (See p. 245.)

„ 4. Casts and epithelial cells, containing fatty matter. (See p. 245.)

„ 5. Intratubular (intra-epithelial) hyaloid casts. From a case of chronic non-desquamative nephritis in a boy, after scarlatina. (See p. 244.)

„ 6. Large waxy intramembranous hyaloid casts. From the urine of a case of chronic gout. (See p. 246.)

Plate IV.

Fig.1.



Fig.2.

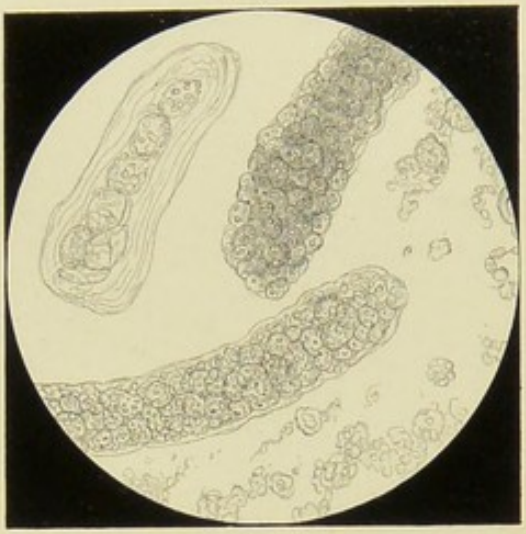


Fig.3.



Fig.4.

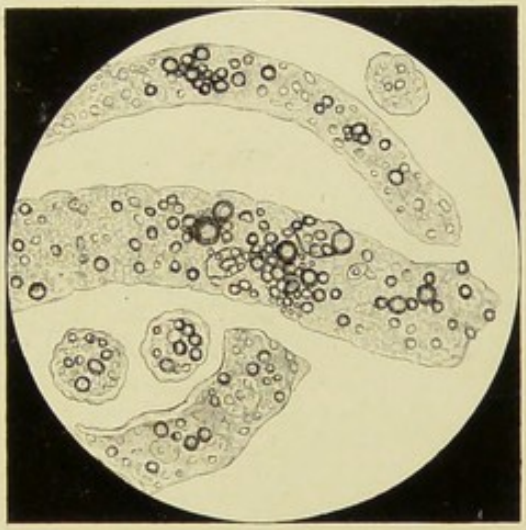


Fig.5.

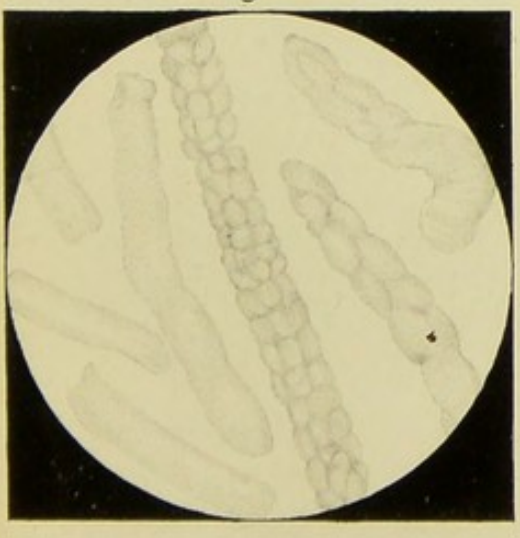
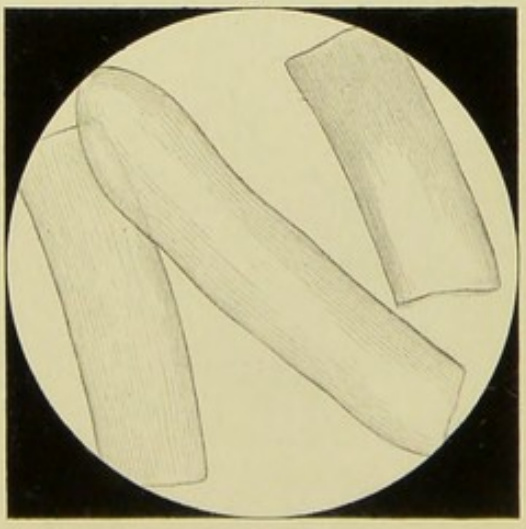


Fig.6.



Lith. Anst. v. Adolph Werner in Leipzig.

PLATE V.

Fig. 1. A piece of the wall of the echinococcus cyst, showing the internal granular surface, and several layers of structureless membrane. Hooklets of echinococci, triple phosphate, oxalate of lime, and uric acid crystals from the contents of the cyst, fill the rest of the field. (See p. 267.)

„ 2. Echinococcus, stretched out at full length; another retracted; a third, in a condition of beginning disintegration. This, and the last figure, are copied from Dr. Barker's plate. (See p. 268.)

„ 3. On the left are figured ordinary pus-corpuscles, varying, however, in size. At the top is represented a group of pus-corpuscles collapsed under the influence of a concentrated solution of sulphate of soda. On the right, some granular, fatty, and disintegrated corpuscles, from an old circumscribed abscess in the kidney, have been sketched.

„ 4. Oxalate of lime, in quadratic octahedra, and quadratic prisms. (See pp. 355, 356, 361.)

„ 5. Various forms of artificial oxalate of lime, from urine described at p. 356.

„ 6. Dumb-bell crystals of oxalate of lime. From the case detailed at p. 368.

Plate V.

Fig. 1.



Fig. 2.

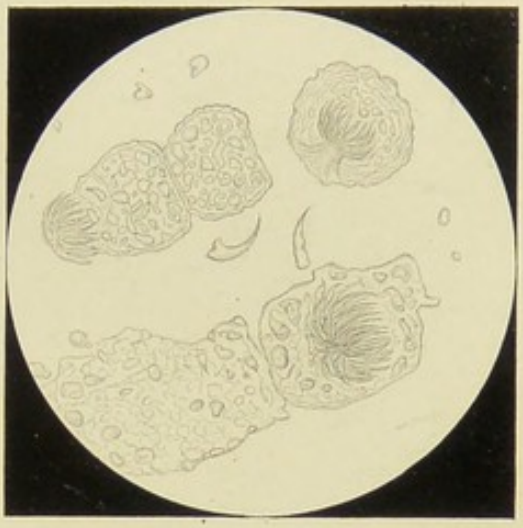


Fig. 3.

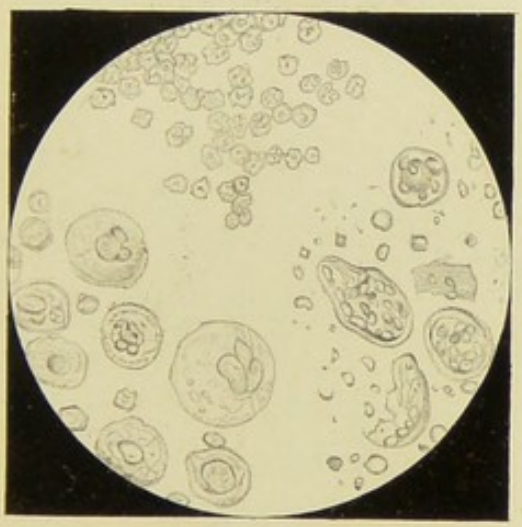


Fig. 4.



Fig. 5.

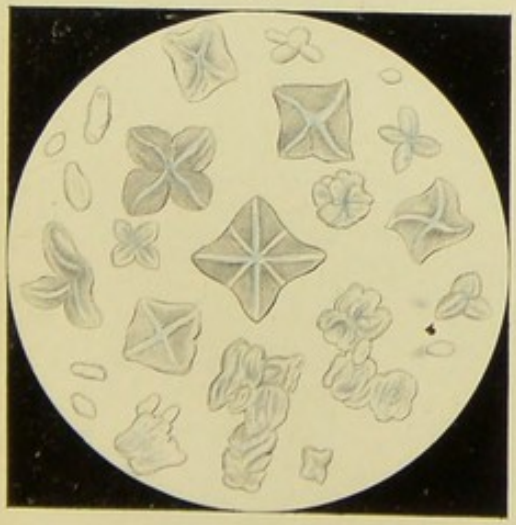
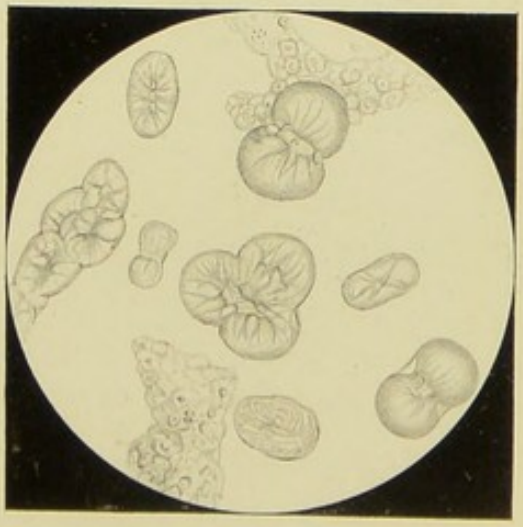


Fig. 6.



Lith. Anst. v. Adolph Werl in Leipzig.

PLATE VI.

Fig. 1. Cystine, precipitated from its ammoniacal solution by acetic acid. (See p. 297.)

„ 2. Sarcina ventriculi, from human urine. Preserved in creosote water. (See p. 413.)

„ 3. Sulphate of iodo-quinine. The upper crystals are placed on the blue, the lower on the pink selenite stage, with single tourmaline beneath it.

„ 4. Sulphate of quinidine, polarizing between two tourmalines crossed at right angles. This, and the last figure, are copied from Dr. Herapath's plate, in the 'Microscopical Journal.' (See p. 393, et seq.)

„ 5. Leucine in strings and balls of rhombic plates, obtained by sublimation of pure and dry leucine. (See p. 283.)

„ 6. Uroglaucine in petaloid masses, after Heller. Indigo blue by reduction, and subsequent slow oxydation. Indigo blue in plates, by sublimation. (See pp. 330, 333.)

Plate VI.

Fig. 1.

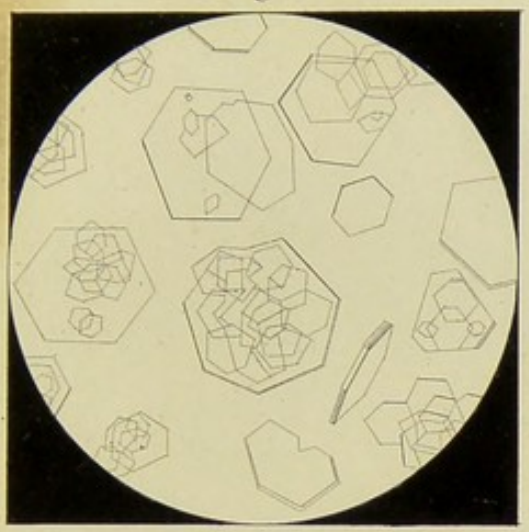


Fig. 2.

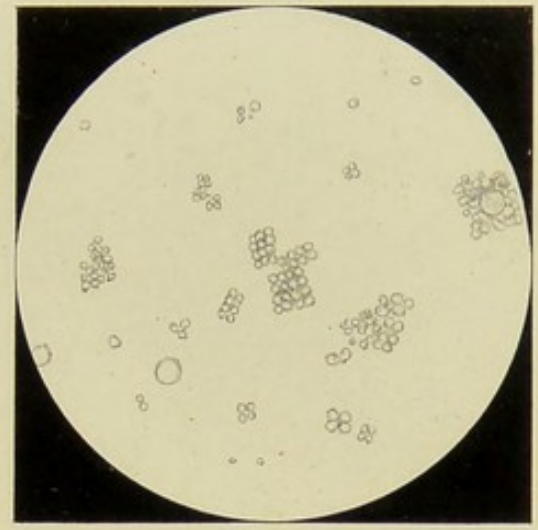


Fig. 3.

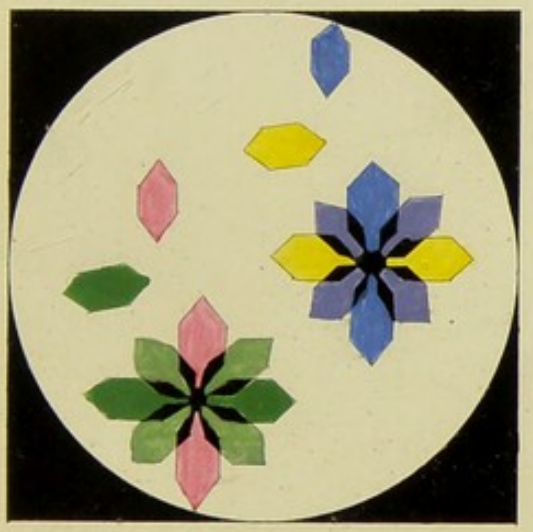


Fig. 4.

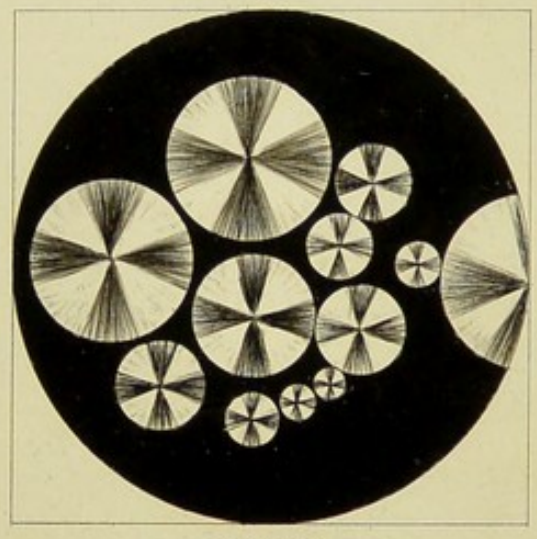


Fig. 5.

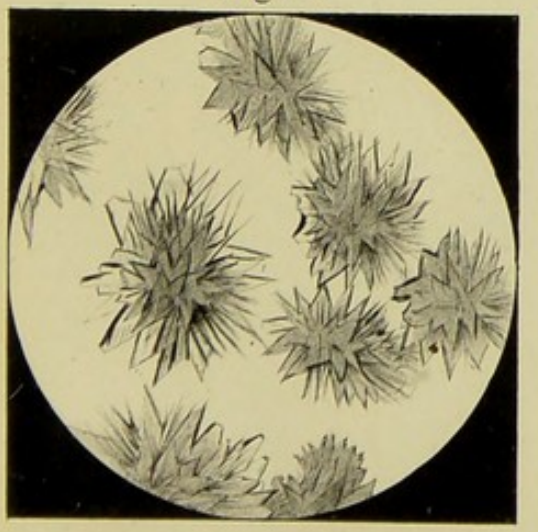


Fig. 6.



Lith. Anst. v. A. Werl in Leipzig

PLATE VII.

Vogel's Table for the determination of the quantity of Uræmatine in urine.

I. First Group. *Yellowish Urine.*

The colour is yellow (gamboge, mixed with a greater or lesser amount of water). Starting with the perfectly colourless urine, this group has three gradations or nuances:

1. Pale yellow (gamboge with much water).
2. Light yellow (gamboge with less water).
3. Yellow (gamboge with very little water).

II. Second Group. *Reddish Urines.*

With the yellow there is mixed a greater or lesser amount of red (gamboge with crimson lake). These urines are generally termed "highly coloured." There are again three varieties of this group:

4. Reddish-yellow. An admixture of some red to the prevailing yellow (gamboge with a little crimson lake).
5. Yellowish-red. The red colour becomes more prominent in the yellow body of the fluid (gamboge with more crimson lake).
6. Red. The red colour is prevalent, but there is still a slight admixture of yellow (crimson lake with little gamboge).

III. Third Group. *Brown (dark) Urines.*

The red colour passes through brown to almost black tints (gamboge, crimson lake, and more or less Prussian blue).

7. Brownish-red. Red with an admixture of a little brown.
8. Reddish-brown. There is more of the brown colour than in the last.
9. Brownish-black. Almost black, but with a touch of the reddish-brown.

Plate VII.

Fig.1.



Fig.2.



Fig.3.



Fig.4.



Fig.5.



Fig.6



Fig.7.



Fig.8.



Fig.9.



A TREATISE

ON THE

PATHOLOGY OF THE URINE,

ETC.

CHAPTER I.

GENERAL CHARACTERS OF URINE.

PHYSICAL CHARACTERS OF URINE.

The urine which has just been voided by a healthy individual is a clear fluid, of yellow colour, of the temperature of the body, of an odour which is peculiar to it, and is therefore termed urinous; it has a saline taste, with an admixture of some bitterness, and reddens blue litmus paper. A short time after the fluid has come to rest in the vessel into which it has been passed, a small, light cloud, of a grayish-white colour, may be observed settling towards the bottom of the vessel. This cloud consists of the mucus and epithelium of the urinary passages.

Clearness and Turbidity of Urine.

Turbidity of urine depends upon the admixture of solid and insoluble substances. The flocculent, small cloud of healthy mucus may be distinguished from other matters by its being easily diffused by agitation, and by its insolubility in nitric acid. So great a turbidity or thickness of the whole mass of urine, however, as after an interval of repose to cause the subsidence of a deposit to the bottom of the vessel or on the side, must be considered as abnormal, and therefore attracts attention. We then proceed to investigate its nature, which, taken together with the other properties of the urine containing the sediment, will often afford great

assistance in the inquiry into the seat and cause of the disorder, of which the turbid condition is a symptom.

In considering a specimen of urine with regard to its turbidity, great care must be taken in ascertaining whether it was passed in a turbid state, or whether the turbidity and sediment supervened after its emission, or after a lengthened period of rest. The prognosis of many cases is determined by this circumstance, an accurate knowledge of which, not always easily to be acquired, is therefore of practical importance.

We must guard against considering simple clearness of the urine as a sign that there is nothing wrong in that fluid. Many abnormal substances, the products of disease, are found in clear urine, and many pathological alterations in the quantities of the normal ingredients occur in a limpid fluid.

At the end of this volume are given some tables for discovering the nature of urinary deposits by chemical reagents and the microscope. The appearance in the form of sediments of the separate bodies, normal and abnormal, their reactions and their general behaviour, are given under each body.

Tints of Urine.

The normal amber-yellow colour of urine is due to a certain amount of colouring matters, which enter into the composition of that fluid. Though great progress has of late been made in the analysis of these bodies, and many valuable facts have been ascertained with relation to them, yet their nature is not so well defined as is desirable. For observation at the bedside gives ample proof that the colour of urine is frequently an exponent of the nature and amount of functional disturbance, and indicates to the physician the direction in which his further examination should proceed.

Starting from the fact that the normal colouring ingredients of urine are capable of generating a series of tints, varying, according to the degree of dilution, from a nearly colourless water-like, through the common pale amber, with an admixture of red, to red, reddish-brown, and up to deep brown; and, assuming as the standard scale of colours the table of Vogel, which is affixed to this volume, we have at once gained a basis which will secure uniformity of observation and description on this subject. Supposing, then, the different tints enumerated to be due to different degrees of dilution of the normal colouring matter, whether in

the urine of a patient or in that of a healthy person, then the colour is designated as of a normal character, its degree only being ranged amongst the pathological facts. These degrees of colour, as applied to the determination of the amount of colouring matter present, will be treated of in the chapter on Uræmatine. Here it may suffice to indicate the general practical conclusions which may be drawn from the different colours as regards the other characters of the urine, and the condition of the organism by which it has been voided.

Pale urine varies from nearly colourless, through a faint greenish tint, up to straw-yellow. It is the urine of early infancy, and is common in adults after the ingestion of large quantities of water or watery fluids. It is mostly neutral, less frequently alkaline, rarely acid. It is common in chlorosis and other anæmic conditions, and then contains a small amount of urea, and of solids generally. In diabetes, however, the pale colour does not admit of any conclusion as to the amount of solids generally. Practically the general rule holds good, that *as long as a patient secretes this description of urine, he is not affected by any severe illness of a febrile and acute nature.* (Vogel.)

Amber-coloured urine is the common urine of health. Its occurrence excludes all diseases of which either the pale or the very highly coloured urine is a usual symptom.

Highly coloured urine ranges from a reddish-yellow colour to red, and is of a decidedly acid reaction, and high specific gravity, indicating the presence of a large amount of solids, particularly urea. Concentration being the principal and uniform feature of this sort of urine, it is well to bear in mind that it may be produced in four different ways. 1. Either the person voiding such urine has taken very little liquid, and in that case the whole amount of concentrated urine will be very small. 2. Or the water of the blood has been evaporated by the skin in the form of perspiration. 3. The third way in which a concentrated highly coloured urine may be produced in healthy individuals, is by the ingestion into the blood of a large amount or an excess of nutritive nitrogenous matter. It is therefore of frequent occurrence with those who partake of sumptuous dinners, and who, like old Father Noah, "have a dislike to water, because all sinful men and beasts were drowned in it." 4. The fourth mode of formation of this description of urine is the more rapid disintegration of tissue and waste of matter in febrile diseases. Here the indication is the more valuable, as other symptoms, such as the temperature of the body or the state of the pulse, cannot always

be exclusively relied upon as exponents of the intensity of the febrile process. It need scarcely be mentioned that several of the circumstances enumerated may combine in producing a highly coloured urine, such as fever and perspiration, or large meals, and violent exercise. In all cases, however, the absolute amount of solids discharged in a given time should be regarded as the prominent indication. The solids must pass through the kidney; the water may be discharged by kidneys, lungs, and skin.

Of the *tints of urine* due to *abnormal substances*, those will be first mentioned which are strictly *accidental*, viz., produced by introduction into the stomach of articles of food, or beverages, or drugs, the colouring principles of which are absorbed into the blood, and afterwards discharged by the kidneys in the urine. The urine may be very deeply tinted by the colouring principle of coffee, when a tolerably strong infusion of the unadulterated roasted berry is taken even in moderate quantity. The colouring matters of several drugs, such as the chimaphila or pyrola, hæmatoxylum, senna, rhubarb, enter the urine very readily, and a short time after having been taken into the stomach. Urine coloured by rhubarb is sometimes mistaken for bilious urine (G. Bird). The error can be at once detected by the addition of liquor ammoniæ, which converts the dark orange into a crimson colour. Vogel recommends the addition to the urine of mineral acids in cases where the presence of the pigments of either rhubarb or senna is probable or suspected. The acids change the brownish or dark-red colour into a bright yellow; while uræmatine, if changed at all, is rather darkened by their influence.

Black or *blackish urine* has several times been observed after the internal use of *creosote*, and the inunction of tar over the whole surface of the body. A fuller account of this phenomenon will be found under *Carbolic Acid*.

The second class of abnormal tints of the urine comprises the *pathological* ones. The scale of tints is from lemon-yellow on the one hand, and deep blue on the other, through all varieties of yellowish-green, apple-green, brownish-green, red (blood colour), through brown, brownish-black, up to black of ink. The lemon-yellow colour, sometimes met with in cholera, or in spinal disease, is due to the presence of an excess of *uroxanthine*, with deficiency of uræmatine (Heller's urophæine).

The blue colour may be due to *cyanurine* (uroglaucine), which is sometimes the product of the decomposition of uroxanthine in the ammoniacal decomposition of the urine

in the bladder, and has been observed in cystitis and Bright's disease. Another produce of the decomposition of uroxanthine is *urrhodine*—a red substance. When uroxanthine is occurring together with *uroglaucine*, or any other blue pigment, it forms a greenish, apple- or grass-green, or if *urrhodine* prevail, violet solution, with a variety of modifications, caused by the admixture, in various proportions, of normal colouring matter or uræmatine.

The effects of *purpurine* (G. Bird; uroërythrine, Heller), a pathological product, which frequently indicates the presence of serious pathological conditions, are a red, rosy, or pink colour of any sediment of uric acid, urate of ammonia, or urate of soda that may occur in the fluid. The urates seem to have a particular affinity for it. Purpurine in a blue or lemon-yellow urine would produce the same changes of colour as urrhodine.

The sediments stained with purpurine, and the sediments which the blue pigments usually form with part of their substance, and all sediments whatsoever, must be filtered off before determining the colour of the solution.

A *greenish-yellow* or *greenish-brown* urine indicates the presence of the *colouring principles of bile*. I have, however, seen bilious urine voided by a gentleman of seventy-six, when suffering under one of his frequent attacks of the passage of gall-stones, which was of the *red* colour of Vogel's table. On other occasions of the kind his urine would be of greenish-brown colour; but then he was jaundiced, which he was not with the red urine.

Dark urine of a brownish, or brown porter-like colour, sometimes like ink, more rarely of a blackish-gray colour, is the result of severe pathological action in the body, and indicates a rapid disintegration of the red blood-corpuscles, the result of which is the appearance in the urine of an abnormal pigment, or perhaps several pigments at one time. Sometimes the pigment of dark or black urine is coagulable, thus indicating its being dissolved *hæmatine*.

In the following table I have arranged the different tints of urine in the succession from light to dark. The cause of the colour, its shortest test, the concomitant characters of the urine, and the general pathological indications, have been entered in separate columns of the table, which may therefore be useful as a guide to the ready physical and chemical distinction of the substances and conditions causing the various colours.

Table illustrative of the Tints of Urine.

Colour.	Substance to which the Colour is due.	Shortest Chemical Test.	Concomitant characters of Urine.	Pathological Indications.
Pale yellow hue to straw-yellow.	Uræmatine, smallest amount.	——	Reaction mostly neutral. Little urea and solids (except diabetes, when sugar augments solids.	Much water drunk. Anæmia, chlorosis, diabetes. Excludes febrile and acute diseases.
Lemon-yellow.	Uroxanthine.	Drop twenty to forty drops of urine into two or three drachms of fuming hydrochloric acid. Reddish-violet colour to blue is produced.	Deficiency of uræmatine.	Occurs in cholera and spinal disease.
Amber colour.	Uræmatine.	Add to boiling urine one fourth of its bulk of hydrochloric acid. Pink or purple colour produced.	Mostly normal.	Being the urine of health, this colour excludes all diseases of which either pale or very high-coloured urine is a symptom.
Yellowish-green and brownish-green.	Pigment of bile.	Let a drop of nitric acid fall in the centre of a thin layer of urine on a white plate, when a transient play of colours in rings of pink, violet, and green is produced.	Very acid.	Obstruction to the passage of bile from liver and gall-bladder into the intestines; presence of the constituents of bile in the blood.
Greenish to grass-green.	Mixture of uroxanthine with any of the blue pigments.	Several tests of these substances.	Alkaline, decomposed; much carbonate of ammonia.	Has occurred in cystitis and Bright's disease.
Reddish-yellow to red.	Uræmatine, large amount	Hydrochloric acid.	Reaction acid. Large amount of solids, particularly urea.	Little liquid taken. Excess of nutritive, nitrogenous matter; free perspiration. *Fever.*

Red to brown, and deep brown.	Colouring principles of hæmatoxylum, chimaphila, coffee.	Coffeurine may be known from the characteristic odour.	Subject to accident.	The ingestion into the stomach of hæmatoxylum, chimaphila, senna, rhubarb, and coffee, or their extracts and infusions.
	Senna.	Mineral acids change the dark red or brownish colour of this and rheine into light yellow.		
	Rhubarb.	Liquor ammoniæ converts the dark orange or brown into crimson.		
	Pigment of bile.	Nitric acid.		
Pink, or rosy.	Purpurine(uroërythrine)	Is precipitated with deposits of urate of ammonia and soda, and may be combined with them artificially.	Urine always acid, making mostly a deposit of urates on cooling.	Indicates frequently the presence of serious lesions. Rest problematical.
Red to purple.	Urrhodine.	Is a product of decomposition of uroxanthine, and with blue pigments makes the urine violet.	——	——
Blue.	Cyanurine (uroglaucine); indigo.	Let urine decompose, or add concentrated NO_3, or HCl. Pigment is destroyed on evaporation of urine. Concentrated SO_3 $\frac{1}{8}$ to $\frac{1}{4}$ volume, produces a test, like that of Pettenkofer for bile. Indigo not affected by boiling with HCl.	Ammoniacal decomposition in the bladder.	Observed in cystitis and Bright's disease. Cyanurine sometimes discharged during apparent health. In that case the urine is of amber colour, and the pigment only appears on addition of acids.
Violet.	Mixture of the red and blue pigments, normal and abnormal.	Those of the separate substances.	——	——
Reddish-brown to brown, porter-like.	Hæmatine.	Coagulable by heat (sometimes); precipitated by acids in flocculi.	——	Typhus. Breathing of arsenuretted hydrogen.
Blackish-gray, black like ink.	Hæmatine, and blood becomes black in putrid urine. Tar and creosote, or carbolic acid.	Sometimes as deposit in clear ordinary urine.	——	The ingestion of carbolic acid into the blood, through the stomach or skin.

Odour of Urine.

Healthy urine has a peculiar odour, which rises with the vapour of water after emission. It is almost indestructible by any of the chemical processes usually applied to urine, and therefore accompanies the operator through the whole course of an analysis.

The odour is due to the presence of a series of volatile acids, which may be obtained by distillation of large quantities of urine. In this way Städeler succeeded in proving the presence in the urine of man and animals of phenylic (or carbolic), taurylic, damaluric, and damolic acid. The common modifications of the smell of urine are probably due to the preponderance of one or several of these acids.

Several articles of daily consumption, as coffee, onions, and garlic, communicate to the urine their peculiar odour. Asparagus gives it a peculiar odour, which is not exactly the odour of the stem when it stands hot on our plate. Oil of turpentine, when taken internally, or breathed in any quantity, communicates to the urine a violet odour. The odoriferous principles of saffron and cubebs may easily be distinguished, when they have been taken internally.

Taste of Urine.

The taste of urine is a mixture of the tastes of its constituents, of which two, however, characterise it—urea and chloride of sodium—the one imparting a bitterish cooling flavour, the other its saline taste. The phosphatic alkalies are of a cooling, weak saline taste, and so far resemble the chloride of sodium. The odorous acids develop their flavour on the tongue to great advantage. To taste urine is more a matter of curiosity than of scientific value, as it reveals no fact from which a conclusion might be drawn. I only record it in compliance with the usage of authors. The discovery of diabetes mellitus was formerly made by tasting only. This the reader should consider before he smiles at my speaking of the taste of urine. In diabetes the taste of the urine is SWEET.

CHEMICAL REACTION OF URINE.

As the chemical reaction of healthy urine is acid, any deviation from this condition becomes at once an anomaly. It has been ascertained that the neutral or alkaline condition is due

not so much to the absolute absence of the acid, as to its neutralization by bases; the nature of the latter, and their origin, determine whether the neutral or alkaline state be within the limits of health, or a symptom of disease, or a disease *per se*.

It is most probable that the acid reaction is due to the presence of acid salts, such as the phosphates and sulphates of potash and soda, the acid urates and hippurates, and accidentally to free organic acids, such as the oxalic, malic, and tartaric (Buchheim, Wöhler), and their acid salts.

Regarding the physiological processes which produce the ordinary acid reaction much remains to be determined by observation. Dr. Bence Jones[1] has made it probable that the amount of acidity in the urine stands in an inverse proportion to the amount of acid secreted by the stomach during digestion. In his analyses the quantity of free acid has been calculated for 1000 parts of urine, and not for the urine secreted in a given time. It is for this reason that Vogel objects to relying upon the conclusions drawn therefrom. The quantities of free acid discharged per hour in every hour of the twenty-four ought to be the standard round which to rally such examinations. As the result of his own researches, and those of others working under his guidance, Vogel ascertained that the highest amount of acid discharged with the urine per hour occurred during the night, the lowest in the forenoon, and the medium amount in the afternoon, being after the dinner of the operators.

The degree of acidity of healthy and pathological urine can be determined by an easy volumetrical process, of which the details are given in a subsequent chapter.

The neutral state or alkalinity of the urine is the consequence of the admixture of fixed or volatile alkalies. Before speaking of the circumstances, however, under which neutral or alkaline urine may be *discharged* from the bladder, we must advert to the fact that urine, which when passed was acid, may soon become alkaline under the influence of decomposition of urea. This conversion is sometimes effected within an hour after emission (G. Bird). It must be considered as an essentially morbid feature, because normal urine, though it almost always becomes alkaline during its decomposition, yet does not do so within the first twenty-four hours after its emission.

But the alkaline decomposition of even healthy urine may

[1] 'Animal Chemistry,' London, 1850, p. 41.

be favoured by certain circumstances requiring the most scrupulous attention of the practitioner, the neglect of which will make him liable to grave mistakes. Urine which is already in a state of alkaline decomposition, when added even in small quantity to healthy urine, will, like a ferment, induce and hasten the decomposition of the normal fluid. The vessels, therefore, in which the urine is collected, must be washed and scalded with great care; otherwise the small quantities of decomposing urine adhering to their walls may induce fallacious conditions of the fluid collected.

There are other circumstances which may make the acid urine alkaline in a shorter period than usual. Such are the presence of mucus and pus, which undoubtedly play the part of a ferment in many cases. This may be proved by dividing a specimen of acid urine into two parts, filtering the one immediately, leaving the other as it is, and letting both stand side by side. The filtered urine will often present its original acid reaction, when the portion which has not been filtered is already alkaline. I have found that decanting the clear fluid from the settled cloud of mucus serves the same purpose.

High temperature and great dilution favour the process of decomposition. A concentrated acid urine of fever, on the contrary, of a specific gravity of 1025, containing much urea, will, when decanted from the deposits, retain for days, if not its entire character, certainly its acid reaction and its ordinary appearance.

Though a certain amount of ammonia, in combination with acids, is present in all healthy urine, yet that quantity is never sufficient to produce an alkaline reaction. When ammonia produces the neutral or alkaline reaction, as it always and exclusively does when the alkalinity has supervened after emission, it is the product of the decomposition of urea into ammonia and carbonic acid. To undergo this conversion, one equivalent of urea combines with two equivalents of water, and then separates into two equivalents of carbonate of ammonia; thus:

$$\underbrace{C_2\,H_4\,N_2\,O_2}_{\text{1 equiv. of urea.}} + 2\,HO = \underbrace{2\,(NH_3 + CO_2}_{\text{2 equiv. of carbonate of ammonia.}}$$

Having now ascertained the causes of alkaline changes occurring in the urine after emission, we are the better prepared to appreciate the processes by which the urine may become alkaline *before* emission. We have already remarked that this may be effected by volatile or by fixed alkalies; and

accordingly alkaline urines may be divided into two great groups. The alkalinity of the first group is always due to the presence of carbonate of ammonia from the decomposition of urea in the urinary passages, particularly the bladder, after its secretion from the kidneys. This may be taken as the general rule; though it is possible, but not proved, that in uræmia, and some other diseases, or when taken internally as a medicine, carbonate of ammonia may be discharged from the blood by the kidneys. Carbonate of ammonia restores the blue colour to reddened litmus paper,[1] but, as it evaporates on drying, its neutralizing influence disappears on the dried test-paper, which therefore again becomes red. The fixed alkalies, on the contrary, impart a permanent blue colour to red test-paper. Both descriptions of alkaline urine effervesce with acids, and froth or lather when containing albumen.

The alkaline decomposition of urine in the urinary passages, particularly the bladder, may be referred to a series of causes, all of which have one effect in common, namely, that of preventing the complete emptying of the bladder at one time. A part of the otherwise healthy urine being thus retained longer than it can resist alkaline decomposition under ordinary circumstances, acts as a ferment on all urine subsequently entering the bladder. Upon this point, the experiments and arguments of Dr. Snow[2] are quite conclusive. About half a

[1] The requirements for *test-paper* are a *thin layer* of colour, on a thick, substantial, *pure, non-bibulous paper.* Bibulous test-paper is bad, because it contains too large an amount of colour, and hence is not delicate for weak solutions.

The colour of what may be called neutral litmus is violet. It indicates acidity by becoming more or quite red, and alkalinity by becoming intensely blue. Vogel prepares it by exposing a watery infusion of litmus to the influence of the air, until the commencing acid fermentation of the fluid has imparted to it the violet hue. With this tincture he stains strongly sized paper, and dries it in the shade.

The article now commonly sold for neutral test-paper is, however, not violet, but red, becoming of a lighter red under the influence of acid, and blue under that of alkali. This paper is very good for testing for alkali; but does not generally indicate weak acids. It is well known in optics, how difficult it is to distinguish between the different gradations of one and the same tint, if they are lying near together: *e. g.*, to say that one red is more or less red than another. But the slightest hue of blue beside red is easily distinguished To redden the paper, however slightly, beyond the violet, spoils its delicacy for acids; on the other hand, the perfectly red paper is the most delicate for alkalies.

However desirable it may be to have one paper indicate either acidity or alkalinity, the attempts to make a neutral paper remind one of the popular saying, that it is impossible to make the state-coach serve the purposes of a privy, without making it inconvenient for both destinations.

[2] Some Remarks on Alkalescent Urine and Phosphatic Calculi, 'London Medical Gazette,' Nov. 20, 1846.

pint of newly voided urine was put into a glass vessel which terminated at the lower part in a tube of minute calibre, through which it dropped into a glass jar below, at the rate of about twelve drops in a minute, which is about an ounce and a half in an hour, that being not far from the quantity usually passing into the bladder from the ureters. The vessels were kept near the fire at the temperature of 100° F. (37·7° C.) At the end of six or eight hours, when the urine had all dropped into the lower vessel, it was emptied, all but about thirty drops, and the upper glass, which served as a funnel, again replenished. It was found that the urine in the lower vessel became decomposed generally in about twenty-four hours,—in about the same time, in short, as urine preserved at the same temperature from the beginning of the experiment, the time varying according to the quality of the urine. It generally became quite fetid in two or three days, at all events highly alkalescent, and remained so as long as the experiment was continued; it was always fresh and acid in the upper vessel, provided this was washed out occasionally; and was always decomposed in the lower one, although the urine, except a small fraction of it, was of the same age in both.

Among the causes which may prevent the complete emptying of the bladder, and produce alkaline, *i. e.*, ammoniacal urine, *foreign bodies* in the bladder claim our attention. "One of the symptoms of their presence is the occasional sudden stoppage of the stream of urine before the bladder is emptied; in addition to this, it is evident that the bladder can seldom contract around a foreign body so exactly as completely to expel all the urine; and, moreover, calculi, and nearly all other foreign bodies which gain admittance to the bladder, are porous, and contain urine imprisoned in their pores; accordingly, it is a general law, with extremely few exceptions, that foreign bodies in the bladder become incrusted with the earthy phosphates." (Snow.) A catheter, which is left in the urethra and bladder for some days, has soon the effect of foreign bodies, and makes the urine ammoniacal and phosphatic, by allowing a small quantity of urine to remain in the bladder. Enlargement of the prostate and stricture of the urethra act in a similar way. Ammoniacal urine is the almost invariable result of weakness, partial or total paralysis of the bladder, more strictly of the detrusor urinæ, such as occurs in paraplegia and spinal diseases and injuries, in the decrepitude of extreme old age, and comatose conditions in the course of certain diseases, such as typhus. (Simon.)

It is probable that the inflamed condition of the mucous

membrane of the bladder, which we mostly observe along with ammoniacal urine, is the *consequence* of this condition of the urine. If ammoniacal urine acts as a caustic upon the epidermis and cutis, causing excoriations and extensive soreness, how much more liable must the mucous membrane of the bladder be to similar affections! The alkaline urine causes positive ulceration on the mucous membrane in cases of extroversion of the bladder, on the enlarged uterus in cases of prolapse,—nothing is then more natural, than that the offended surface of the cavity of the bladder should, for its protection, first pour out a large quantity of mucus, and when the cause continue for a length of time, pass into a state of chronic inflammation, with croupy exudations, attended by great misery.

In very few cases the mere presence of a calculus or foreign body in the bladder causes inflammation of itself, it mostly requires the presence of ammoniacal urine. The symptoms of a calculus not attended by ammoniacal urine are far less severe than those of a concretion accompanied by such urine; and in many cases the presence of a calculus in the bladder is neither observed nor suspected before the appearance of ammoniacal urine and its attendant suffering, which, from the beginning of the phosphatic incrustation, can be shown to have taken place only at a time when the calculus had already attained a considerable size.

We must here mention two more conditions in which the partial retention of urine may cause ammoniacal urine and its consequences. The one is a so-called sacculated bladder, or rupture of the mucous membrane protruding through the muscular coat. The other occurs in insane persons, who have a tendency to retain their excretions as long as possible. When forced to pass water, either by natural necessity or by attendants, they will only allow the passage of a part, retaining another. In one such case, I could frequently observe the urine become ammoniacal fifty hours after the beginning of the paroxysm. The researches of Drs. Rigby and Sutherland show, that this condition is frequent among the inmates of lunatic asylums.

The most efficacious treatment of all cases of ammoniacal urine is the washing out of the bladder with warm water by means of a syringe and double canula. In all cases where the operation has been carried out properly, the urine immediately loses its ammoniacal condition, and in most cases is clear and acid, thus proving the correctness of the above views by demonstration.

In many cases of acute total retention, the urine does not

become ammoniacal, but becoming concentrated by the absorption of water, remains acid, but forms deposits of various kinds. These cases have evidently no analogy with those of partial retention, and can therefore not tell against the views here adopted.

Ammoniacal urine is always fetid, pale, and turbid, from the precipitation of triple phosphate and phosphate of lime. The smell, and the presence of the crystals of ammonio-phosphate of magnesia, easily distinguish it from urine which is only turbid by alkalinity from fixed alkali, and contains a precipitate of phosphate of lime, or phosphate of lime and magnesia. Urine which is alkaline from the presence of bicarbonates (after Vichy water) is mostly clear, the earthy phosphates being soluble in the second equivalent of carbonic acid, which easily separates from the carbonate.

We have thus advanced to the consideration of that group of alkaline urines which impart to red test-paper a permanent blue colour, showing that they are produced by fixed alkalies. When the alkali is present in quantity sufficient only to neutralize the free acid of the urine, then the latter exerts no influence upon any test-paper; it is neutral. But it must be borne in mind that the reaction of healthy urine being acid, neutrality of the fluid in itself denotes alkalinity.

While, on the one hand, the presence of volatile alkalies in the urine is always pathological, the alkalinity from fixed alkalies on the other hand, though it may be, and in many cases is of a morbid nature, occurs more frequently within the range of perfect health. Certain descriptions of vegetable food, such as apples, lemon-juice, and a series of acid fruits, make the urine alkaline in a very short time. Dr. Bence Jones found that 120 grains of the dry tartrate of potash, dissolved in four ounces of water, made the urine alkaline after thirty-five minutes. The alkalinity had disappeared after two hours. A gentleman ate an apple for experiment, and found his urine alkaline in less than an hour. The acetates, tartrates, citrates, and malates, in fact the salts of many of the organic acids, are, by the oxydizing influence of the chemistry of the body, converted into the carbonates of their respective bases, and being as such discharged with the urine, give it their characteristic reaction. It is for this reason, and some others, that the urine of herbivora is always alkaline.

In man this description of alkalinity, which may occur for hours or days, or at a certain time after meals, is of no practical importance. It becomes so, however, when it is the consequence of the use, as medicines, of the caustic alkalies,

soda and potash,[1] and of the earths, magnesia and lime, or their carbonates. This artificial disease not unfrequently occurs when patients to whom alkaline remedies have been prescribed by their medical advisers, continue to take them on their own account for an unreasonable length of time.

I have already stated that the neutral or alkaline condition is of frequent occurrence with the pale urine discharged in anæmic conditions. Of the reason of the alkaline reaction in these cases we can as yet give no satisfactory account. But it seems probable that the depression of the organism in these cases, accompanied as it is by faulty nutrition of the muscular and nervous systems, does not allow of the accomplishment of that chemical process, by the completion of which, in health, acid combinations are discharged from the tissues and blood. It is in this direction that we may have to search for the truth. Meantime, we may safely adopt the empirical, but highly practical doctrine of Rademacher,[2] which Vogel[3] himself adopts, admitting its merit; namely, that a constantly alkaline (and let me add, constantly pale) urine requires the employment of tonics, particularly iron.

The continuance of the alkalinity of urine from any cause, but particularly from alkaline fermentation and the maladministration of fixed alkalies, for any length of time, is to be considered a serious matter. For the phosphates of magnesia and lime, being precipitated, and mixing with the increased amount of mucus, may at any time, and unawares, form a stone, with all its consequences; or the turbid and caustic condition of the urine may give rise to diseased states of the bladder, which it is afterwards frequently a matter of great difficulty to remove.

Table showing the Substances which cause the Reaction of Urine expelled from the Bladder.

A. Acid Reaction: imparting a permanently red colour to litmus paper. Common in health: due to—

a. Free acids.

- *α.* Oxalic
- *β.* Malic
- *γ.* Tartaric

} acids, and their acid salts, when taken in large and repeated doses. (Buchheim.)

- *δ.* Free acid (nature unknown).
- *ε.* Phenylic acid
- *ζ.* Taurylic acid
- *η.* Damaluric acid
- *ϑ.* Damolic acid

} questionable.

[1] See 'Fatty Tumours: action of Liquor Potassæ.' Letter from Dr. Thudichum, 'British Medical Journal,' Aug. 15, 1857, p. 702.

[2] 'Rechtfertigung der verstandesrechten Erfahrungsheillehre,' 2d ed., vol. ii, p. 211, *et seq.*

[3] Loc. cit., p. 177.

b. Acid salts.

α. Phosphates
β. Sulphates
γ. Urates (acid)
δ. Hippurates
} of alkalies.

c. Neutral salt with acid reaction.

a. Chloride of ammonium (questionable).

B. NEUTRAL OR ALKALINE REACTION: occurring in health occasionally, more frequently in disease: due to—

a. Fixed alkali, imparting a permanently blue colour to red litmus paper.

α. Carbonates of the alkalies, potash and soda, derived from the salts of organic acids—acetates, citrates, tartrates, malates, lactates, &c.; or introduced directly, *e. g.*, in mineral waters of Vichy, Aix-la-Chapelle.

β. Carbonates of the earths, lime and magnesia.

γ. Pus, blood, and serum.

b. Volatile alkali—ammonia; carbonate of ammonia, from decomposition of urea, being a result of—

α. Uræmia (questionable).

β. Retention of urine, caused by weakness, or paralysis of bladder, or by obstruction to discharge of urine, as from enlarged prostate: the ferment being mucus, or a retained portion of the already fermented urine.

γ. Decomposition of urea, under the influence of a continued discharge of fixed alkalies by the urine.

c. Deficiency of phosphoric and sulphuric acids, in alkalinity or neutrality of pale urine, occurring in anæmic conditions.

CHANGES ON COOLING.

In colour the urine becomes a trifle darker on cooling; its peculiar smell becomes very weak, partly because it does not evaporate any longer with the vapour of water, partly because there is less of it.

The epithelia collect in masses and clouds towards the bottom of the vessel, leaving the supernatant fluid perfectly clear and transparent.

If the urine have been concentrated and dark, it will frequently deposit a reddish crust against the walls of the vessel containing it. This crust, and the pulverulent deposits of urates, which are formed at different stages of the process of cooling, may occur in persons enjoying apparently perfect health.

As a general rule, it may be said that the more coloured a deposit of urates is, the longer time has it required for its formation. A lady having lost her child, was obliged to retain the milk in her breasts. When the painful swelling of the bosom had ceased, she discharged urine, which, on touching the vessel in which it was received, became white

like milk, and was brought to me as milk. When only a small quantity was passed, the milk-like condition was at once apparent; the vessel withdrawing a sufficient amount of warmth from the urine to precipitate the urate. But when a larger quantity was passed, the first portion made a precipitate, which was redissolved as the larger portion was added. Ten minutes, however, were sufficient to make the precipitate appear, which consisted of snowy-white urate of ammonia. Dark-coloured urines mostly throw down the urates after standing during some time. In a case of heart-disease with dropsy, the brownish-red urate only fell after twenty-four hours; in a case of colic, only after twelve hours. In these three cases the temperature could not have been the only influence exerted upon the urine, because in each case the urine must have been of the temperature of the air long before the deposit fell, and in the first case the deposit fell before the urine was of the temperature of the (warmed) room.

In some few cases the urine may become alkaline during the process of cooling (*vide* p. 9).

If sediments are discharged with or formed in the urine they subside towards the bottom of the vessel. Among the sediments, besides mucus, the urates, uric acid, and the oxalate of lime are most common. Most other deposits are due to the decomposition of urine, and of the urates in some cases.

CHAPTER II.

QUANTITY OF URINE AND INGREDIENTS.

MODES OF COLLECTING THE URINE.

To collect urine is not an easy task, and requires great attention. The requirements are to collect the whole of the urine without losing any portion, and to collect it in such a manner as to preserve its purity. It is essential to keep all vessels used for the purpose scrupulously clean, and to wash and scald them at least once a day. If practising among the poor, the physician will find it necessary to order that the chamber-vessel be kept covered when not used, in order to protect the urine from the admixture of dirt and rubbish falling from the patient's bed. In many diseases it is desirable to collect in separate vessels the several portions of urine passed at different times of the day and night. Several small pots will best suit this purpose.

In hospitals and other public institutions a very convenient form of glass is in use. The glass consists of a flat body which easily lies on its bottom, a turned-up narrow neck, and a mouth fitted to the requirements of the sex. For men it is therefore funnel-shaped; for women the funnel is made ellipsoidal, so as to receive the vulva.

If the urinals described were combined with a pan of a suitable construction, the urine might be collected in a most easy manner. The pan requires only to have such a gap in its front border and wall as will admit the neck of the urinal standing in front of it. In men, the penis will lie easily in the neck of the urinal; and if women take the trouble of sitting a little closely on the oval funnel of the urinal, not a drop of urine can possibly be lost.

These glasses should be graduated upon at least 50 c.c. every division, of which there ought to be 40, equal to a measure on the whole of 2000 c.c. Graduation upon single fluid ounces up to fifty or sixty serves the same purpose. The physician on coming to the bedside would then be enabled to inform himself by a glance of the total quantity of urine collected; and, if none were lost, of the whole bulk discharged.

In some hospitals the ancient urinal is still in use; its only advantage over the ordinary vessel is its being made of glass; its shape is much less convenient than that of the glasses described above, which admit of the discharge of urine in the recumbent or any other posture.

In many cases the difficulties in the way of collecting the whole of the urine discharged in twenty-four hours are very great. Any one of my readers will easily find them out by trial upon himself; with women and children they are still greater. Unless a special apparatus be employed, a certain loss at every motion is nearly unavoidable. To empty the bladder when the rectum is pressing is difficult, and frequently impossible, or interferes with the function of the bowel, and then becomes injurious to health. But the quantities so lost are very small indeed when compared with the total collected by all available means, and may safely be made up for by an estimate.

The matter becomes more embarrassing in cases of severe illness, where, unfortunately, with the importance of the indications to be derived from the quantity and quality of the urine, the obstacles to a complete collection become greater. Patients in a delirious, or unconscious, or paralysed state will retain or pass unconsciously a part or the whole of their renal and alvine excretions. Here we must estimate the losses from known and collected quantities in proportion to time and from the evidence to be derived from inspection. Allowing 20 per cent. for error in the estimate, the known quantities will reduce this error to 10 or 5 for the whole amount in the worst cases.

In this manner the practical man may obtain the nearest possible approach to truthful observation. Unless, however, all the cautions are employed, we would strongly recommend that too nice conclusions should not be based upon such incomplete observations, though they even give to the thinking practitioner points of evidence to which he may append his reflections, and which may be taken into account in forming the prognosis of a case, or in tracing out a plan for therapeutical proceedings.

TOTAL QUANTITY OF URINE DISCHARGED IN A GIVEN TIME.

Any attempt to make a quantitative analysis of the urine for the purposes of physiological or pathological research must be based upon the knowledge of the total amount of urine discharged in a given time. It is the neglect of this point which makes all analyses useless which are calculated upon thousand parts of urine, regardless of the time in which it was passed. Hence we must, though with regret, exclude from consideration, by this sweeping objection, the vast number of analyses made and published till within a period of three or four years ago. And not only on this ground are these analyses excluded, but the want of accuracy in the methods makes them so much lost labour. Some authors, though perfectly well aware that in all cases where any approach to accuracy in the determination of the specific gravity is required, an average sample from the urine passed in twenty-four hours into the same vessel must be selected, —have yet formed no settled idea of the necessity of knowing the whole amount of urine discharged during the twenty-four hours. It could have been only by losing sight of this point that they recommended the determination of the average density of the urine from the density of a mixture of the urine passed immediately before going to bed, and of that voided on rising in the morning. But of what use is it to know density at all, if from the density we cannot calculate the whole of the solids discharged in a given time? For this we must know the whole amount of urine.

We may either collect the whole bulk of urine passed in twenty-four hours, or in every single hour, or in as many portions of the twenty-four hours as convenient. But it should always be expressed in a value calculated upon the twenty-four hours, or upon every single hour. In many chronic and acute diseases we must collect and analyse the urine for several days in succession, in order to arrive at a correct conclusion upon the average condition.

The amount of urine is best determined by measuring in the graduated urinals; or, if more accuracy is desirable, in high graduated cylinders of a capacity varying from 500 c.c. to 2000 c.c., or from 10 to 50 fluid ounces. The large cylinders have marks for every 10 c.c., and a practised eye will easily estimate one fourth of a division; it is, therefore, possible to determine the entire quantity to within 25 c.c. in a very short time. The small cylinders, which are to serve

for measuring the quantities of urine of a shorter period, say one hour, should be divided into single cubic centimetres, or into fluid drachms.

Both descriptions of cylinders must be provided with lips for pouring out their contents. Their upper borders must be ground in an horizontal plane, so that a glass disc, with the assistance of a little tallow, will make an air- and water-tight cover, and prevent all loss by evaporation. The foot of the cylinder must be ground so correctly that the vessel may be perfectly perpendicular when standing on a horizontal plane. If the latter is not at hand, a tripod or disc with elevating screws and two spirit levels will be the easy means of placing the cylinders in a perfectly horizontal position. These tripods are easily obtained, as they are now commonly used in photography.

If it is desirable to know the weight of a certain bulk of urine, it is only necessary to multiply the number of cubic centimetres found by measure into the figure expressing the specific gravity; the result will give the quantity in grammes, thus—

1000 c.c. × 1·025 (spec. gr.) = 1025 grammes.
250 c.c. × 1·021 „ = 255·25 „

QUANTITY OF URINE DISCHARGED IN HEALTH.

In valuing the physiological effects of the variations of the discharge of urine, the fact must always be borne in mind that the water discharged in the urine is only a part of the water excreted by the whole body. According to our best estimates, one half of all the water ingested into the body goes away by the kidneys; the other half by the lungs, the skin, and the fæces together.

I have considered it useful to add some observations on the total quantity of urine discharged by healthy individuals, to the observations already existing. They were made upon two individuals; the one, *A*, a man twenty-eight years of age, and weighing 70 kilogrammes; the other, *B*, a man twenty-eight years of age, and weighing 72 kilogrammes.

A, æt. 28, *weighed* 70 *kilogrammes. Quantities of urine from* 12 *midnight to* 12 *midnight, twenty-four hours each.*

The figures designate cubic centimetres.

Nov. 16.	2014		1654	Dec. 29.	2250	Jan. 13. 1049	2310
	2094		1987		2216		1790
	2072		2080		2440	„ 23. 1860	1820
	2125		1618	Jan.	1. 1570	1585	2450
	2061		1287		1557	2850	1910
	1765		1650		1500	2030	2920
	2097		2422		2082	1540	1766
	2505		1239		1312	2860	2160
	1843		2683		2160	1860	1638
	1980		1468		1410	650	2215
	2373		2210		1435	1736	2520
	1715		1490		2050	Feb. 1. 1610	1820
	2539		2590		2220	2473	1550
	2612		1810		1660	1450	1530
„	30. 1930		1815		2326	2210	2136
Dec.	1. 2202	Dec. 17.	1785				

Seventy-six days, with one interruption of twelve days and one of ten days.

$$\frac{148{,}211}{76} = 1950.$$

The quantity of urine discharged by *A* is therefore 1950 c.c. per day, as the average of seventy-six days. Maximum, 2920 c.c. Minimum, 1049 c.c. The minimum of 650 c.c. I must assume as abnormal; the individual on that day had a cold and headache.

B, æt. 28, *weighed* 72 *kilogrammes. Quantities of urine from* 12 *midnight to* 12 *midnight, twenty-four hours each.*

Dec. 17.	2432		1580		2000		2440		2235
	1528		2000		1670	Jan. 30.	1485		2040
	1873		1335	Jan. 19.	1585				1685
	1642		1445						1380
	1812		1355			Feb. 1.	1420		1100
„	22. 1874	Jan. 9.	2190	„	21. 2080		1515		1760
					1895		1445		1065
„	29. 1720	„	11. 1975		1420		1292		1680
	1880		1970		1622		1293		1710
„	31. 2020		1482		2655		1750		1530
Jan.	1. 1700		1590		2540		1500		1040
			2350		1820		1110	Feb. 25.	1790
„	3. 1980		2020		1830		1100		

Fifty-seven days, with five interruptions, of eight, one, one, one, one day respectively.

$$\frac{98{,}235}{57} = 1723.$$

The quantity of urine discharged by *B* is therefore 1723 c.c. per day, as the average of fifty-seven days. Maximum, 2655 c.c. Minimum, 1040 c.c.

The quantity of urine discharged in twenty-four hours by healthy adult persons has been determined by various other observers. The results of their observations, together with the results of my own, are arranged in the following table—

Table showing the total quantity of Urine

Observer.	Subjects.	Found in One hour.											
		Cubic centimetres.			English fluid measure.								
		Min.	Med.	Max.	Minimum.			Medium.			Maximum.		
					℥	ʒ	♏	℥	ʒ	♏	℥	ʒ	♏
Lecanu . .	—	—	—	—	—	—	—	—	—	—	—	—	—
Valentin .	Himself, medium of three days.	—	—	—	—	—	—	—	—	—	—	—	—
Lehmann .	Himself under ordinary circumstances.	—	—	—	—	—	—	—	—	—	—	—	—
Ditto . . .	Himself, when living irregularly.	—	—	—	—	—	—	—	—	—	—	—	—
Bischoff, Vogel, and others.	Well-fed persons who drink much.	60·0	—	70·0	2	0	54	—	—	—	2	3	43
	Well-fed persons who drink less.	50·0	—	60·0	1	6	5	—	—	—	2	0	54
	For one kilogramme of weight of adult.	—	1·0	—	—	—	—	0	0	16·9	—	—	—
	For 100 centimetres of length of adult.	—	40·0	—	—	—	—	1	3	16	—	—	—
Thudichum .	*A*, man, æt. 28; weight, 70 kilos., seventy-six days.	43·0	81·0	121·0	1	4	6·7	2	6	48·9	4	2	4·9
Ditto . . .	*B*, man, æt. 28; weight, 72 kilos., fifty-seven days.	43·0	71·0	110·0	1	4	6·7	2	3	59·9	3	6	59
Ditto . . .	One kilogramme of weight of adult man.	—	1·1	—	—	—	—	0	0	18·5	—	—	—
Ditto . . .	100 centimetres of length of adult. [*A*+*B*=346 cent.]	—	44·0	—	—	—	—	1	4	23·6	—	—	—

One cubic centimetre = 16·9

The values obtained by my observations, extending over larger than those of former observers. They may therefore urine secreted by adults, and of the lowest and highest amount

ischarged in given times by healthy individuals.

Found in Twenty-four hours.										Reference.
Cubic centimetres.			English fluid measure.							
Min.	Med.	Max.	Minimum.			Medium.			Maximum.		
			℥	ʒ	♏	℥	ʒ	♏	℥	ʒ	♏	
743·0	1268·0	2271·0	—	—	—	—	—	—	—	—	—	‘Handb. d. Phys.,’ 2d edit., vol. i, p. 655.
—	1447·7	—	—	—	—	—	—	—	—	—	—	
—	1057·8	—	—	—	—	—	—	—	—	—	—	Wagner’s ‘Handwörterb. d. Phys.,’ vol. ii, pp. 16-18.
909·0	—	1202·5	—	—	—	—	—	—	—	—	—	
1400·0	—	1600·0	49	4	0	—	—	—	56	2	40	Bischoff, ‘Der Harnstoff als das Maass des Stoffwechsels.’ Vogel, ‘Semiotik des Harns.’
1200·0	—	1400·0	42	2	0	—	—	—	49	4	0	
—	24·0	—	—	—	—	—	—	—	—	—	—	
—	960·0	—	—	—	—	—	—	—	—	—	—	
1049·0	1950·0	2920·0	—	—	—	68	5	15	—	—	—	Observations detailed above.
1040·0	1723·0	2655·0	—	—	—	60	5	18·7	—	—	—	
—	26·0	—	—	—	—	—	—	—	—	—	—	
—	1061·0	—	—	—	—	—	—	—	—	—	—	

nims imperial measure.

33 days of two individuals, are throughout considerably : said to extend our knowledge of the average quantity of nsistent with healthy function.

Among the influences which determine the quantity of urine, many are inherent in the mode of life, others are entirely independent of any act of the individual. Of the former are the quantity and quality of food and drink, and the amount of perspiration caused by activity.

The ingestion into the system of large quantities of water, tea, coffee, beer, (weak) wine, &c., may in a short time raise the hourly quantity of urine from 60 or 70 c.c. to 300, 600, 700 c.c. (from 2 to 10 or 20 fl. oz.) and more. I recollect that, when at College, I used to bet with one of my fellow-youngsters as to which of us could drink the largest quantity of water within the hour, from two to three in the afternoon, having taken dinner between twelve and one. At first I beat him, drinking four litres. The quantity of urine discharged was of course correspondingly great, and certainly not less than two litres per hour. After a week my opponent beat me hollow, drinking six litres during the appointed hour.

I recollect a student who drank fifteen half litres of weak beer within the hours from eight to eleven at night, an entire half litre at a time, and felt nothing the worse for it. A patient at one of the German spas used to take sixteen half-pint glasses of weak saline water between the hours from six to eight in the morning. In both cases the quantity of urine discharged within the next hour amounted to about one half of the quantity of fluid consumed during that hour, and in all cases the excess of fluid seemed to be discharged within two hours and a half after the last ingestion.

The quantities of water consumed by patients in some hydropathic establishments are something extraordinary. It is the same in many English and Continental spas, where patients make it their avocation to drink warm and cold water. A discharge of urine up to 1000 c.c. (35 fl. oz.) per hour is there of common occurrence after drinking.

Abstinence from drink, on the other hand, diminishes the secretion of urine; but this diminution is not exactly in inverse proportion to the increase by drink. The urine does not sink below a certain quantity, even in cases of total abstinence from food and drink. With a dry diet the urine may, as observed by Mosler on four males of from twenty to twenty-five years of age, sink from the medium of 86·0 c.c. (3 fl. oz.) per hour under their ordinary diet to 37·0 c.c. (10 fl. oz.)

The temperature of the atmosphere, the amount of moisture diffused in it, and its tension as expressed by the barometer, are influences over which the individual has only partial control. The amount of moisture, therefore, which is exhaled

by the lungs and skin—though of course dependent in part on the amount of water present in the blood, on the relative excretory activity of the organs, and on the bodily state of the individual, such as exercise, rest, sleep, and so on—is partly determined by atmospheric influences.

Certain regular variations in the hourly quantity of urine are produced by the cosmic influences of day and night. During the sleep of night only 58·0 c.c. (15 fl. dr.) of urine per hour are excreted; in the morning the medium is 69·0 c.c. (18 fl. dr.); after dinner, if taken early, or after luncheon, the amount of urine becomes largest—77·0 c.c. (2½ fl. oz.), and sinks again in the evening to 73·0 c.c. (19 fl. dr.), when even a late dinner will not influence it so much as might be supposed from the observations after an early dinner. Nothing could better demonstrate the influences of activity and rest upon the quantity of urine than these facts. Not only is there a greater production of effete matter, during waking and exercise, requiring to be discharged from the blood than during sleep, but also the excretory activity of the kidney is higher, in consequence of the transference of the nervous stimulus, and from the stimulant action of certain substances of aliment, such as coffee, porter, onions, and a host of other articles of diuretic property. This transferred nervous and direct stimulus may be brought to bear upon the kidneys at any hour of the day or night, and it is therefore that persons working with either mind or body during the night, discharge as much urine as during the same activity in the daytime. On the other hand, sleep and inactivity in the daytime will diminish the quantity of urine.

To recapitulate: the physiological quantity of urine is dependent, on the one hand, upon the amount of water introduced into the blood, or abstracted from it by other excretory organs; and, on the other hand, upon the excretory activity of the kidneys in its widest sense, as we have already stated.

QUANTITY OF URINE DISCHARGED IN DISEASE.

Though in patients all the influences which determine the quantity of urine in health may combine with the influences of the disease, yet as a general rule the consideration of the total quantity of urine in a great number of diseases will convince us that its variation, or a certain mode of variation, forms one of their essential symptoms. In the long run the character of the disease will determine the character of the

urine, however the satisfaction of an accidental thirst of the patient may increase it for a time, or however much it may have been diminished by vomiting, diarrhœa, perspiration, or increased pulmonic exhalation.

In the previous remarks we have seen the maximum, medium, and minimum quantities of urine discharged in given times by given weights of individual. This must form the basis of any attempt at judging whether the quantity of urine in a given case of disease is less or more than the same individual would be likely to discharge during health. The only caution necessary is to allow a sufficient margin for accidental variations. If we do so, the practical conclusions arrived at from a consideration of this point are as valuable as any of the most pathognomonic objective symptoms. As an example, we will assume the case of an average adult individual. We know he does not drink a great deal when well, and may therefore put down his medium quantity of urine for twenty-four hours as 1300 c.c. (42 fl. oz.) This individual has become ill, and we now ascertain that his urine for twenty-four hours only amounts to 400 c.c. (13 fl. oz.) We are at once justified in the conclusion that the disease has brought about a diminution of the bulk of the urine to less than one third its ordinary medium. Experience teaches us the consequences likely to follow the condition of the system, of which this lessened quantity of urine is a symptom. The symptom therefore has a high diagnostic and prognostic value, as we shall presently more particularly show. An increased amount of urine, on the other hand, to about 2500 or 3000 c.c. (80½ or 96½ fl. oz.), in a patient who in health would discharge from 1600 to 1700 c.c. (51½ to 55 fl. oz.), is an evident excess, which, if not traceable to any special accidental cause, and if permanent, as in diabetes, is the main and principal symptom of the disorder, and therefore the almost exclusive means of its diagnosis.

We will presently show to the reader the *use* of observing these variations in every case; but science requires that we should observe everything offered to our senses by a case, even should we not see the immediate use of it.

It is a fact, derived from general experience, and which may be verified any and every day, *that the quantity of the urine is diminished in all acute febrile diseases*, viz., in exanthemata and zymotic diseases, in low gastric fevers and typhus, in rheumatic fevers, in all inflammatory diseases, such as pneumonia, pleuritis, and bronchitis, and in the inflammatory fevers of tropical climates or miasmatic regions. In all these diseases, and in many more, *a constant dimi-*

nution of the quantity of urine is accompanied by, and therefore pathognomonic of, a constant increase in the intensity of the disorder. When the quantity of urine remains very low (below 800 *c.c.,* 25¾ fl. oz., *per day) for any length of time, then we may conclude that the intensity of the disease has not abated. A constant increase in the quantity of the urine, however, is a favorable symptom, and shows that the patient has passed the acme, and that the diseased action is abating* (vide Vogel, loc. cit., p. 226). *During the period of convalescence the quantity of urine becomes normal, or exceeds in some cases the normal quantity.*

Professor Vogel observed the following case, illustrative of these points. It is the more interesting, as the normal quantity of the urine discharged by the patient during health had been measured for a certain period just before he became ill. He was an attendant in the hospital, and became the subject of typhus fever. During the first three days of the illness, the total quantity of urine in twenty-four hours, amounting to 1800 c.c. (58 fl. oz.) during health, fell gradually to 200 c.c. 6½ fl. oz.) : it rose during the next five days regularly up to the normal 1800 c.c. (58 fl. oz.), exceeded the amount soon up to 2200 c.c. (70¾ fl. oz.), and then returned gradually to the usual average quantity.

When a disease, acute or chronic, takes a fatal turn, the quantity of urine becomes frequently very low, or remains in a fluctuating low state. This is the case in all diseases ending with or by exhaustion of the material of the component parts of the body. In cases, however, the fatal termination of which is due to a more sudden interference with the powers of the nervous system, or with the mechanical action of the lungs and heart, the quantity of the urine is not usually very much diminished.

The quantity of urine is materially diminished in dropsical diseases, with or without diseased kidneys. Common practice has made the amount of urine discharged by such patients the index of their improvement or otherwise, and has made a small quantity of urine, in cases in which the cause of the disorder is not the kidney itself, a therapeutical indication for the administration of diuretics.

The quantity of the urine is materially increased in those diseases which we commonly term diabetes. In these cases, however, as in cases of diseased kidneys, it is necessary to give particular attention to the quality of the urine at the same time, when the distinctions between hydruria, diabetes insipidus, and diabetes mellitus will become prominent.

SOLIDS AND WATER—SPECIFIC GRAVITY.

The direct way of determining the amount of solids contained in a given quantity of urine is by the evaporation of the water. This is best done under the receiver of the air-pump, care being taken not to make the urine boil, in order to prevent loss from the bursting of the bubbles evolved. By placing with the urine to be dried any body capable of freely absorbing water, such as sulphuric acid or quicklime, the vapour may be absorbed as soon as evolved, and in this way a vacuum for air and vapour may be kept up, under the influence of which the urine will rapidly get dry. When nearly dry, the residue may be mixed with a weighed quantity (1 to 2 grammes, 15 to 30 grains) of finely ground spongy platinum. This makes the drying considerably easier.

The vessel in which the urine is exposed should be rather flat, so as to give the largest possible surface for evaporation, and should be provided with ground edges, so that it may be rendered air-tight by greasing them and applying a glass disc. This caution is required in order to prevent the residue from absorbing water from the air, on being transferred from the receiver to the scales for weighing. The weight is now determined in the closed box of the chemical scales, the air surrounding which is kept dry by the presence of sulphuric acid and chloride of calcium. Then the vessel with the residue is again removed to the receiver of the air-pump; after it has been exposed for a time to the evaporating influence, the covered vessel is again weighed; and if it have lost nothing during the last exposure, the residue is considered to be perfectly dry. Of course, if it have lost in weight between two weighings, it must yet be brought repeatedly into the vacuum, until the weight remains stationary.

This process is one of extreme difficulty and great expense of time; but it is the only one which gives accurate absolute results. Less accurate is the following method, in which the evaporation of the water is effected by the assistance of heat. The objection to the application of heat in this process is, that it decomposes a certain amount of urea, which is volatilized in the form of ammonia and carbonic acid. This objection is so well founded, that if the products of evaporation are caught in a cooler, it will almost always be possible to find traces of ammonia in the condensed distillate by the delicate test I shall describe under Ammonia. This ammonia, of course, must not be confounded with the ammonia proper of the urine. By always keeping the urine acid

during evaporation, the decomposition of urea may be limited to a minimum; but alkalinity of the urine will favour the destruction of urea during the application of heat. However, where no air-pump is at hand, and where ordinary results only are required, the method now to be described is still of considerable use.

The operator pours about 12 or 15 grammes (or 4 to 5 drachms) of urine by weight or measure into a porcelain or platinum capsule, which, with a well-closing cover, has been counterpoised beforehand. It is then fitted into the ring of the water bath, so that the greater part of its outer surface is surrounded by the hot water.

If the solids only are to be determined, the best plan is to take a flat, small evaporating dish for the operation. The best vessel for a water bath is a semi-globe of copper, with handles, and with rings on the top to fit every size of evaporating dish, and with an opening for replenishing the supply of water. Another water-bath is that which combines the advantages of the one just described with those of an air-bath warmed by water. The top is provided with four holes, admitting as many evaporating dishes or capsules of different sizes. Any hole not used is closed by its cover. The warm air-bath at the front has two compartments, a door, with a rosette for admitting air if required, a ventilator at the top for carrying away the moisture, and an opening, into which a thermometer may be fixed with a cork, if it be desired to keep the temperature at a certain point.

When the urine has evaporated to an apparently dry residue, the capsule must be transferred to an air-bath,—a round box of copper, with double walls and a lid on its upper surface. The substances to be dried are placed upon a sieve of perforated copper, which is placed in the interior of the box in such a manner as to prevent any heat conducted by the metal, particularly the bottom, from reaching the substances. Thus they can only be affected by the hot air, the temperature of which is ascertained by a thermometer, placed with its bulb inside the box, and surrounded outside by a glass tube, in order to prevent the small column of mercury from being affected by any external currents of air.

The capsule being in the air bath, the air is now heated with a spirit- or gas-lamp, under the box, to 230° F. (110° C.), and is kept at that temperature from half an hour to an hour. Being ready for weighing, the capsule is covered, and allowed to cool over sulphuric acid, in the apparatus in which it is carried to the scales. This apparatus is a strong cylindrical glass with ground edges, containing about an inch in depth

of strong sulphuric acid. Over this, the capsule is placed upon a tripod made of strong lead wire. The glass is closed by a glass disc, with the assistance of a little tallow.

After the weight of the capsule and contents has been ascertained, it is again exposed to the temperature of 230° F. (110° C), and if, after some time, a second weighing does not show a further loss, the residue may be considered as dry.

We now find by easy calculation the amount of water evaporated, and the amount of solids contained in a given quantity of urine. If the total quantity of urine discharged in twenty-four hours be known, the total of solids discharged therewith is readily found : for the quantity of urine (u) taken for evaporation stands to residue (r) found, in the same proportion as the total quantity of urine (U) discharged in twenty-four hours stands to the (R) solids dissolved in it.

$$u : r :: \mathrm{U} : x; \text{ hence } x = \frac{\mathrm{U}\,r}{u} = \mathrm{R}.$$

For example, let the quantity of urine experimented on be 10 grammes, the quantity of solid residue in it 0·23 grammes, the total quantity of urine discharged 1000 grammes, then

$$\frac{0{\cdot}23 \times 1000}{10} = 23 \text{ grammes},$$

the total quantity of solids dissolved in the urine.

As the urine is a solution of several substances in water, their amount, viz., the amount of solids contained in any given quantity, may be ascertained by finding the specific gravity; for the specific gravity of any watery solution is higher than pure water in proportion to the amount of solids dissolved, the solids in solution giving up their own individual specific gravity, and influencing the specific weight of the solution by their absolute weight only. This is proved by the fact already mentioned; namely, that the absolute weight of a given bulk of urine may be found by multiplying the bulk, as expressed in cubic centimetres, by the figure expressing the specific gravity (p. 20).

The best mode of discovering the specific gravity of the urine is to compare the weight of a certain bulk with the weight of an equal bulk of water. For this purpose any phial of convenient size may be used; but best of all vessels is the pycnometer, a small glass bottle, the elongated ground in stopper of which is a capillary tube. The advantages thereby obtained are, that no air can be inclosed in the bottle (certainly not, as some fancy, because the air, when included, can escape by the capillary tube, which it could not,

from its great adhesion; but because no air is ever inclosed, being displaced by the rising water when the stopper sinks into the full bottle); and that the bottle can be accurately filled with the same bulk of fluid every time. The larger and better kinds of pycnometers are, moreover, provided with a thermometer, the bulb of which lies in the body of the stopper, and the tube in the elongation.

The weight of the pycnometer, and of the water required to fill it, being each ascertained, are written upon the glass with a diamond. The weight of the urine required to fill the pycnometer is then ascertained. Then the weight of water : weight of urine : : specific gravity of water: specific gravity of urine. Or, the specific gravity of water being 1,

$$\frac{\text{weight of urine}}{\text{weight of water}} = \text{spec. grav. of urine.}$$

Ex. A pycnometer held 50 grammes of water, and 5·21 grammes of urine.

$$\frac{51{\cdot}2}{50} = 1{\cdot}024 \text{ spec. grav. of urine;}$$

Or, 50 : 51·2 : : 1 : x

$$x = \frac{51{\cdot}2}{50} = 1{\cdot}024.$$

Another and more convenient mode of finding the specific gravity of the urine is founded on the fact of immersed solids displacing a bulk equal to their own. For this purpose a solid glass ball is used, the loss of which, when weighed in water, is known, and inscribed on it with a diamond. It is then weighed while immersed in urine, and its loss, as compared with its weight in air, is ascertained. Then its loss when weighed in the urine, divided by its loss when weighed in water, will be the specific gravity required.[1]

Ex. A glass ball lost 50·0 grammes when weighed in water, and 51·2 when weighed in urine.

$$\frac{51{\cdot}2}{50{\cdot}0} = 1{\cdot}024.$$

Though the two methods last described do not require so much time and weighing as the first two methods, still they

[1] Bird and Brooke, 'Nat. Philos.' p. 193, § 378.

are sufficiently troublesome to exclude them from universal application. The only method of ascertaining the specific gravity of urine for the practical purposes of diagnosis and prognosis at the bedside, is the use of the gravimeter, or areometer, which, when destined to be used for the urine only, should be called urogravimeter, but has been wrongly styled urinometer. The mode of action of this instrument depends upon the fact of solids of a given weight sinking deeper in light than in heavy fluids.

The urogravimeters are made of various materials, generally glass or metal, each of which have their peculiar advantages, which have not yet been combined in any material. Metal is most durable; but by frequent use and drying it loses a little of its weight. This does not so much apply to instruments made of solid gold or platinum, and well polished and hardened, as to a manufacture now frequently sold, the material of which is brass with a gilt surface. This electro-gilt layer is rubbed off in a very short time; and of course the instrument becomes incorrect, and requires to be sent to the gilder. Whoever uses such an instrument must frequently try its accuracy by immersing it in distilled water, in which it will sink to zero when correct, and not so deep when incorrect.

Instruments made of glass are apt to break; but their advantages are, cheapness, and the property of the glass to compensate by expansion or dilatation for any diminution of the density of the urine by a higher temperature between 60° and 80° F. (15·5° and 26·6 C.) Ackland.

The gravimeter just described only admits of a reading in half divisions; and if the instrument is small, these divisions come so near together, that it is sometimes impossible to say which division is the proper level of the fluid. In order, therefore, to obtain more accuracy, by having more divisions between the points of *a* and *b*, or 0 and 30, it is advisable to divide the scale upon two gravimeters, of which the one may range from 0 to 18, the other from 18 to 30 or 38, which is beyond the density of almost any urine. In this manner we double the length of the scale, and may now mark and read quarters of a division.

There are two sources of error, arising out of the use of these instruments, which must be corrected before determining the amount of solids after the reading from the gravimeter. The first source of error is in the instrument itself, and consists in the division of the scale into *equal* parts. This of course goes upon the assumption that the strata of the fluid in which the gravimeter is immersed are also of *equal* density. But as the density increases with the depth

from the surface, the graduations of the scale ought to be corrected upon the different densities of the respective columns of urine. This may be done in every case by calculation, but much better by using a gravimeter, the scale of which has been graduated with reference to compensation, by the machine of Mr. Ackland, invented for that purpose.

The second source of error is the variable temperature of the urine, the gravimeters in general use being graduated for water and urine at a temperature of 60° F. (15·5° C.) It is therefore necessary in any case to determine the temperature of the urine by the aid of a thermometer; and if it is not at 60° F. (15·5°C.), to bring it artificially to this, or to correct the reading of the gravimeter by a compensating calculation based upon the temperature found. For this purpose the following table of Mr. Ackland may be referred to.[1]

A Table for reducing the indications at a higher temperature of a glass gravimeter to the standard temperature, 60° F. (15·5° C.)

Ex. Suppose the urinometer to float in urine of 73° temperature at 21. On referring to the table opposite 73° will be found 1·20, which is to be added to the indication 21, making the true specific gravity = 1022·2.

Temperature.		No. to be added to the indication.	Temperature.		Addition to indication.
F.	C.		F.	C.	
60	15·55	·00	73	22·78	1·20
61	16·11	·08	74	23·33	1·30
62	16·67	·16	75	23·89	1·40
63	17·22	·24	76	24·44	1·50
64	17·78	·32	77	25·00	1·60
65	18·33	·40	78	25·55	1·70
66	18·89	·50	79	26·11	1·80
67	19·44	·60	80	26·67	1·90
68	20·00	·70	81	27·22	2·00
69	20·55	·80	82	27·78	2·10
70	21·11	·90	83	28·33	2·20
71	21·67	1·00	84	28·98	2·30
72	22·22	1·11	85	29·44	2·40

From the specific gravity so found, the quantity of solid matters present in the urine is calculated with the aid of a formula, which must be ascertained from the results of the more accurate methods we have described. Among the many formulæ so given two only appear to me sufficiently well proved to advise their adoption in practice. The first and most convenient formula is that of Trapp:

d = difference between 1000 and specific gravity of urine.

[1] Dr. G. Bird, loc. cit., p. 46.

Formula : $d \times 2 = x$ (total of solids in 1000 parts) ; or

Rule : To find the amount of solids in any given bulk of urine, double the last two figures of the number expressing the specific gravity : the product shows the number of parts of solids contained in any thousand parts of urine. This formula seems to be particularly applicable to urine of a low specific gravity[1], from 1000 to 1018, being the range of the first gravimeter.

The second formula, which is best suited for urine of a higher specific gravity, from 1018 to 1038, the range of the second gravimeter, is that of Dr. Christison.[2] It is : $d \times 2{\cdot}33 = x$. It is the same as that adopted by Dr. Day[3] and Dr. Hæser, and means, in other words : multiply the last two figures of the number expressing the specific gravity by 2·33, and the result is the total of parts of solids in any 1000 parts of urine. The results of the calculations with this formula are embodied in the following table :

Sp. gr.	Solids in 1000 parts.	Sp. gr.	Solids in 1000 parts.	Sp. gr.	Solids in 1000 parts.
1018	41·94	1026	60·58	1034	79·22
1019	44·27	1027	62·91	1035	81·55
1020	46·60	1028	65·24	1036	83·88
1021	48·93	1029	67·57	1037	86·21
1022	51·26	1030	69·90	1038	88·54
1023	53·59	1031	72·23	1039	90·87
1024	55·92	1032	74·56	1040	93·20
1025	58·25	1033	76·89		

Having in this way found the number of parts of solids in any thousand parts, grains or grammes of urine, we may easily calculate the whole amount of solids secreted with the urine in twenty-four hours, if we have ascertained the quantity so secreted. And as it is necessary to know the weight of the whole bulk of urine for finding the weight of the total of solids contained in it, the weight is first ascertained from the specific gravity, by multiplying the figure expressive of the bulk by the figure expressive of the specific gravity. By the specific gravity, therefore, we may obtain two kinds of information : 1, the weight of a given bulk of urine; 2, the amount of solids contained in urine.

[1] Vogel, loc. cit., p. 229.
[2] 'Library of Practical Medicine,' London, 1840, vol. iv, p. 248.
[3] 'The Lancet,' 1844, p. 370.

Ex. A patient passed in twenty-four hours two and a half pints, or 1250 grammes, of urine of the specific gravity 1020. 1000 grains (or grammes) of this urine hold dissolved 46·6 grains (grammes) of solids, and a pint will weigh 8925 grains: then

Grains. Grains. Grains.
1000 : 46·6 :: 8925 × 2·5 : x (total amount of solids).

2·5
44625
17850
22312·5
46·6
13 387 5 0
133 875 0
892 500

1,000|1039,762·50| = $1039\frac{7\,6}{1\,0\,0}$ = 1039·76 grains.

Or,

1000 grammes : 46·6 gr. :: 1250 gr. : x

46·6
75 0 0
750 0
5000

1,000|5825,0·0| = 58·25 gram. = x.

Ex. A patient passed on the average 60 c.c. of urine per hour, of the specific gravity 1012. 1000 parts of this urine hold dissolved 24 parts of solids. What is the amount of solids in 60 c.c.?

1000 : 24 = 60 : x

24
240
120

1000|1440| = 1·44 grammes.

This is the place to state that in calculating the solids from the specific gravity, we are liable to commit an error amounting to one tenth or one seventh of the solids actually contained in average healthy urine; and the error may be either above or below the amount actually contained. In concentrated urines and the urine of disease, however, the difference between the calculation from the specific gravity

and the real quantity may amount to one fifth, or even one fourth (Vogel), of the solids actually contained. It is therefore possible to find 30 or 50 parts of solids in a number of parts of urine which positively only contain 40. This is the worst case; but it shows that to slight fluctuations in the specific gravity, and the amount of solids calculated therefrom, we can in practice accord no importance. If we find, for example, that an individual discharges on an average 55 grammes of solids per twenty-four hours in his urine, a rise to 60 grammes, or a fall to 50 grammes, per twenty-four hours, cannot be considered abnormal, because it may be that the difference is only due to the error of calculation to which the method is subject; and the individual may actually have discharged his 55 grammes, or any number of grammes between the 50 and 60. If we find, however, from the specific gravity, that a person who on the average discharged 60 grammes per twenty-four hours, discharges only 30 grammes, we are perfectly justified in drawing the conclusion that this person voids a much smaller amount of solids in the urine than he did before; and though we cannot positively say whether he actually discharges 30, or 25, or 35 grammes, yet 30, 25, or 35 are so greatly different from 50, 55, or 60 grammes, that the diminution cannot be due to the faults of the method, and may with propriety be used as evidence for the diagnosis, or as an indication for the treatment of the case.

This uncertainty in the results obtained by the gravimetrical method is most likely partly the consequence of the fact that the various constituents of the solid residue of the urine do not always stand in the same proportion to each other. There is also the error to which the calculation of the temperature makes us liable; further, the error arising from the different densities of the different strata of fluid, as already stated; further, the difficulty of making the scale of the gravimeter sufficiently long to allow of an accurate reading of the level of the urine, which may assume different curves as the different densities of the urine determine a greater or less adhesion to the sides of the vessel and to the stem of the gravimeter. What with having to employ two gravimeters, to compensate and calculate for temperature, and density from depth, and being after all subject to inaccurate reading and the varying proportions of the solids in urine—errors which in the aggregate amount to a difference from reality of from one tenth to one fourth,—I must say, that I think the trouble of the methods with the balance and air-pump nearly equalled, and yet the result of a hundred

gravimetrical analyses is scientifically and practically not worth one accurate analysis.

The reader is now in possession of the facts which will enable him to attribute its proper value to the gravimetrical method of determining the amount of solids in the urine. The following observations are recorded in tabular order as being the best of their class :

Observers.	Men.						Women.					
	Average quantity of urine in twenty-four hours.			Average density.			Quantity.			Density.		
	Min.	Med.	Max.	Min.	Med.	Max.	Min.	Med.	Max.	Min.	Med.	Max.
	oz.	oz.	oz.					oz.				
Prout	30	40	—	—	1020	—	—	—	—	—	—	—
G. Bird . . .	—	—	—	—	1020	—	—	—	—	—	—	—
Becquerel . .	—	43	—	—	1·0189	—	—	47	—	—	1·0151	—
Routh, eighteen observations .	20	35	50	—	1·021		mean 1·017					

According to the older estimates, the kidneys seemed to excrete from 600 to 700 grains of solids in twenty-four hours (mean 650, Dr. G. Bird). However, all the late authors coincide in making 1020 the average specific gravity of urine, and if of this urine from 1400 to 1600 grammes (49 to 56 fl. oz.) are discharged during twenty-four hours, the gravimetrical method gives a mean amount of solids of from 55 to 66 grammes, or 850 to 1020 grains for twenty-four hours.

100 kilogrammes of individual discharge on an average 4·1 grammes of solids per hour, 100 centimetres discharge 1·5 grammes (Vogel).

For the generality of diseases the gravimetry of urine gives very meagre results as yet, but there can be no doubt in the abstract that an accurate knowledge of the whole amount of solids would be of high practical value in every case of illness. The amount of nourishment acquired from ingested food, the intensity of the destruction of matter serving the purposes of life, as found by the comparison of times and quantities, the activity of the secreting organs themselves—all these factors are summed up in the total quantity of solids contained in the urine. It is natural then that *in disease*

generally, where little solid food is being taken, the amount of solids sinks from the daily 60 *to* 50 *and* 40 *grammes* (600 grains), and even then is made up less of the produce of the destruction of fresh nourishment in the blood and muscles than of disintegrated tissues and their interstitial juices; in other words, is formed mostly at the expense of the body, as is entirely the case in simple inanition. A patient lives on his own fat partly during his illness, as the proverb says, like a badger during the winter. The consequences are clear—emaciation.

I have now spoken of disease generally; and the remarks made of course apply to the two great classes of disease, acute and chronic, with equal force. But the fluctuations in the amount of solids occurring in both are of a very different prognostic value; for in chronic disease, with a limited amount of solids, a rise in their amount is, as a general rule, a forerunner of considerable and mostly lasting improvement, and indicates that the chemistry of the body is actively employed in renewing the material of the organs and rectifying their functions. To this rule diabetes mellitus alone forms an exception, where a rise in the amount of solids indicates an exacerbation of the disease; and, in this respect, diabetes forms the transition from chronic to acute disease, in which, on the whole, a rise in the amount of solids in the urine during the acme is an unfavorable symptom, indicating an excessive disintegration of the tissues and juices of the body, which must necessarily lead to exhaustion of the material substrata of life. Under all circumstances, a constant and gradual decrease of the amount of solids is as unfavorable a symptom as the decrease of the total quantity of urine discharged, because it indicates the decay of life, and a probable fatal termination of the case.

The indications of the solids become more varied as soon as they are considered with relation to the amount of other excreta. First, as regards the amount of water by which they are accompanied in the urine, four distinct classes of cases must be borne in mind. If a very small amount of solids is contained in a similar amount of water, we may conclude upon a corresponding amount of anæmia in the individual, always provided that disease of the kidney be not present. In the latter case, a small amount of solids indicates the retention of urea, which may probably end in uræmia.

If a small amount of solids is contained in a larger or large amount of water, it may possibly be the consequence of excess of drink of some kind. Many cases of hysteria,

of anæmia with hysterical symptoms, are accompanied by this description of urine. It is the essential symptom of a decided improvement in many cases of hydræmia and dropsy, and when it occurs in a patient with no particular cause to account for it, it has properly been termed *hydruria*. Of this disease Professor Vogel observed a very decided, and therefore illustrative case. A man, thirty-five years of age, of a powerful frame, and suffering from rheumatism of the neck, discharged a quantity of urine, amounting to 2983 c.c. (104 fl. oz.) per day in the mean of twenty-four days. But its specific gravity was very low, varying between 1005 and 1012; and the average quantity of solids discharged per day accordingly only amounted to 42 grammes (630 grains). This case was therefore clearly one of hydruria. The patient did not seem to suffer under this excessive discharge of fluid.

When the amount of solids becomes larger, but still remains below the standard of health, and the amount of water is at the same time diminished—in other words, in diseases with a small amount of urine of high specific gravity—the acuteness of the pathological process is clearly indicated. Beginning with the physiological excessive perspiration, there are many pathological conditions, as the sweat of fever, thirst, starvation, diarrhœa, and fever of essential or symptomatic nature, of which this condition of urine is a regular symptom.

In the fourth class of cases, both the solids and the water of the urine are present in excess. They form a special and specific class of diseases, to which the generic name of diabetes has been given. The genus has, however, only two species, of which the one is distinguished by the presence in the urine of sugar, and therefore goes by the name of diabetes mellitus; the other subdivision comprises cases where, in a large amount of water, the increased amount of solids is made up of other solids than sugar, termed diabetes insipidus. In both classes of diabetes, the wear of the body is considerable, and either at intervals, or throughout the course of the disorder, surpasses the amount of nutriment taken in. Diabetes mellitus, from its chemical interest, and the facility with which it may be artificially produced in animals, has been favoured with more attention of late than diabetes insipidus, a disease with which perhaps many difficult cases of hysterical anæmia and intractable ailments will have to be classed hereafter. If the total quantity of urine amounts to more than 3000 c.c. (105 fl. oz.) per day, and if the specific gravity shows an excessive amount of solids, ranging from the normal

60 grammes (926 grains) up to 130 grammes (2006 grains), or even more, giving on an average about 80 grammes (1234 grains) per day, we may then with perfect safety ascribe the excessive destruction of the constituents of the body to this excesssive secretion, and place to its account a number of symptoms usually following in its train, such as the pale looks and the headache of anæmia, vertigo, the tenderness of certain dorsal vertebræ on pressure, and spasms in the muscles of the neck, such as were observed by Vogel in a marked case of this description.

We have now considered in its bearings the observation of the amount of solids in relation to the water in which they are contained; it only remains to draw attention to the important conclusions to be derived from comparing the amount of solids secreted by the kidneys with the excreta of the skin, lungs, and bowels. In many cases of dropsy, the bowels will spontaneously compensate partly for a diminished discharge of urine; and it is, in fact, by this vicarious discharge that drastic purgatives are of service in disease of the kidneys. The skin will elimiñate urea in cholera in such quantities that it may be collected by washing and crystallization, and its amount may even be determined. The lungs will, perhaps, in many cases take on increased action, and discharge, not only water, but also carbonic acid, to compensate for a diminished secretion by the kidneys and skin. A diminution in the amount of solids in the urine requires therefore to be checked by the amount of vicarious discharges. And should we be able to determine at the same time the amount of the ingested nutritive matters, we should at once be in a position to balance the income and expenditure of the body, and thereby not only to foresee the probable result, but also to be in possession of the indication for part of our treatment. But in this direction so much remains to be ascertained by fact, that it would be dangerous to the practical tendency of these pages to mix up prospective speculation with the real advantages to be derived from observation of the amount of solids discharged in the urine.

CHAPTER III.

UREA.

Symbol: $\overset{+}{U}$. Formula: $C_2H_4N_2O_2$.

Composition:		
2C	.	20·000
4H	.	6·666
2N	.	46·667
2O	.	26·667
		100·000

The best physiological definition of urea is perhaps the following: Urea is the principal product of the metamorphosis in the body of nitrogenized food. It is essentially excretory matter, incapable of any longer serving the purposes of life, because it cannot be more highly oxydized; and when retained becomes a poison to the system,[1] both directly, and, perhaps, by the products of its decomposition. Its regular occurrence in healthy blood, and in the juice of flesh of animals and man, has established the opinion that it is formed in the tissues (muscles), and carried by the blood to the kidneys to be discharged. Hence, when the action of the kidneys is partially or totally suspended, urea naturally accumulates in the blood, and accompanies the serum effused into the cellular tissue and the cavities of the body.[2] In this way its occurrence in the dropsical fluid of Bright's disease, as first discovered by Rayer and Guibourt,[3] and confirmed by subsequent observers,[4] and in the blood of animals after extirpation of the kidneys (Prevost and Dumas), is satisfactorily explained. In cholera the condition of the blood forms the obstacle to the excretion of urine, and in consequence urea is found in the blood,[5] and in the viscid perspiration of the skin. Urea has been discovered in the vitreous and aqueous humours of the eye.[6] It has been found in the

[1] Gallois, 'Essai physiologique sur l'Urée et les Urates.' Thèse offerte à la Soc. d. Pharm. 'Journ. de Pharm. et de Chim.,' 3me ser., tome xxxii, p. 64. 'De l'action toxique de l'Urée.'

[2] S. Picard, 'De la présence de l'Urée dans le sang, et de sa diffusion dans l'organisme.' 'Thèse. Strasbourg,' 1856, Canstatt's Jahresber., p. 169.

[3] Desire, 'Gaz. Méd. de Paris,' 1836, Juill.

[4] Marchand, Müller's 'Archiv,' 1837, p. 440.

[5] Marchand, Erdmann's 'Journal,' 1837, xi, p. 449.
Millon, 'Compt. Rend.,' xxvi, p. 121.

liquor amnii by Wöhler,[1] but is certainly present in exceptional cases only, as I have shown in an essay to which the Faculty of Medicine of the University of Heidelberg awarded a prize medal.

I must not overlook some observations said to be made of the occurrence of urea in milk, in blister-serum, in the perspiration of persons with diseased kidneys, and in the copious evacuations from the intestines of such patients, produced by the action of elaterium.

If we had been favoured by the authors of these statements with the particulars of the process adopted for obtaining the urea, and of the proofs that the substances obtained were really urea and nothing else, there would be no difficulty either in admitting these observations, or rejecting them upon the basis of analytical criticism. But at present they are mere assertions, the correctness of which can in no way be controlled. The greatest chemists do not allow themselves to throw assertions upon their readers, without giving the whole of their analytical proofs. The more we must demand similar and even more stringent proofs of men, who, whatever their professional standing, must acknowledge themselves more liable to error than a Berzelius, a Graham, or a Liebig. One fact will show the necessity of this caution. It goes the round through all the handbooks and encyclopædias of all nations, that Marchand found urea in the blood of the cow or calf. The indiscriminate authors do not inquire how he found it. On referring to the original article,[2] or Gmelin's 'Handbuch,' we find that Marchand concluded upon the presence of urea from the crystallization in octahedra of the chloride of sodium. We now know that that occurrence by no means justifies us in the assumption even of the merest trace of urea, and, consequently, the assertion that Marchand found urea in the blood of the calf is devoid of foundation. We could not have corrected this error, had Marchand been credited with his statement upon the mere value of his name as a chemist.

History.—Urea, in an impure state, was first obtained from urine in 1773, by Rouelle, jun., who called it *extractum saponaceum urinæ*. It was first obtained pure by Fourcroy and Vauquelin in 1799. Its chemical composition was doubtful, even after its decomposition to ammonia and cyanic acid had been proved. In consequence of this discovery, a successful attempt was made by Liebig to produce urea artificially; and we are now in possession of several methods

[1] 'Ann. d. Chem. und Pharm.,' lviii, p. 98.
[2] Erdmann's 'Journal,' 1838, p. 500.

whereby it may be produced in any quantity, and more pure than it can be obtained from urine, without much difficulty.

As pure urea is a necessary instrument for preparing the test-fluids by which the chlorides and urea of the urine are determined quantitatively, it may be of use to the reader to have the mode of artificially making urea described in this place.

Mix intimately 28 parts of dry ferrocyanide of potassium with 14 parts of manganese, and heat on an iron sheet plate over an open fire, until the mixture ignites and is slowly burned through. Extract the blackish-gray mass which remains with cold water; add to the filtered liquid 20½ parts of dry sulphate of ammonia; let it stand, in order that the sulphate of soda may crystallize; separate the crystals from the solution containing urea; evaporate the latter to dryness, and extract with alcohol, which leaves the rest of the sulphates undissolved, and, on evaporation, gives perfectly pure and white urea.

Two new methods for the artificial preparation of urea, by Natanson and Regnault, have been described.[1]

Urea is formed by evaporating a mixture of cyanic acid and ammonia $(H_3N+HO+C_2NO)=(C_2H_4N_2O_2)$. It is a product of the decomposition, by oxydizing agents, such as peroxide of lead, of uric acid; and, by another process, of creatine; and the regularity with which this transformation is effected has established the opinion that urea is contained in uric acid, as it were, in a preformed condition, or that uric acid is only a preparatory state of urea.

Physical properties.—Of the physical properties of urea, its *form of crystallization* deserves our attention for a moment. The crystals of artificial urea, or of urea obtained from urine by the process of purification to be described, are known well enough as white silky needles, or white transparent prisms, square on section, striated, and of a silky lustre. One or two inclined planes form the ends of the prisms.[2] Much more perfect crystals, however, than are obtained by any of these modes, are occasionally produced by the simple spontaneous evaporation of a drop of urine on an object-glass.

The urine of fever-patients, which has a high specific gravity, and contains a very small proportion of inorganic salts, is very suitable for this experiment. The rapid formation of the prisms and their combinations, and their solubility in water, glycerine, and preserving solutions, ensures the

[1] 'The Lancet,' July 26, 1856, p. 144.

[2] *Vide* Dr. L. Beale, 'The Micros. in Clin. Med.,' p. 264, fig. 215. Funke, 'Atlas d. phys. Chemie,' taf. ii, fig. 4. See also Plate I, fig. 1.

diagnosis. They polarize with a weak blue colour, which is much like the glare of the sea in moonlight.

Urea crystallizes in quadratic prisms, from a solution in water with a rectangular terminal plane, from a solution in alcohol with octahedral planes. The long four-sided prism becomes six-sided when two of its diagonal edges are replaced by two vertical planes of a secondary prism, and eight-sided when the other two edges are also replaced by the secondary prism. These relations must be borne in mind when examining crystallizing solutions under the microscope with a view to diagnose urea. On the object-glass, one of the planes, by coming in contact with the surface, is pre-eminently large, and its two adjoining planes are very much narrower, thus showing that the crystal was prevented from growing in the direction of the glass. A secondary plane may in this way become larger than its diagonal one, and one or more primary planes may be prevented from obtaining the size of their correlatives.

Urea is colourless, of a bitterish, cooling taste, like saltpetre, which has been mentioned as being in part the taste of urine. When dry, it is not changed by exposure to the air, and then attracts very little moisture. A pure solution in water, even when dilute, does not undergo any spontaneous chemical change. It has no reaction on vegetable pigments. It is soluble in its own weight of water of 15° C., in five parts of alcohol, of 0·816 specific gravity, at the ordinary temperature of the air, and in its own weight of boiling alcohol. It is almost insoluble in ether, and quite insoluble in oil of turpentine.

Decompositions.—Urea may be decomposed by the influence of heat, acids, alkalies, salts, putrid animal matter, and yeast. When exposed to a temperature of 120° C. (248° F.) it fuses, but the temperature being raised a few degrees, ammonia and carbonate of ammonia are evolved, leaving ammeline, an amorphous white matter, then cyanate of ammonia, cyanuric acid and its derivatives, until at last the residue chars, and on raising the temperature to red heat, burns without leaving any residue.

Nitrous acid, and nitric acid coloured red by the presence of the former, decompose urea into carbonic acid, nitrogen, and water.

$$C_2H_4N_2O_2+2NO_3=2CO_2+4N+4HO.$$

The same decomposition is produced by a solution in nitric acid of the nitride of the suboxyde of mercury. This decomposition is employed in the quantitative analysis of Millon.

Urea, when fused with potash, or treated with concentrated sulphuric acid, is transformed into carbonic acid and ammonia.

$$C_2H_4N_2O_2+2HO = 2CO_2+2NH_3.$$

The quantitative analysis of Heintz and of Ragsky is based upon this influence of sulphuric acid upon urea.

The same decomposition of urea may be produced by the influence of heat in the presence of water. A solution of urea, when enclosed in a glass tube, by the assistance of the blow-pipe, and kept for several hours in an oil bath or well-regulated air bath, at a temperature of 140° C. (288° F.), will decompose in this manner; and if a sufficient amount of hydrate of baryta be present in the tube, the decomposition at a temperature of from 210° C. (410° F.) to 240° C. (468° F.) will be accelerated by the alkali, and the carbonic acid evolved will be immediately fixed by the baryta. From the quantity of carbonate of baryta so produced, we may ascertain the quantity of urea present in the fluid before the experiment. This is the process employed in the method of Bunsen.

The decomposition of urea into carbonic acid and ammonia is further the result of true fermentation, induced by ferments, such as yeast, or decomposing mucus of the urinary bladder (*vide* alkaline urine, p. 11), or any other putrefying animal matter, such as albumen.

A solution of urea, when heated with caustic lime, or magnesia, to a temperature of above 50° C. (122° F.), will evolve ammonia. Below 50° C. (122° F.), lime and magnesia exert no influence upon urea in solution, and may therefore be employed with safety for the quantitative analysis of ammonia in urine.

A solution of urea, when mixed with liquor sodæ chlorinatæ, evolves the whole of the urea in the form of nitrogen, carbonic acid, and water. As the carbonic acid is immediately absorbed, nitrogen only is left, the bulk of which, on measuring, is a ready means of determining the amount of urea of which it was a part. (Method of E. W. Davey.)

A mixture of urea and nitrate of silver in solution is on evaporation transformed into nitrate of ammonia and crystalline cyanate of silver. This experiment is the reverse of the process by which urea is produced artificially. Its formula is thus:

$$C_2H_4N_2O_2 + AgO, NO_5, = NH_4O, NO_5 + AgO, CyO.$$

Combinations of Urea.

Urea enters into combination with several bases, acids, and salts. Of these compounds, those are of great importance which, by being insoluble in water and watery

solutions, enable us to transform dissolved urea into a precipitate, and thereby determine its quantity.

Urea and protoxyde of mercury.[1]—*a. With two equivalents of protoxyde of mercury.* $\overset{+}{U}+2HgO$.—On adding to a warm solution of urea, oxyde of mercury diffused in water, we observe the first portions of the oxyde to be perfectly dissolved; an excess of the oxyde of mercury is in the fluid gradually changed into a white or yellowish-white powder; the filtrate from the latter, after the elapse of twenty-four hours, deposits thin hard crusts on the walls of the vessel. These crusts and the powder have the above composition. The preparation frequently contains some cyanate of mercury.

b. With three equivalents of protoxyde of mercury. $\overset{+}{U}+3HgO$.—On adding to a solution of urea, caustic potash, and then a solution of bichloride of mercury, with a renewed addition of potash ley, so that the fluid is always kept alkaline, a thick, gelatinous, snowy-white precipitate is obtained, which, when perfectly washed out and in its moist condition transferred into boiling water, transforms into a sandy or granular powder of a yellow or yellowish-white colour. After drying the powder is reddish-yellow. When heated while moist it frequently explodes, with evolution of light, water, carbonate of ammonia, and metallic mercury. The powder is soluble without effervescence in hydrocyanic and hydrochloric acid; in the latter solution alkalies produce a whitish-yellow precipitate.

c. With four equivalents of protoxyde of mercury. $\overset{+}{U}+4\,HgO$.—If, instead of a solution of bichloride of mercury, a solution of nitrate of protoxyde of mercury is precipitated by an alkaline solution of urea, a white and less voluminous precipitate is obtained, which in boiling water shrinks to a sandy powder.

Urea and chloride of sodium. $\overset{+}{U}+NaCl+2HO$.—This salt crystallizes in clino-rhombic prisms of great lustre, when a mixture of solutions of urea and chloride of sodium is evaporated. The same salt is obtained in large coloured crystals on evaporation of human urine. (Strecker.)

Urea and nitric acid. $\overset{+}{U}+NO_5$.—If we mix a concentrated solution of urea, or urine concentrated by evaporation, with an excess of colourless nitric acid, the mixture will immediately crystallize into an almost solid mass of white shining scales or plates (yellow from urine) of nitrate of urea. This

[1] Liebig, 'Ann. d. Chem. und Pharm.,' lxxx, p. 123; lxxxi, p. 128; lxxxii, p. 232; lxxxv, p. 189.

crystallization may be completed or accelerated by exposing the mixture to the influence of cold—by putting it into ice or a freezing mixture.

Nitrate of urea crystallizes in the rhombic system. If a pure crystallization be obtained, the rhombic prisms may be seen to perfection. Neubauer[1] says that on letting pure nitric acid combine with urea under the microscope, flat rhombic octahedra are formed at first, which, by apposition of crystalline matter, become converted into rhombic plates. This metamorphosis, however, most improbable in itself for crystallographical reasons, has not been observed by me, or by any other writer on the subject as far as I know. The rhombic prisms are either flat, single, and primary, or combinations of several prisms; like those of pure urea, becoming hexagonal, and ultimately thin plates. (See Plate I.)

The nitrate obtained from urine directly, almost always crystallizes in large plates, of which many lie upon each other, mostly with their principal crystallographical axes parallel to each other. This parallelism is observed also in crystallizations of pure urea: the plates only show the prismatic character a little more.

The crystals obtained from urine are pressed between bibulous paper, until the paper is no longer stained. They may then be washed on a filter with some water containing a little nitric acid, in which they are not very soluble, and may then be pressed a second time. They are then almost white, and of a silky gloss, or satin-like lustre, resembling mother-of-pearl.

Nitrate of urea is not changed by the influence of the air. It is soluble in water. Heated on platinum foil it explodes, when the temperature has been raised quickly to a high point; but if only heated to 284° F. 140° C. it decomposes, carbonic acid, suboxyde of nitrogen, urea, and nitrate of ammonia being produced.

Urea and oxalic acid. $\overset{+}{U}+\overset{-}{O}$. ($2C_2H_4N_2O_2$, $C_4H_2O_8$ Gerhardt.)—Oxalic acid has a stronger affinity for urea than nitric acid, so that when it is added to a solution of the nitrate, oxalate of urea will be formed, which not being very soluble in water containing nitric acid, is precipitated. Oxalate of urea crystallizes in rhombic prisms and rhombic plates,[2] some varieties of which are very much like the prismatic plates of nitrate of urea. But frequently the oxalate has

[1] Loc. cit., p. 7. He refers to Funke's 'Atlas,' taf. ii, fig. 5; but there only prisms, and not a single octahedron, are to be seen.

[2] *Vide* Dr. Beale, 'The Microscope,' p. 264, fig. 214. O. Funke, 'Atlas,' taf. ii, fig. 6. Bowman, 'Med. Chemistry,' p. 5, fig. 1.

more tendency to produce crystals in which the axes are of a more equal length; these crystals, though smaller in outline, have then more body. (See Plate I.) To the naked eye a precipitate of the oxalate of urea appears as a white crystalline mass of plates. This salt is soluble in 23 parts of water of a temperature of 59° F. (15° C.), but is soluble in a much smaller quantity of boiling water.

Urea and nitrate of mercury.[1]—On adding to a solution of urea a solution of nitrate of mercury, a white flocculent precipitate is immediately produced, which contains urea, oxyde of mercury, and nitric acid. According to the proportion in which both solutions are mixed, and the amount of free acid contained in the solution of mercury, one of three compounds or a mixture of three compounds is produced, which are distinguished from each other by containing different quantities of the protoxyde of mercury.

These three different combinations have the following characters in common: On combustion with oxyde of copper they develop a mixture of gases, in which nitrogen and carbonic acid are present in the proportion of three volumes of the one to two volumes of the other. This is the same proportion as in the nitrate of urea. On removing the oxyde of mercury by sulphuretted hydrogen, there remains in the fluid after filtration from the precipitate, pure nitrate of urea, which crystallizes to the last drop. These combinations, therefore, only differ from each other by a varying amount of protoxyde of mercury; they are entirely soluble in hydrocyanic acid and hot nitric acid. In the latter solution, potash produces a white precipitate. If the dry precipitate of one of them is heated for a length of time in a current of warm air, a decomposition takes place; it assumes a yellowish colour, and the solution in nitric acid gives now a yellowish precipitate with potash. The formulæ of these three combinations are—

$$A.\quad NO_5,\ \dot{U}+4HgO$$

$$B.\quad NO_5,\ \dot{U}+2HgO$$

$$C.\quad NO_5,\ \dot{U}+3HgO$$

From these formulæ, and the manner in which they are decomposed by sulphuretted hydrogen, sulphuret of mercury being precipitated and nitrate of urea going into solution, we may consider these bodies to be combinations of one

[1] Justus Liebig, 'Ueber eine neue Methode zur Bestimmung von Kochsalz und Harnstoff im Harn,' Heidelb., 1853. 'Annal. d. Chem. und Pharm.,' lxxxv, p. 294.

equivalent of nitrate of urea, with four, two, and three equivalents of the protoxyde of mercury respectively. The first of these combinations is produced in the quantitative analysis of urea in the urine.

Diagnosis of Urea in Urine and other Animal Fluids.

To demonstrate the presence of urea urine, the following modified method of Liebig[1] should be adopted: A quantity of urine should be mixed with about half its volume of a solution of baryta (consisting of two volumes of saturated solution of baryta or baryta water, and one volume of a saturated solution of nitrate of baryta), or a quantity of that solution sufficient to precipitate the phosphoric and sulphuric acids. The fluid is then filtered from the precipitate, neutralized with nitric acid, and evaporated to dryness on the water bath; the residue is extracted with alcohol; the alcoholic extract is again evaporated, and exhausted a second time with absolute alcohol. This last solution contains the urea very pure, so that it crystallizes out in colourless needles. This process may be employed for producing urea directly from urine without precipitating it by either nitric or oxalic acid, and may serve as a mode of finding the quantity of urea in any fluid, particularly when the apparatus and test-fluids of the Centigrade analysis should happen not to be at hand.

The presence of albumen in urine requires a modification of this process. It is not advisable to remove the albumen by boiling, with the addition perhaps of some drops of acetic acid, in cases where accuracy is desired. For albumen, on passing from its dissolved into an insoluble condition, incloses into its substance a certain amount of urea, which cannot afterwards be separated from it without great loss of time and trouble. This fact must always be borne in mind in analysing fluids containing a small amount or only a trace of urea; as in that case the whole of the urea may adhere to the coagula of albumen, and the fluid may appear to have contained no urea at all; or urine may in this way be made to appear to contain a smaller amount of urea than it actually does. To avoid erroneous conclusions, therefore, albuminous urine, after precipitation with the solution of baryta, should be extracted with absolute alcohol, which, having a stronger affinity for urea than albumen has, takes

[1] Loc. cit., p. 23.

the former into solution in the same moment as it renders the albumen insoluble. The alcoholic extract may then be evaporated to the bulk of the urine employed, and the amount of urea determined by means of the mercurial test-fluid; or it may be evaporated to dryness, the residue extracted a second time, when, on a second evaporation, the whole of the urea will be obtained in a crystalline state ready for weighing.

It is mainly owing to the oversight of this fact that urea has not been found either in blood or in the juice of flesh by many observers, since it is always present in both.

Liebig's Method of ascertaining the Absolute Quantity of Urea in Urine.[1]

This mode of ascertaining the quantity of urea dissolved in urine is equal in accuracy to any hitherto in use, but has the great advantage over them of requiring much less time for its execution, and no particular ability on the part of the operator—two circumstances which pre-eminently qualify it as a means for the diagnosis of certain pathological conditions of the system. It is based upon the property of urea to be precipitated by the addition of nitrate of mercury, in combination with one equivalent of nitric acid and four equivalents of the oxyde of mercury, three equivalents of nitric acid remaining free in solution.

On gradually adding to a dilute solution of urea a dilute solution of nitrate of mercury, and neutralizing the free acid of the mixture from time to time, by the addition of some baryta water or a dilute solution of carbonate of soda, a flocculent, bulky, snowy-white precipitate is obtained, which is insoluble in water. If the alternate addition of the nitrate of mercury and carbonate of soda be continued as long as a precipitate is formed, there will be a point at which the mixture, or the spot where the drop of the solution of the carbonate falls into the mixture, will assume a yellow colour, owing to the formation either of oxyde of mercury, or basic nitrate of mercury, or carbonate of mercury. If the fluid is now filtered, it does not any longer contain any appreciable quantity of urea; the whole of the urea has been precipitated. The precipitate is composed of one equivalent of urea and four equivalents of oxyde of mercury. By mixing solutions of urea and nitrate of mercury, both of known strength, we can easily convince ourselves that precipitation

[1] Liebig, loc. cit., p. 19.

of the yellow oxyde or carbonate by the addition of carbonate of soda does not take place until we have added, for ten parts of urea in the solution of urea, a volume of the solution of mercury, in which there are contained seventy-seven parts of the oxyde of mercury. This amounts to four equivalents of the oxyde for one equivalent of urea.

If we continue adding a solution of nitrate of mercury to a solution of urea so long as a precipitate is produced, the mixture will remain *white* on the addition of carbonate of soda. But if the original mixture be allowed to stand for several hours, the precipitate after the lapse of that time will have changed its properties, and have become crystalline. One may now easily recognise the six-sided plates of the combination of urea with one atom of nitric acid and three atoms of the oxyde of mercury; and the clear fluid which stands over the precipitate, and which, on the admixture of an alkali, gave a white precipitate, is now precipitated *yellow* by the same alkalies. In the acid fluid the combination, containing four atoms of the oxyde of mercury and one of nitric acid, is reduced to a combination containing less oxyde, because a part of the oxyde is redissolved by the free acid of the fluid.

In order to recognise whether an amount of the solution of the nitrate of mercury sufficient to produce the combination of urea with four atoms of the oxyde of mercury has been added, the neutralization with carbonate of soda after the addition to the solution of urea of the mercurial solution becomes necessary. If a drop of the mixture, when added to a drop of a solution of carbonate of soda on a watch-glass, or on a flat piece of glass, remains white, we may be quite sure that there still is uncombined urea in the mixture. When, however, on the two drops mixing, a yellow pellicle is produced, then we have added a sufficient amount, or rather a little more than sufficient, of the mercurial solution to precipitate the whole of the urea. It requires only a small excess of the salt of mercury to indicate that the quantity sufficient to precipitate all the urea has been added. It is therefore evident, that if we know the amount of mercury contained in the solution of it, we may, from the quantity of this solution used for precipitating urea in the manner described, determine the quantity of urea contained in solution; or if, for precipitating a *known* quantity of urea, say 100 milligrammes, we have used a certain volume of the solution of mercury, this same volume of the same solution will indicate the same quantity of urea in fluids containing an unknown amount of urea. From the volume of the mer-

curial solution used in this way, the amount of urea present may then be calculated; a consumption of half the volume shows half the amount of urea, of twice the volume double the quantity of urea, to be contained in the fluid.

The results obtained by this analysis are equal in accuracy to those obtained by the methods of Bunsen and Ragsky; but these latter methods, though giving excellent results, are not available for practical purposes, on account of the time and attention required to carry out the operations. If it be required to make many analyses of urea at one and the same time, the method of Bunsen may not take more time than that of Liebig above described, though the operator must be expert at weighing, and not lose much time with the scales, or this one proceeding will take as much time as the whole of the titre analysis. As the analysis of Bunsen is not only absolutely correct, but also a beautiful conception, I have lower down given it in full; that of Ragsky being, though good, not easy of application, is omitted.

Preparation of the Solution of Mercury for precipitating Urea from Urine.

Four grammes of pure urea are first dissolved in water, and this solution is diluted with water to exactly the bulk of 200 c.c. By dissolving four grammes of urea in 200 c.c. of water, 201·75 c.c. of solution would be obtained, being 1·75 c.c. in excess.

Of the solution of nitrate of mercury, which is to serve for the purpose of precipitating urea from the urine, 20 c.c. are to be just sufficient to indicate exactly the amount of urea contained in 10 c.c. of the solution just described, namely, 200 milligrammes of urea; one cubic centimetre, therefore, of the mercurial solution must correspond with 10 milligrammes of urea. To this end, the solution of mercury must contain an amount of oxyde sufficient to produce, with 10 milligrammes of urea, the nitrate containing four equivalents of the oxyde of mercury, and further, it must contain a trifling excess of the oxyde of mercury, in order to indicate the complete precipitation of the urea. This is the case when, after the addition of the last drop of the 10 c.c. of the mercurial solution to the solution of urea, a solution of carbonate of soda produces a distinctly yellow-coloured precipitate.

According to calculation, 100 milligrammes of urea require for precipitation 720 milligrammes of the oxyde of mercury (in the form of nitrate); but in order to produce a distinct

reaction of oxyde of mercury in dilute solutions of urea, the 10 c.c. of mercurial solution necessary to precipitate the 100 milligrammes of urea must contain an excess of oxyde amounting to 52 milligrammes, or in all 772 milligrammes of oxyde. Every cubic centimetre of the solution, therefore, must contain an excess of 5·2 milligrammes of oxyde.

The simplest mode of obtaining the test-fluid is by dissolving in a beaker-glass one part of pure metallic quicksilver in five parts of nitric acid of 1·425 specific gravity, and frequently adding a little nitric acid, keeping the mixture at a gentle heat, until the evolution of vapours of nitrous acid has entirely ceased. The solution is then evaporated on the water bath until it assumes the consistence of a syrup. This syrup is then diluted with water until 100 c.c. of this dilute fluid contain exactly 7·140 grammes of mercury. This is the case, if 100 grammes of mercury, after transformation into the nitrate of the protoxyde, are dissolved in so much water that the bulk of the solution amounts to exactly 1400 c.c.

If we use for the preparation of the protoxyde the crystallized nitrate of the suboxyde of mercury, which may with greater facility be obtained pure and is more free from other metals than metallic mercury, the concentrated solution of the protoxyde obtained is of unknown strength. The quantity of protoxyde contained in it must therefore be determined; and this being done, the solution is to be diluted to the strength already stated.

There are several methods of finding the amount of protoxyde of mercury contained in a solution of the nitrate. It may be found in a direct way by diluting a known volume of the concentrated solution or syrup with ten volumes of water, and precipitating the protoxyde of 10 c.c. of this solution by the addition of potassa. Or a precipitate of the sulphide of mercury may be obtained by mixing the nitrate with a solution of sulphate of soda, and decomposing the precipitated sulphate of protoxyde of mercury by a current of sulphuretted hydrogen.

A third proceeding, which dispenses with scales, is the following:

Episode: Mode of ascertaining the amount of protoxyde of mercury contained in a solution of nitrate of mercury.— On mixing a solution of the nitrate of protoxyde of mercury with a solution of phosphate of soda, a white flocculent precipitate of phosphate of protoxyde of mercury is immediately produced, which, on being allowed to stand in the liquid, rapidly becomes crystalline.

A solution of corrosive sublimate may, however, be mixed with the alkaline phosphate, without any turbidity being produced.

If to the mixture of the two first-mentioned salts we add a solution of chloride of sodium, before the precipitate has had time to become crystalline, the latter immediately decomposes with the chloride of sodium, corrosive sublimate and phosphate of soda being produced; the precipitate disappears, and the fluid becomes perfectly clear.

This test is the basis of the following method, by which the amount of protoxyde of mercury contained in a solution of the nitrate may be ascertained with tolerable accuracy. One equivalent of phosphate of mercury requires for its redissolution one equivalent of chloride of sodium. It follows from this that if we know the amount of chloride of sodium which it has been necessary to add for redissolving the phosphate of mercury, we also know the amount of protoxyde contained in the solution of the nitrate.

As the equivalent of the chloride of sodium is only about one half of that of the protoxyde of mercury, a slight error in the addition of the chloride of sodium will be doubled in the calculation of the mercury. This analysis is therefore not so accurate as its reverse, the determination of chloride of sodium by the mercurial solution. But it is sufficiently accurate for the purpose here intended.

Episode in episode: Preparation of the standard solution of chloride of sodium to be employed in ascertaining the amount of mercury in solution.—A saturated solution of chloride of sodium is first prepared by pouring water over pure, transparent rock salt in coarse pieces, and letting it stand for solution at a temperature of from 54° to 75° F. (12·2 to 23·9°C.) If the mixture be frequently shaken it will, after the elapse of twenty-four hours, be perfectly saturated, and in every case will contain an invariable amount of salt, viz., 3·184 grammes in every 10 c.c. The solution, after decanting and filtering, is ready for use.

Of this solution we take with a pipette	20·0 c.c.
And add water . .	566·8 c.c.
Whereby we obtain of dilute solution of chloride of sodium .	586·8 c.c.

Which in all contain 6368 milligrammes of chloride of sodium, viz., the amount contained in 20 c.c. of the saturated solution. In 10 c.c. of this dilute solution there are consequently contained 108·52 milligrammes of chloride of sodium, corresponding to 200 milligrammes of protoxyde of mercury (1 c.c.

dilute solution=20 milligrammes of protoxyde of mercury). This calculation is based upon the equivalents of protoxyde of mercury=108, and chloride of sodium=58·6, which stand to each other in the same proportion as 200 of the oxyde to 108·52 of chloride of sodium.

Mode of ascertaining amount of protoxyde, &c. (continued). —In order to determine with some degree of accuracy the amount of oxyde contained in a solution of the nitrate, the latter must not be too concentrated, partly because a larger bulk admits of more accurate measurement, partly because the end of the reaction is much more perceptible in dilute than in concentrated fluids. It is therefore desirable that the mercurial solution, which is to serve for the test, should in 10 c.c. not contain more than from 180 to 200 milligrammes of protoxyde of mercury.

The following preliminary experiment is therefore made, for the purpose of ascertaining the concentration: 10·0 c.c. of the solution of chloride of sodium are mixed with 4·0 c.c. of a solution of phosphate of soda (the officinal salt) saturated at the ordinary temperature. To this mixture the mercurial solution is now poured from a burette, until a precipitate is formed which does not disappear on shaking the fluid. Let us suppose that we have used for that purpose 2·4 c.c. of the mercurial solution; they accordingly contain 200 milligrammes of oxyde; 10 c.c. of the solution therefore contain more than 800 milligrammes, when they should only contain 200 milligrammes at the outside. This solution, therefore, before the actual testing begins, must be diluted with three times its own volume of water.

Of this dilute solution of mercury we now measure 10·0 c.c. into a beaker, add 4·0 c.c. of the above-mentioned solution of phosphate of soda, and pour from a burette the graduated or standard solution of chloride of sodium into this mixture, which is kept in constant agitation, until at last the white precipitate, which is formed on addition of the phosphate to the mercurial solution, is entirely redissolved.

The addition to the mercurial fluid of the solution of phosphate of soda must be followed immediately by that of the chloride of sodium; for if we suspend the addition of the latter only for a few minutes, the phosphate of mercury becomes crystalline, and now either dissolves not at all, or with difficulty only. The solution of mercury, moreover, must not contain too much free acid. It contains the proper amount, if, after the addition of the phosphate of soda, the mixture no longer reddens litmus. If it has, however, an acid reaction, the mercurial solution must, previously to the testing, have a

part of its acidity neutralized by the addition of a few drops of a solution of carbonate of soda, until basic salt begins to be precipitated, which may be redissolved by a drop or two of dilute nitric acid.

As a matter of course the errors in this analysis are mainly due to our adding a drop or two more of the chloride of sodium than is actually required to dissolve the precipitates. The greater the quantity of solution of chloride of sodium added to a given bulk of the mercurial solution, the more oxyde this solution will appear to contain. The error, consequently, which we have just pointed out, increases the apparent real amount of oxyde contained in the solution. As the phosphate of mercury is slightly soluble in the fluid, and as, after all, the solution of chloride of sodium is graduated with regard to this error, the latter is generally very slight. If the proceeding be reversed by pouring the mercurial solution into a mixture of the solution of chloride of sodium and the alkaline phosphate, a slight excess of the mercurial solution must always be added, for the purpose of producing the precipitate, which is not permanent until the fluid has been saturated with the mercury. This proceeding, therefore, would give too low an indication of the amount of oxyde.

These analyses become still more correct, if we combine both methods, and proceed in the following manner:

(Method I.) We measure 10 c.c. of the solution of mercury into a beaker, add from 3 to 4 c.c. of the solution of phosphate of soda, and, taking care not to let the precipitate become crystalline, we immediately pour from the burette into the fluid the solution of chloride of sodium, until the precipitate has disappeared. Let us suppose that we have used for that purpose 12·5 c.c. of the solution of chloride of sodium, we now—

(Method II.) Measure 12·5 c.c. of the same solution of chloride of sodium into a beaker, add from 3 to 4 c.c. of the phosphate of soda, and pour into this mixture from a burette the amount of the same solution of mercury, which is just necessary for the production of a commencing precipitate. Let us suppose that we have used of it 10·25 c.c., then its real strength is—There have been used for

I.	10·0 c.c. of the merc. sol.	12·5 c.c. sol. of chl. of sod.
II.	10·25 c.c. ditto.	12·5 c.c. ditto.
	20·25 c.c. merc. sol.	25·0 c.c. sol. of chl. of sod.

As every c.c. of the graduated solution of chloride of sodium

indicates 20 milligrammes of oxyde of mercury, it follows that the 25 c.c. used indicate $20 \times 25 = 500$ milligrammes of oxyde, which are contained in 20·25 c.c. of mercurial solution.

In this manner has been ascertained the amount of oxyde contained in the solution (diluted with three volumes of water). I will now proceed to give the description of the other proceedings necessary for producing a solution graduated for urea.

Preparation of Mercurial Solution graduated for Urea (continued).

A known volume of the concentrated solution or syrup, in a part of which, after dilution with three volumes of water, the amount of oxyde of mercury has been ascertained, is now diluted with so much water as will bring it near to the point of concentration required for urea. The correctness of this dilution must be checked before its application for determining the amount of urea in urine, by means of the solution of pure urea mentioned above, which, in 10 c.c., contains 200 milligrammes of urea.

In diluting the concentrated mercurial solution, it is advisable not to add the whole bulk of water, which by calculation has been found necessary, all at once. It is better to add a little less water, then to test with the solution of urea, and after thus checking the correctness of the analysis, to add the rest of the water.

To recapitulate the entire proceeding :

We take 10·0 c.c. of the concentrated solution or syrup, dilute it with five or ten times its bulk of water, according to its concentration, and in 10·0 c.c. of this dilute solution we approximately ascertain the amount of oxyde by means of the phosphate of soda and the graduated solution of chloride of sodium.

Let us suppose that, for 10·0 c.c. of the solution diluted with five times its own bulk of water, we have used 18·5 c.c. of the solution of chloride of sodium, the amount of water to be added can then easily be calculated.

For 10·0 c.c. of the concentrated solution, there ought to be used 38·5 c.c. of the graduated solution of chloride of sodium (corresponding to 772 milligrammes of oxyde of mercury). We have, however, in reality used $5 \times 18{\cdot}5 = 92{\cdot}5$ c.c. of the graduated solution. If for 10·0 c.c. of the concentrated mercurial solution there are required 92·5 c.c. of the graduated solution of chloride of sodium, 4·16 c.c. of the former will

exactly be necessary to neutralize 38·5 c.c. of the latter. If therefore

416 vol. of the concentrated merc. solut. are mixed with
584 vol. of water, we obtain

1000 vol. of a dilute solution,

10·0 c.c. of which exactly correspond to 38·5 c.c. of the graduated solution of chloride of sodium.

As has been already stated, it is not advisable to add the whole amount of water (the whole 584 volumes) at once. It is better to allow a margin. We now measure 10 c.c. of the graduated solution of urea into a beaker, add from a burette the solution, which has been diluted to not quite the calculated strength, until a drop of the mixture, when brought into contact with a drop of a solution of carbonate of soda on a glass plate or a watch-glass, gives a distinct yellow reaction. In case we have used for that purpose 19·25 c.c. of the solution of mercury,

We now add, upon every	192·5	c.c. of the latter,
Water to the amount of	7·5	c.c.
Whereby we obtain a total of solution =	200·0	c.c.

We now make the final experiment with this solution.

If after the addition, to 10 c.c. of the solution of urea, of 20 c.c. of the mercurial solution, the yellow colour appears distinctly, the solution of mercury may be used for ascertaining the amount of urea in urine.

We must bestow all possible care upon the correctness of the test-fluid, as it is intended to replace the balance, which, when faulty, will make the error appear the larger, the smaller the difference of weight we wish to determine. In the case of an incorrect balance, the error may be met every time we use it—it is possible to weigh correctly with it. But a graduated fluid must be corrected once for all before use. The volume of the fluid does not increase the trouble of preparing it; and it is therefore advisable to prepare the largest possible quantity at one time.

The small excess of the oxyde of mercury in the fluid is like the hand of the balance; the yellow colour is its deflection, the amount of which must be carefully impressed upon the memory.

Analysis of Urea in Urine. Special Proceedings.

We first prepare a mixture of two volumes of baryta water, and one volume of a solution of nitrate of baryta, both saturated at the ordinary temperature. Of this alkaline fluid, one volume is mixed with two volumes of urine. For this purpose a small glass cylinder of a capacity of about 15 c.c., or any other convenient size, may be used. This cylinder is ground round the edge, so as to admit of being closed hermetically by a plate of glass. It is then twice filled with urine to overflowing, the excess being each time removed by covering it with the glass plate. The same cylinder is afterwards *once* filled in the same manner with solution of baryta, and the latter is poured on the urine in a beaker. The precipitate which forms when the two fluids mix, is removed by filtering. Of the filtered fluid, 15 c.c., corresponding to 10 c.c. of urine, are taken for each analysis.

To this volume of urine we now, without neutralizing, add from a burette the graduated solution of the nitrate of protoxyde of mercury, keeping the mixture agitated all the time, and test the mixture as soon as we perceive that no further precipitate is formed, and that the fluid does no longer become thick on the addition of the mercurial solution. For this purpose we take with a glass rod a drop out of the mixture, and add it to a drop of a solution of carbonate of soda, of which there are several in readiness on a glass plate lying on a sheet of white or black paper. If after the lapse of a few seconds the mixture of the two drops remain white, the addition of the mercurial solution must be repeated, until, on a new trial, a drop of the contents of the beaker exhibits a distinct yellow colour on being added to the drop of solution of carbonate of soda.

We now read on the scale of the burette the number of cubic centimetres of the mercurial solution used; and from this is ascertained, by the simplest calculation, the amount of urea contained in 10 c.c. of urine, and hence in the total quantity discharged in twenty-four hours.

Modification of this method required by an excess of urea in urine.—The mercurial test-fluid is graduated for a solution of urea containing 2 per cent. of this substance: 15 c.c. of the solution of urea require for precipitating the whole of the urea, and for the production of the test indicative of the completion of the precipitation, 30 c.c. of mercurial solution. We thus obtain 45 c.c. of a mixture in which on the whole there are 30 times $5{\cdot}2 = 156$ milligrammes of free protoxyde of

mercury; every cubic centimetre therefore contains 3·47 milligrammes of protoxyde of mercury.

If the 15 c.c. of solution of urea contain 4 per cent. of urea, and we add 60 c.c. of the mercurial solution, a mixture amounting to 75 c.c. is produced, in which there are contained 312 milligrammes of the oxyde of mercury, viz., 4·16 milligrammes in every cubic centimetre, being an excess of 0·69 milligrammes of protoxyde in every cubic centimetre above what is required to produce the original colour.

It has been shown by careful experiment that, in analysing urine containing a larger amount of urea, an error is committed which makes the amount of urea appear smaller than it really is. In the case just now given as an illustration, we would not add 60 c.c. of the mercurial solution for the production of the original colour, but only 59·37 c.c. In order to remove this error, we have only to make the mixture more dilute by the addition of water. As soon as we have found out that the urine contains a higher percentage of urea than the mercurial solution is graduated for—for example, if more than 30·0 c.c. of the mercurial solution are used for 15 c.c. of urine—we must, for the number of cubic centimetres of the mercurial solution above 30·0 c.c., add half the number of cubic centimetres of water *before testing with carbonate of soda.* If, for instance, we have used 20 c.c. more than 30, we add 10 c.c. of water. It will always be found that, after the addition of the water, a few more drops of the mercurial solution must be added, before the proper indication is obtained.

Modification required by the urea sinking to 1 *per cent.*—If the quantity of urea in urine amounts to 1 per cent. only, it will be necessary to add to 15 c.c. of urine not 15 c.c. only, but 15·3 c.c., which would unduly increase the apparent amount of urea. To avoid this error in working with dilute urine, we must, for every 5 c.c. of mercurial solution which have been used less than 30 c.c., subtract 0·1 c.c. from the sum of cubic centimetres actually used. If therefore for 15 c.c. of urine 25·0 c.c. of mercurial solution have been used, the *real* amount of urea being 249 milligrammes, is expressed by 24·9 c.c. of mercurial solution.

Modification required by the presence in urine of chloride of sodium.—A series of experiments has shown that, when the chloride of sodium contained in urine amounts to 1 or 1·5 per cent., it interferes with the analysis of urea by means of the mercurial solution. If to 10 c.c. of the solution of pure urea 20 c.c. of the graduated mercurial solution are added, carbonate of soda will produce a distinct yellow precipitate of protoxyde

of mercury in the mixture. If to the latter we now add from 100 to 200 milligrammes of chloride of sodium, and test again with carbonate of soda, the yellow colour will not appear, and for its reproduction will require a further addition of from 1·5 to 2·5 c.c. of the mercurial solution; which, if taken as representing urea, would increase the apparent amount of the latter by 15 to 25 milligrammes.

It is the same in urine. The chloride of sodium contained in it increases the apparent amount of urea unduly by 20 or 30 milligrammes in 10 c.c. In case the amount of chloride of sodium rises above 2 per cent., the error is not increased in proportion to the quantity, but remains the same, with certain fluctuations.

As we shall see more particularly in treating of the determination of chloride of sodium by means of the nitrate of protoxyde of mercury, a solution of urea containing chloride of sodium is not precipitated until all the chloride of sodium present is decomposed, and corrosive sublimate is formed. In a solution of 200 milligrammes of urea and 100 milligrammes of chloride of sodium in 10 c.c. of water, to which 20 c.c. of the mercurial solution have been added, the excess of the mercury, which otherwise would have given the yellow reaction on addition of carbonate of soda, is not present in the form of nitrate, but of corrosive sublimate; by the formation and presence of which, it is evident, the change in the test is caused. Instead of 3·46 milligrammes of oxyde of mercury in the form of nitrate, the mixture contains the same amount of mercury in the form of sublimate.

On diluting a solution of corrosive sublimate with water until it yields a distinct brownish-yellow precipitate of oxychloride of mercury on the addition of carbonate of soda, and on then mixing the same solution of sublimate with a drop of nitric acid, and then adding it in drops to a solution of carbonate of soda, the mixture will remain clear. No precipitate will be formed; and, if any, it consists only of a slight whitish turbidity, from which, after prolonged standing, some few brownish-yellow plates are deposited. In this condition, the excess of corrosive sublimate exists in the mixture of the solutions of urea and of mercury, the greater part of the nitric acid of which is in a free and uncombined state.

This free nitric acid converts part of the carbonate of soda into the bicarbonate, which does not precipitate corrosive sublimate. When the mixture, in consequence of a larger amount of chloride of sodium having been present in it, contains a larger amount of corrosive sublimate, the quantity of

carbonic acid set free is not sufficient to totally prevent the precipitation of protoxyde of mercury, and a brownish-yellow precipitate is produced. This appears to be the reason why the presence of a certain amount of chloride of sodium defers the indication of the complete precipitation of urea, and why a further increase in the amount of chloride of sodium does not interfere with the test after having reached a certain height.

In operating upon urine containing from 1 to 1·5 per cent. of chloride of sodium, the number of milligrammes of urea contained in 10·0 c.c. of urine may at once be correctly obtained by simply subtracting 2 c.c. from the total cubic centimetres of mercurial solution used. The results thus obtained are relatively correct as regards the differences of the amounts of urea, even when the quantity of chloride of sodium varies in the urine of different individuals. There is only a slight error in the absolute quantity of urea, which, if left uncorrected, may amount to 15 or 20 milligrammes in 10 c.c. of urine.

If, therefore, we require to know the absolute quantity of urea in urine, the chlorine must be removed from the urine, and the chloride of sodium converted into the nitrate of soda. This is done by the agency of a graduated solution of nitrate of silver. 11·601 grammes of fused nitrate of silver are dissolved in water, and diluted until the volume of the fluid amounts to 400 c.c. One cubic centimetre of this solution contains 29·01 milligrammes of nitrate of silver, corresponding to 10 milligrammes of chloride of sodium.

The solution of mercury which will be described under the head of chloride of sodium corresponds to this solution of silver. Equal volumes of both will on use indicate equal quantities of kitchen salt. If, therefore, to 10 c.c. of urine we had to add 12·5 c.c. of the mercurial solution just alluded to, for producing the turbidity indicating that all the chloride of sodium is converted, then 12·5 c.c. of the solution of silver, on being added to 10 c.c. of urine, will precipitate the whole of the chlorine without any silver being left in solution.

As, by means of the mercurial solution, we can ascertain in a few seconds how much of the solution of silver it is necessary to add to urine containing chloride of sodium, for the purpose of removing the latter, this operation, which otherwise would be laborious and take much time, is divested of all inconvenience.

Let us suppose that, for 15 c.c. of urine precipitated with the solution of baryta, corresponding to 10 c.c. of the original

urine, we have used 17·5 of the mercurial solution graduated for kitchen salt. We now measure with a pipette

30·0 c.c. of the same urine, add
35·0 c.c. of the solution of silver,

65·0 c.c.

and throw the mixture on a filter.

Of the filtered liquid we now take for the test of urea always one half of the number of cubic centimetres of the mixed fluid, viz., 32·5 c.c., in which there are contained 10c.c. of urine, less phosphates and chlorides. These are now mixed with the mercurial solution graduated for urea; and the quantity of the latter is thus ascertained, regard being always had to the dilution in consequence of the addition of the solution of silver.

Modification required by the urine containing ammonia.—For common urine, one volume of solution of baryta to two volumes of urine is generally sufficient for precipitating the whole of the phosphoric and sulphuric acid present, and leaving a small amount of baryta in solution. If, however, the urine becomes alkaline from the presence of an alkaline carbonate, which most commonly is carbonate of ammonia, from the decomposition of urea, one volume of solution of baryta to two volumes of urine is in most cases insufficient to precipitate the whole amount of carbonic acid. It therefore will be necessary to add a larger amount of the solution of baryta.

If three volumes of the solution of baryta are mixed with four volumes of urine, 17·5 c.c. of the filtered fluid, corresponding to 10 c.c. of urine, will have to be taken for the analysis of urea by precipitation. Of a mixture of equal volumes of solution of baryta and urine, 20 c.c. must be taken for the test; and so on in the same proportion.

The influence of the decomposition of urea will in many cases not prevent the same results from being obtained in putrid urine as were arrived at in the same urine when fresh. Two or three days' standing will generally make no difference; but after that, the analysis with the mercurial fluid cannot any longer be depended upon.

If exact analyses of ammoniacal urine be required, we may either fix the carbonic acid, and transform the urea present into the same acid and ammonia by subjecting a quantity of urine to Bunsen's analysis; or we must determine the ammonia and urea each by a separate process in two separate portions of urine, and calculate the amount of urea from the ammonia by which it is represented.

For the analysis of urea in this kind of urine, it is not precipitated with the mixture of solution of baryta, but with baryta water only. From the filtered fluid a portion is taken corresponding to 10 c.c. of urine, and heated in a water bath, until ammonia is no longer evolved. This expulsion of ammonia is easily effected, because, after the addition of baryta water, which, when added in sufficient quantity, combines with the whole amount of carbonic acid present, the whole amount of ammonia is contained in the form of caustic ammonia. In the fluid thus freed of ammonia, urea is determined by the mercurial fluid.

In another portion of the urine the ammonia has to be determined by one of the ordinary alkalimetrical methods. The most convenient test is dilute sulphuric acid, which may be procured by mixing 16·333 grammes of pure hydrated sulphuric acid with as much water as will raise the whole of the mixture to 500 c.c., or 1000 half c.c. Of this sulphuric acid 0·5 c.c. exactly saturate 5·66 milligrammes of ammonia, being the quantity produced by the decomposition of 10 milligrammes of urea. Every cubic centimetre of sulphuric acid, therefore, used for neutralizing the ammonia of urine, corresponds to 20 milligrammes of urea originally contained in the urine.

The analysis becomes more accurate if we subject a known quantity of urine (after treatment with baryta) to distillation, collect the product in a receiver containing a known volume of the graduated sulphuric acid, which must be more than sufficient for neutralizing the whole amount of ammonia that passes over. The quantity of free acid left is then determined by means of a dilute solution of ammonia, graduated upon the dilute and graduated sulphuric acid. If, for example, we have put into the receiver 40 c.c. of dilute sulphuric acid, and if, after partial saturation by the distillate, we yet require 15·0 c.c. of the graduated solution of ammonia for neutralizing the acid, then a quantity of ammonia has passed over by distillation which has neutralized $40 - 15 = 25$ c.c. of the graduated sulphuric acid, and represents 250 milligrammes of urea.

Modification required by the presence in urine of certain nitrogenized matters not being urea.—Besides urea some other bodies are precipitated by the solution of nitrate of protoxyde of mercury. One of them is *allantoine*, as has been shown by Dr. Limpricht.[1] It has been stated by Professor Städeler that he found allantoine in the urine of

[1] 'Annal. d. Chem. und Pharm.,' 1853, October, p. 99.

dogs labouring under difficulties of respiration. Allantoine is present in the urine of the sucking calf; but it has never as yet been found either in the normal or pathological urine of man. Even under circumstances where its occurrence was most probable, as after the ingestion into the stomach of uric acid or urate of ammonia, when the usual products of the decomposition by oxydation of that body are found in the urine, viz., urea (an excess) and oxalic acid, the third produce of the artificial process, allantoine, could not be found in the urine even by such a chemist as Wöhler.[1] We may therefore be quite safe that our analyses will not easily be made inaccurate by the presence of that body.

There are, however, some nitrogenized matters, forming an insoluble precipitate with the nitrate of mercury, which are of more frequent occurrence, particularly in the urine of patients. Kletzinsky,[2] in his comparative experiments on the value of different methods for determining the quantity of urea, found that there is a substance present in urine, which, by its property of being precipitated by a solution of sugar of lead, manifests itself as different from urea, and yet is precipitated along with urea by the mercurial solution. This substance, in five experiments made upon healthy urine, amounted to 2, 2, 3, 3, and 4 per cent. of the urea; but in the urine of patients it would rise to 12 per cent. of the urea present. Professor Vogel[3] is of opinion that the error in some cases might amount to 20 per cent. of the urea present.

This error must be avoided by the following proceeding:

Of a solution of sugar of lead, acidulated with a few drops of acetic acid, a sufficient quantity is added to urine to precipitate the whole of these nitrogenized matters. Some of them are nearly related to the colouring matter of urine, which is itself precipitated by acetate of lead. Any excess of the solution of lead must be removed by a current of sulphuretted hydrogen. After filtering, the urine may be used for the test for urea, due allowance being made for the dilution.

Bunsen's method of ascertaining the absolute quantity of urea in urine.[4]—I have already stated the principle of this accurate method. Its advantages are, that it may be used

[1] 'Annal. d. Chem. und Pharm.,' Bd. 65, pp. 340—341.
[2] Heller's 'Archiv,' 1853, p. 252.
[3] Loc. cit., p. 244.
[4] 'Annal. d. Chem. und Pharm.,' Bd. 65, p. 375.

for any description of urine, without requiring either correction or modification, as neither uric, hippuric, or benzoic acid, nor sugar, albumen, colouring or other nitrogenous matters, exert any influence over the results.

Thirty or forty grammes of urine are weighed or measured into a balloon; from 8 to 10 grammes of a very concentrated solution of chloride of barium mixed with a little ammonia are added; the balloon is closed with a cork, and the mixture is well shaken. After it has stood until the precipitate has settled to the bottom, the mixture is filtered through a filter of known weight on a funnel, the tube of which is drawn to a long, thin point. Of the clear fluid, 25 to 30 grammes are allowed to run into a strong glass tube, closed at one end, and containing about 3 grammes of solid, chemically pure chloride of barium. The weight of the tube and contents is determined before filling. The walls of this tube round the upper aperture must be kept quite dry. The weight of the urine filled into the tube is then ascertained, after which the tube is closed by the blowpipe, 1″ or 1½″ above the level of the fluid. The tube so closed is now put into an oil bath, and for three or four hours exposed to a temperature of from 428° to 468° F. (220° to 242° C.) After the tube has again cooled, it is opened by means of a file and live charcoal; the crystals of carbonate of baryta are placed on a filter, washed carefully with water which is free of carbonic acid, and, after drying, are weighed. One part of carbonate of baryta corresponds to 0·4041 of urea.

The precipitate formed on mixing the urine with the ammoniacal solution of chloride of barium, and which remained on the filter, is then also washed, dried at 212°F. (100° C.), and weighed. The weight of this precipitate, subtracted from the weight of the urine and solution of chloride of barium, gives the total weight of the fluid, of which we have put from 25 to 30 grammes into the glass tube. From the urea found in the latter, that contained in the whole or any amount of urine may be calculated.

It is shorter to precipitate the phosphates and sulphates with the mixture of solutions of baryta water (two volumes) and nitrate of baryta (one volume), as described for Liebig's method. Of the filtered fluid a known quantity by measure, say 25·0 c.c., is poured into the tube. The precipitate on the filter is left out of the question, and thereby a great deal of trouble in washing and weighing is saved. The analysis certainly is thereby made less accurate, but so trifling is the error, that it may safely be allowed to pass.

Dr. Davey's method of determining the amount of urea in urine.[1]—This method is founded on the fact that urea is very readily decomposed by the hypochlorites of soda, potash, or lime, and its constituent nitrogen is evolved in the gaseous state. From the quantity of gas evolved the amount of urea is estimated.

A strong glass tube, about twelve or fourteen inches long, closed at one end, and its open extremity ground smooth, and having the bore not larger than the thumb conveniently can cover, holding from two to three cubic inches, each divided into tenths and hundredths by graduation on the glass, is filled more than a third full of mercury, to which afterwards a measured quantity of urine to be examined is poured, which may be from a quarter of a drachm to a drachm or upwards, according to the capacity of the tube; then holding the tube in one hand near its open extremity, and having the thumb in readiness to cover the aperture, the operator fills it completely full with a solution of the hypochlorite of soda (taking care not to overflow the tube), and then instantly covers the opening tightly with the thumb, and having rapidly inverted the tube once or twice, to mix the urine with the hypochlorite, he finally opens the tube under a saturated solution of common salt in water, contained in a steady cup or small mortar. The mercury then flows out, and the solution of salt takes its place, and the mixture of urine and hypochlorite being lighter than the solution of salt, will remain in the upper part of the tube, and will therefore be prevented from descending and mixing with the fluid in the cup. A rapid disengagement of minute globules of gas soon takes place in the mixture in the upper part of the tube, and the gas is there retained and collected. The tube is then left in the upright position till there is no further appearance of minute globules of gas being formed, the time being dependent on the strength of the hypochlorite and the quantity of urea present; but the decomposition is generally completed in from three to four hours; it may, however, be left much longer, even for a day if convenient, and having set the experiment going, it requires no further attention; and when the decomposition is completed, it is only necessary to read the quantity of gas produced off the scale on the tube. In cases where great accuracy is required, due attention must be paid to the temperature and atmospheric pressure, and certain corrections made if these should deviate from the usual standards of comparison, at the time of reading off the volume of the gas; but in

[1] 'Philosophical Magazine,' June, 1854, p. 385; also 'Dublin Hospital Gazette,' June 1, 1854.

most cases sufficiently near approximations to accuracy may be obtained without reference to those particulars.

From a number of experiments, Dr. Davey has ascertained that the quantity of gas evolved from different amounts of urea, treated in the way just described, very closely approximates to the quantity of nitrogen gas which should be furnished from the urea by calculation. Thus, the fifth part of a grain of urea should furnish by calculation 0·3098 parts of a cubic inch of nitrogen gas at 60° F.° (15·5° C) and 30″ bar.; the same quantity of urea treated as described furnished in one experiment 0·3001, and in another 0·3069 parts of a cubic inch of gas at the same temperature and pressure; which shows that the calculated quantity of nitrogen differs from the amount of nitrogen gas obtained by only a few thousandths of a cubic inch.

If the relation that exists between a certain quantity of urea and nitrogen be known, we can, from the quantity of gas evolved in any case, easily calculate the amount of urea present by the simple process of rule of three. Thus the fifth part of a grain, or 0·2 of a grain of urea, gives by calculation 0·3098 parts of a cubic inch of nitrogen gas. Then 0·3098 : the volume of gas found : : 0·2 : the required quantity of urea; or, multiplying the first and third terms by 5, we have 1·549 cubic inches of gas representing one grain of urea, which is a simpler proportion.

Comparative experiments, which Dr. Davey made with his method and that of Liebig, seemed to agree very closely. In each of the following experiments one fluid ounce of urine yielded the respective quantities of urea in grains.

	Liebig's.	Davey's.
1.	3·680	3·712
2.	5·328	5·472
3.	4·976	4·976

In the first and second experiments with Liebig's test, the quantity of common salt present in the urine was taken into account, as it increases the apparent quantity of urea in the urine. In the third, this was not taken into consideration, and the quantity of urea was compared with the mean of two results obtained by Dr. Davey's method.

The hypochlorite of soda is preferable to that of potash as a decomposing agent, because the soda salt is an article of the pharmacopœia under the name "sodæ chlorinatæ liquor," and therefore can be easily procured; whereas the potash salt, not being used in medicine, would require to be specially made for the purpose. The hypochlorite of lime is not so

effectual, and has the disadvantage of soiling the sides of the graduated tube by the carbonate of lime formed in the reaction.

In reference to the quantity of hypochlorite of soda to be employed, it should always be used in excess. About five or six times the volume of the urine employed will be found generally to be quite sufficient, and ensure there being an excess of the hypochlorite. The amount required may be easily determined also by direct experiment, by adding to a certain quantity of urine to be examined in a glass, a measured quantity of the hypochlorite, and leaving it for a short time till the evolution of gas is nearly over; then if, on the addition of more of the hypochlorite, the effervescence is renewed, it shows that there was not enough of the decomposing liquor first employed, and more must be added from time to time till no further evolution of gas is produced, and the quantity of hypochlorite used to arrive at this point indicates the amount necessary. One grain of urea requires somewhere about half a fluid ounce of the ordinary sodæ chlorinatæ liquor for its complete decomposition. The amount of mercury employed should, as a general rule, be never less than the volume of gas produced; for if the volume of gas evolved be more than that of the mercury used, it will be more than that of the solution of salt, and therefore some of the mixture of urine and hypochlorite will be forced out of the tube before it is completely decomposed, and consequently some of the gas will be lost; so that, if this occur, we must repeat the experiment, using either a larger quantity of mercury, if our tube will allow, or diminishing the quantity of urine employed.

It might be supposed, on first sight, that this method would be liable to the following source of error, viz., that some of the gas would be evolved and lost during the pouring in of the hypochlorite; but this is not the case, as several seconds elapse before there is any apparent reaction or evolution of gas on mixing the hypochlorite with the urine, and there is therefore full time to perform the experiment without any loss of the gas. Dr. Davey has also ascertained that the acid reaction of the urine does not affect his method. But there are some slight sources of error connected with it, the principal one being, that ammonia, if it exist in the urine, gives rise to nitrogen gas, and therefore increases the apparent amount of urea: but the same objection holds equally in Liebig's and Ragsky's methods, the two most accurate at present known. Uric acid also is similarly affected by the hypochlorite; but it and ammonia ordinarily occur in such

small proportion in urine, that the error produced from these substances would be but trifling, and is partly corrected by taking the calculated quantity of nitrogen, which is, as has been shown, something more than that obtained from a certain quantity of urea by direct experiment.

In cases where ammonia or uric acid occur in more than ordinary quantity, these substances must be separated by the usual means employed before having recourse to this method. This object would be effected by gently heating the urine with a certain quantity of baryta water as long as the odour of ammonia is disengaged, and then filtering the solution (see p. 66).

Another source of error is that, if a solution of the hypochlorite of soda alone, or standing over mercury, be exposed to the light for several days, it will very gradually evolve a minute quantity of oxygen, which shows that in determining urea we should not allow the experiment to go on for too long a time; but, if left for a day, or even two, it will scarcely make any appreciable effect on the quantity of gas evolved in testing for urea.

The reaction which appears to take place in the process seems to be the following: The hypochlorite of soda acting on the urea gives rise to the formation of carbonic acid, water, and chloride of sodium, together with the evolution of nitrogen gas. Thus

$$\underbrace{C_2H_4N_2O_2}_{\text{Urea.}} + \underbrace{3(Cl,O.\,NaO)}_{\text{Hypochlorite of soda.}} = 2CO^2 + 4HO + 3Cl\,Na + 2\,N.$$

The nitrogen is evolved, and the carbonic acid is absorbed by some of the hypochlorite of soda in excess, which absorbs carbonic acid very quickly without evolving any other gas; and Dr. Davey failed in several experiments to detect the smallest portion of carbonic acid in the gas produced by acting on urea, though he always noticed the presence of a very minute quantity of oxygen in the nitrogen gas.

Dr. Davey has also ascertained that several of the substances found in urine during disease, as, for example, sugar, albumen, biliary and excess of urinary colouring matter, produce scarcely any effect on the results obtained by this method.

We here give the literature of other methods for ascertaining the quantity of urea in urine:

Lecanu, 'Journal de Pharm.,' vol. xvii, p. 651.—In the form of nitrate.

Heintz, 'Poggend. Ann.,' vol. lxvi, p. 114.; vol. lxviii, p. 393; *Ragsky,* 'Annal. d. Chem. und Pharm.,' vol. liv, p. 29.—In the form of (sulphate of) ammonia.

Millon, 'Compt. rend.,' vol. xxvi, p. 119.—In the form of carbonic acid and nitrogen.

Draper, 'Journ. of Pract. Chem.,' vol. lx, p. 381.

Physiological quantity of Urea.

Numerous experiments have shown that a healthy man, who lives well, discharges on an average from 30 to 40 grammes of urea in twenty-four hours, which, calculated upon one hour, gives 1·25 to 1·66 grammes. This average must of course vary a little according to the size of the individual; and in the individual it must be dependent on accidental circumstances, which will sometimes change it, and in rare instances will produce extreme maxima and minima. But for practical purposes the above figures are valuable, even though subject to the variations mentioned. It would be a much better basis for comparative researches at the bedside, if the average amount of urea could be expressed in proportion to certain units of weight of the body, say pounds or kilogrammes, or units of measure of length of body, say centimetres. But many experiments will be requisite before such a basis can with safety be given.

It would be useless here to enter into any speculation or theory on the mode and place of formation of urea in the system. We leave it undecided whether it is made in the blood, or blood-corpuscles, or in the muscles, however important the decision of these questions may be. But one great fact is undoubtedly established; namely, that as urea is the principal product of the metamorphosis in the body of nitrogenized food, the quantity of urea must stand in a direct relation to the quantity of food taken; or, if little or no food be taken, to the amount of nitrogenized component parts of the body disintegrated in the place of food. In this sense must be taken the expression that urea is the measure of dissimilation, if I may be allowed to use this term as the antithesis of assimilation. "Der Harnstoff ist das Maass des Stoffwechsels," says Bischoff. And this is so nearly true that (with a slight modification of the sentence) we may say—the amount of urea is the measure of the most important part of the change of matter in the system. The *intensity* of the change is expressed by the *amount* of urea in the urine. More urea is produced during waking, than during sleep; more during

bodily and mental exertion, than during an equal period of inactivity. A large amount of nitrogenized food taken into the stomach will increase the amount of urea above the average; a small amount of vegetable food will make it sink below the ordinary medium.

In calculating the discharge of urea with regard to time, we must take care not to lose sight of the fact that the production of a given quantity within a certain time may appear larger or smaller according to certain circumstances, which retard or facilitate the secretion of the kidneys. If the amount of fluid discharged as urine become very small, the amount of urea discharged in a given time will also be smaller too, owing no doubt to a part of the urea formed being retained in the system, particularly in the blood and muscles. If, on the contrary, the kidneys have to discharge a larger amount of water, the total quantity of urea will be raised above the average; because an amount of urea which, under ordinary circumstances, would be retained in the system for a time, is discharged with this increased bulk of water. This is the case for solids generally, and we may well say that a large quantity of water acts as a diuretic so long as there are soluble substances in the blood to be carried away with it.

Pathological indications.

If the amount of urea remain above or below the average for any length of time, so that the possibility of an accidental variation is excluded, it is a symptom of disease.

I will first consider the excess of urea. It is common in the *stadium incrementi* up to and over the acme of all acute febrile diseases, such as typhus[1] and pneumonia, &c.; and the total quantity of urea discharged in twenty-four hours may amount to 50, 60, or 80 grammes (A. Vogel), being double the amount of that discharged during health. This increase becomes a more important feature of disease, when the ingestion of nitrogenized matter falls to a minimum at the same time; in other words, because these patients have mostly no appetite, and if they have, are obliged to restrain it by the dietetic rules of their medical attendant. As soon,

[1] Dr. Alfred Vogel, Harnuntersuchungen nach Liebig's neuer Methode. Henle und Pfeufer, 'Zeitschrift für rationelle Medicin.,' Neue Folge, Band i, 1854, p. 362. Also the same author's 'Monograph on Typhus.'

For some particulars, see the review of Dr. Stromeyer's work on Typhus, in 'Assoc. Med. Journal,' 1856, p. 46.

however, as the fever has abated, the amount of urea will sink; and that the lower below the normal quantity, the less food the patients are able to take from the continuance of loss of appetite, or from the inadequacy of the organs of digestion to perform their task. But as the patients recover appetite and strength the amount of urea rises to its usual height. The same process is observed during the exacerbations of chronic disease, which in fact constitute an acute episode in the long train of symptoms. So an exacerbation of phthisis may be accompanied by urine similar to that of an attack of pneumonia, containing an excess of urea.

But in diseases which are chronic and accompanied by impaired nutrition, the amount of urea sinks below the average.

The lowest amount of urea which I have ever observed to be discharged by a patient during twenty-four hours, was 75 grains, in 200 fluid drachms of pale, faintly alkaline urine. This was from a lady suffering from an ovarian tumour, for which she had been salivated several years ago. The growth of the tumour had been arrested since that time, but an anæmiated condition of the body had established itself, against which all treatment was tried in vain.

So low an amount of urea as 75 or 90 grains in twenty-four hours generally only occurs towards the fatal end of diseases, when not only the production of urea is very limited, but also the excretory activity of the kidneys begins to become languid.

The diminution of the quantity of urea may, however, be due to the failure of the excretory activity of the kidneys only, though at the same time an excess may be produced in the system. The excess is then retained in the blood, tissues, and juices of the body, and causes the cachexia commonly known as uræmia, which, if it be true that the products of decomposition of urea, namely, ammonia and carbonic acid, are the *materies et causa morbi*, had better be called ammonæmia. When urea is retained water is also mostly retained in part, and, by its effusion into the cavities and cellular tissue, causes dropsical disease. Urea may then be detected in most secretions, excretions, exudations, and effusions. It is the same with dropsical effusions from other causes: they contain in solution an amount of urea derived from the blood, but in these cases the impairment of the excretory activity of the kidneys is a secondary symptom, and scarcely ever causes that amount of retention of urea which may lead to uræmia. And even then the kidneys may be stimulated by diuretics or by exercise, or a spontaneous rally of the system may re-

vive their excretory activity, when, with a large amount of urine, a proportionally large quantity of urea, which has been accumulated in the system, may be discharged. The amount of urea will here indicate the amount of depuration effected, just as in retention of urea the smaller amount discharged will allow us to calculate, taking the whole case into consideration, the amount produced, and, by subtraction, the amount retained in the blood.

CHAPTER IV.

URIC ACID.

Composition and History.

Symbol: $\bar{U}$. The composition of uric acid is the following for 100 parts:

Carbon	.	35·714
Hydrogen	.	1·191
Nitrogen	.	33·333
Oxygen	.	19·048
Water	.	10·714
		100·000

This gives the formula $C_5HN_2O_2+HO$, being half the formula of some authors. We adopt the formula of Gerhardt,[1] $C_{10}H_4N_4O_6+4Aq = C_{10}H_2N_4O_4, 2HO+4Aq$. We shall find this formula more convenient for explaining the composition of the urates.

Uric acid was discovered and described by Scheele[2] in 1776, as the constituent of urinary calculi. As from its properties it appeared to be an acid, Morveau[3] gave it the name of *lithic acid*. The labours of Bergmann[4], and of Fourcroy and Vauquelin,[5] are of importance in the history of this substance, as following and confirming the observations of Scheele. Fourcroy changed the name of *lithic* to that of *uric acid*, the name now universally adopted. The following is the rest of the historical literature:

Brugnatelli, 'Ann. de Chim,' vol. xxviii, p. 56.—Found oxalic acid by decomposition with NO_5.

[1] Loc. cit., p. 544.

[2] 'Kongl. Vet. Acad. Handbl.,' 1776, p. 327. Scheele's 'Chemical Essays,' p. 199.

[3] 'Encycl. Méth. de Chimie,' art. "Acides or, Lavoisier's 'Traité de Chimie,' p. 318.

[4] 'Kongl. Vet. Acad. Handbl.,' 1776, p. 333.

[5] 'Ann. de Chimie,' xvi, 63, and xxvii, 225 and 286.

Pearson, 'Philos. Transact.,' 1798. p. 15.

Gay-Lussac, 'Ann. de Chim.,' vol. xcvi., p. 53.—First elementary analysis.

Henry, 'Mem. of the Lit. and Phil. Soc. of Manchester,' 2d series, vol. ii (1813).

Bérard, 'Ann. de Chim. et de Phys.,' vol. ccxcii (1817).

Prout, 'On the nature and proximate principles of Urine,' 'Medico-Chir. Trans.,' 1817.

Kodweiss, 'Poggendorff's Annal.,' vol. xix, p. 1 (1830).

Mitscherlich, ibid. vol. xxxiii. p. 335.

Liebig, 'Annalen d. Pharm.,' vol. x, p. 47 (1834).

Chevallier and Lassaigne, 'Ann. de Chim. et de Phys.,' vol. xiii, p. 158.

Wöhler and Liebig, 'Annal. d. Pharm.,' vol. xxvi, p. 241; 'Ann. de Chim. et de Phys.,' vol. lxviii, p. 225 (1838).—The nature of uric acid and all its derivatives finally established.

Occurrence of Uric Acid, and methods of obtaining it pure.

Uric acid is a constant ingredient in urine, from which it may be obtained in crystals, and combined with bases, by cautious concentration, or by precipitation with an acid. It constitutes many sediments and urinary calculi, and pathologically is found in the blood and gouty concretions. It is found in the urinary excrements of many animals, from the common snail upwards. The urine of birds chiefly consists of urates, so that 100 kilogrammes (or parts) of guano may be made to yield (by Bensch's method [1]) $2\frac{1}{4}$ kilogrammes (or parts) of chemically pure uric acid. The excrements of serpents consist of almost pure urate of ammonia, and therefore they are the most convenient material for procuring pure uric acid. These excrements, if in large solid white pieces, command a price at present of from nine to ten shillings the pound. For obtaining pure uric acid from them, the following process is used: The excrements, after being reduced to a powder, are

[1] 'Annal d. Chem. und Pharm.,' lviii, p. 264. For other methods to obtain uric acid from calculi, excrements of pigeons, chicken, and even from human urine, see—

Böttger, 'Archiv d. Pharm.,' ix, p. 132.

Landerer, 'Journ. de Pharm.' (3), xix, p. 439.

Arppe (1853), 'Ann. d. Chem. und Pharm.,' lxxxvii, p. 237.

These methods use borax instead of caustic alkali. Arppe obtained 0·33 per cent. of pure uric acid from excrements of pigeons. (Gerhardt, loc. cit., p. 546.)

The method of Delffs is much like the one here described, *vide* 'Poggend. Annal.,' lxxxi, p. 311. Liebig and Kopp, 'Jahresbericht,' 1840, p. 408.

dissolved by means of heat in a ley of caustic potash or soda (one part of solid alkali dissolved in ten parts of water), and boiled until ammonia is no longer evolved. The solution is now filtered through paper, after which a current of carbonic acid is made to pass through it until the precipitate, which at first is jelly-like, becomes granular, and sinks to the bottom of the vessel; that is, until the fluid has become quite neutral. It is advisable to let the fluid with the precipitate stand over night. The precipitate is the acid urate of the alkali; it is put on a filter and washed with cold (iced) water, until the filtered fluid and water used for washing become turbid. This is unnecessary when white excrements of snakes, or even red calculi from man, are employed, as the precipitate is mostly perfectly white. The salt so obtained is again dissolved in the dilute alkaline ley, made boiling hot, and is then poured into dilute hydrochloric acid, which must be more than sufficient to neutralize all the alkali. Perfectly white and pure uric acid is hereby precipitated, and, after decanting, filtering, and washing, is dried. It consists of small scales, being irregular rhombic plates.

Physical properties of Uric Acid.

Uric acid, when crystallizing slowly from a solution, appears in dendritic crystals, which may sometimes attain the length of $\frac{1}{8}$ or $\frac{1}{4}$ inch, and contain 21·5 per cent. = 4 atoms of water, of which a part is given off at the ordinary temperature. On adding to the solution of a urate some hydrochloric or nitric acid, uric acid is precipitated as a jelly-like mass, which is transformed into anhydrous scales by warming the fluid.

When dry, uric acid is a white, light powder, of a satin lustre, and consists of small, delicate scales with irregular outline, the rhombic plate sometimes defined. It is destitute of taste and smell. It is nearly insoluble in cold water, sparely soluble in hot. One part of the acid requires for solution 1800 to 1900 parts of boiling water, and 14,000 to 15,000 parts of water at 68° F. (20° C.) The watery solution faintly reddens litmus paper.

Uric acid is a little more soluble in hydrochloric acid than in water. Boiling hydrochloric acid dissolves a considerable quantity of it; it crystallizes partially on cooling, and completely on evaporation of the acid. In sulphuric acid, uric acid is soluble without decomposition, and is precipitated from this solution by the addition of water.

Uric acid is insoluble in alcohol and ether.

Uric acid is with facility dissolved in a solution of the common or tribasic phosphate of soda, as also in solutions of many other salts of the alkalies, particularly in higher temperatures. In these cases uric acid combines with part of the base, and thereby gives rise to the formation of acid salts, which impart to the solution an acid reaction. Of these processes we shall have to speak when treating of the sediments.

Crystallography.

The most perfect and pure crystals of uric acid that can be obtained are oblong square plates; and if it were not for the combinations, the plates themselves would pass as rectangular and quadratic, but in fact they are rhombic plates with extremely obtuse angles. A secondary prism may take off the angles of the primary plate (plate or scale being only another expression for flat prism, or prism in which only two axes are developed). When the secondary prism begins to predominate, we have an hexagonal plate. In this form uric acid is frequently obtained in precipitating it with acetic acid from its ammoniacal solution. In this form it also crystallizes from its solution in hydrochloric acid. Plate I, fig. 5 and 6.

In many cases the one pair of opposite angles of a plate become more acute, the other more obtuse; and plates may be observed varying from the rectangular form to that of needles. To these elementary forms all the crystals of uric acid occurring either in the form of spontaneous deposits in the urine or as products of a chemical process may be referred.

Occasionally twin crystals, composed of two rhombic plates crossing at right angles, or at an angle of 45°, are observed. There is another multiplication of spinous crystals imitating the square plate, or placed upon the square plate. This modification is usually large, and frequently obtained from urine by the addition of nitric acid.

The reader being thus in possession of the regular forms is enabled to classify all the irregularities usually occurring in spontaneous deposits. He will at a glance be able to put each of the forms in figure 1 on Plate II in its proper place.

The common rhombic plates of uric acid deposits, when formed rather quickly round another substance, such as granules of urates, present holes in their substance, and irregularities, such as usually attend a hasty formation. The obtuse angles frequently become rounded off, less frequently the pointed angles. In both cases the rhombic plates become

oval. This rounding off of the obtuse angles is characteristic of the so-called lozenges.

It would be useless to describe all the varieties of crystallization in which uric acid deposits may occur. If the reader is once acquainted with the types, he will have no difficulty in classing any deposit that may occur to him. As yet no rule has been found according to which one or the other of the varieties of crystals is formed. Concentration and temperature of the urine, the relative quantities of its ingredients, particularly the absence or presence of colouring matter, and its amount, the nature and quantity of the acid by which uric acid is precipitated, determine the nature of the crystallization. It is the same in producing crystals artificially. If the urine be kept in a warm place for that purpose, the crystals will be the largest that can be obtained by any means. I have obtained crystals one quarter of an inch in length.

Uric acid has the property of polarizing light. The large plates obtained artificially polarize only faintly, as they are invariably covered with a sort of dew. But the more transparent the crystals become, the more beautiful will be the colours they exhibit under polarized light. Crystals obtained from urine by acetic acid and from a solution in hydrochloric acid are particularly suited for the experiment on polarization.

Metamorphoses of Uric Acid by different agents.

Under the influence of heat, uric acid is decomposed without being fused. By dry distillation, a sublimate is obtained, consisting of cyanuric acid, urea, carbonate of ammonia, and cyanide of ammonium. At the same time a great deal of hydrocyanic acid escapes, and some carbon remains behind, which is porous and contains nitrogen.

Concentrated nitric acid (4 parts of 1·42 specific gravity) dissolves uric acid (1 part) under effervescence, carbonic acid and nitrogen being disengaged. The reaction consists in the formation of alloxan, urea, and nitrous acid; the latter decomposing urea, in the moment of formation, into carbonic acid and nitrogen (*vide* Urea, p. 46). Alloxan remains in large colourless rhombic octahedra, which are disintegrated under the influence of air, and are readily soluble in water. The solution reddens litmus paper, and imparts a purple colour to the skin.

On dissolving uric acid in dilute nitric acid, alloxantine is obtained, which is distinguished by producing a purple reaction, when ammonia is added to its warm solution.

This colour is due to the formation of murexide, otherwise known under the name of purpurate of ammonia. This reaction is diagnostic of uric acid.

On making uric acid and water into a pap and gradually adding peroxyde of lead, and keeping the mixture near the boiling point, the lead is transformed into the oxalate of lead, carbonic acid is evolved with effervescence, and the filtered fluid deposits crystals of allantoine on cooling. The mother-liquor yields urea.

This reaction consists in the first instance in the transformation of uric acid into allantoine, carbonate of lead being formed. Part of the allantoine is further decomposed into urea and oxalic acid.

$$\underbrace{C_{10}H_4N_4O_6}_{\text{Uric acid.}} + \underbrace{2HO}_{\text{Water.}} + \underbrace{2PbO_2}_{\text{Peroxyde of lead.}} = \underbrace{C_8H_6N_4O_6}_{\text{Allantoine.}} + \underbrace{2(PbO,\ CO_2)}_{\text{Carbonate of lead.}}$$

$$\underbrace{C_8H_6N_4O_6}_{\text{Allantoine.}} + \underbrace{2HO}_{\text{Water.}} + \underbrace{2PbO_2}_{\text{Peroxyde of lead}} = \underbrace{2(C_2H_4N_2O_2)}_{\text{Urea.}} + \underbrace{2(PbO,\ C_2O_3)}_{\text{Oxalate of lead.}}$$

All substances derived from uric acid may be transmuted either into urea and oxalic acid, or into urea and mesoxalic acid. This has led to the assumption of three radicals in uric acid, of which the one, Cy (cyanogen), is the radical of urea; the second one, C_2O_2 (oxalyl), the radical of oxalic acid; and the third, C_3O_3 (mesoxalyl), of mesoxalic acid. Upon this basis the derivates of uric acid have been grouped by Gerhardt[1] as follows:

Uric Acid Group.

a. Cyan-mesoxalic acid sub-group.	*b*. Cyan-oxalic acid sub-group.
Uric acid.	
Alloxan.	Parabanic acid.
Dialuric acid, Alloxantine } Hydrogenized Alloxan.	
	Allantoine.
Mesoxalic acid.	Oxalic acid.
Urea.	

[1] Loc. cit., p. 544.

It will be found useful to have mentioned these relations, as we shall have to explain several phenomena on their basis.

Determination of Uric Acid in Urine.[1]

On adding to the solution of any urate, either hydrochloric, nitric, or acetic acid, uric acid is precipitated. If the solution of the urate is concentrated, the precipitate will fall immediately, and consists of amorphous hydrated uric acid, becoming crystalline by heat or standing. But if the solution is dilute, no immediate precipitate is formed, but crystals of uric acid form after some (twenty-four to forty-eight) hours of standing; and they will be the larger in proportion to the time required for their formation.

To obtain, therefore, uric acid from urine, it is precipitated by the addition of an acid, no matter whether the urine is normal, or contains sugar, albumen, or any of the soluble constituents of blood.[2] If the urine be normal, and contain no albumen, nitric acid is best used, and the urine is allowed to stand in a warm place, a sand-bath, or any warm corner. A temperature of 98° F. (36·67° C.) has, moreover, the advantage of not admitting the precipitation of any urates, which are not easily acted upon by the dilute acid. The crystals formed in higher temperatures are much larger, and therefore much easier to be collected, than those produced at the ordinary temperature. A quantitative analysis, therefore, has better chances of accuracy in this way. I do not recommend hydrochloric acid for precipitating, because, uric acid being more soluble in it than in water, the analysis becomes incorrect. In some instances (for example a case of chronic rheumatism) I have obtained no definable precipitate by hydrochloric acid in a sample of the same urine, in which nitric acid produced a number of large plates on the surface of the fluid and the sides of the glass. Moreover, hydrochloric acid favours the acid fermentation and development of certain descriptions of confervoid vegetations, which act as yeast-cells on the urates, decomposing them very rapidly. This process is entirely prevented by nitric acid. If the urine contain

[1] Heintz, 'Poggend. Ann.,' lxx, p. 122. Lehmann, 'Journ. für Pract. Chem.,' xxv, p. 17; 'Lehrb. der Physiol. Chem.,' 1853, i, p. 197. Demonstration of Uric Acid, *vide* E. v. Gorup-Besanez, 'Anleit. zur Zoochem. Analyse,' 1854, 2d edit., p. 186.

[2] Gerhardt, loc cit., p. 548.

albumen, acetic acid, or the common phosphoric acid, are best used. The crystallization of uric acid may be said to be completed when all the crystals are of nearly uniform size. But as we possess no other indication on this point, the acidulated fluid must be allowed to stand rather longer, to make sure of a perfect precipitation. The crystals are collected into a deposit, washed by decanting, and collected on a filter.

It has been estimated by Heintz that the loss incurred by the imperfect insolubility in acidulated urine of uric acid amounts to 9 parts in 100,000 of the urine used for the analysis, and that this loss is not increased by the presence of sugar, albumen, or the soluble constituents of blood. In all cases this loss is compensated by a certain amount of red or brownish colouring matter, which is mechanically but intimately adherent to the particles composing the crystals. If the urine contain bile, the uric acid crystals may contain so much colouring matter, that it may be necessary to purify them of it. This result is best obtained by the following method of Lehmann:

The urine is evaporated to the consistence of a syrup, which is extracted with alcohol. The insoluble part is treated with a dilute solution of caustic potash; the solution so obtained is made boiling hot, and precipitated by acetic acid, when all the uric acid falls down in a pure state. It is freed from the adherent impure fluid by washing with water containing some acetic acid. To the weight of the uric acid so obtained, the above estimated loss must be added. In speaking of quantities it may be as well to mention that, for the quantitative analysis by precipitation, a measured quantity of urine of not less than 100 c.c., or better, 150 c.c., is necessary. To this in a beaker are added 5 per cent. of the ordinary acids. For this method it is moreover, from obvious reasons, advisable not to use urine of a very low specific gravity; but if the latter be less than 1012, to concentrate the fluid by evaporation on the water-bath to about the normal average specific gravity. For the method of Lehmann, about 50 c.c. of urine will be sufficient to give tolerable results; though here, as everywhere, the relative loss diminishes in proportion to the increase in the quantities operated on.

The precipitate of uric acid obtained by either method, after being collected on a filter of known weight, and there once more washed with water acidulated with acetic acid, is now dried in the hot-water bath. When dry, it is placed between two watch-glasses, fitting closely to each other by ground edges, and held together by brass clips made for that

purpose. This apparatus is now placed over sulphuric acid until cool; its weight and that of the filter being known beforehand, the increase in weight is the weight of the uric acid on the filter, being the amount of uric acid contained in the amount of urine employed.

Volumetrical Analysis for Uric Acid.

This analysis has been introduced by Dr. Scholz, of Blankenburg-am-Harz, and is described at page 365 of Dr. Mohr's treatise.

Uric acid in an acid solution may be oxydized by a solution of permanganate of potash just as easily as the salts of the suboxyde of iron. Urea has no influence upon the permanganate, and cannot be oxydized any further in this manner. Creatine discolours a solution of permanganate of potash or chamæleon only after some time and in a higher temperature. Uræmatine has some influence upon chamæleon. In order to find and determine the equivalent of chamæleon for uric acid, the following experiments were made with a solution of chamæleon, the titre of which was: 1 cubic centimetre of solution of chamæleon = 0·045603 grammes of ammonio-sulphate of suboxyde of iron. (This salt I shall hereafter describe under the name of the double salt of iron.)

I. 0·204 grammes of crystallized air-dry uric acid were dissolved in caustic potash, and the solution was over-saturated with sulphuric acid. This solution required 23·9 c.c. of chamæleon = 1·0899 grammes of doublesalt of iron.

Doublesalt of iron × 0·18717 = uric acid.

II. 0·102 grammes of uric acid required 12·1 c.c. of chamæleon = 0·55179 grammes of doublesalt of iron.

Doublesalt of iron × 0·18489 = uric acid.

III. 0·323 grammes of uric acid required 36·9 c.c. of chamæleon = 1·6827 grammes of doublesalt of iron.

Doublesalt of iron × 0·19194 = uric acid.

IV. 0·398 grammes of uric acid required 46 c.c. of chamæleon = 1·6827 grammes of doublesalt.

Doublesalt of iron × 0·18972 = uric acid.

V. 0·278 grammes of uric acid = 32·1 c.c. of chamæleon = 1·4638 grammes of doublesalt.

Doublesalt of iron × 0·18990 = uric acid.

Leaving the second experiment, in which the quantity of

uric acid employed was too small, the average of the four other experiments is:

Doublesalt of iron × 0·18968 = crystallized uric acid.

The equivalent of crystallized uric acid is 186, which divided by the multiplicator 0·18968, gives 980·59 doublesalt of iron. 186 parts of uric acid, therefore, take up as much oxygen as 980·59 parts of doublesalt of iron. Two equivalents, or 392 parts of the latter, take one equivalent or 8 parts of oxygen, consequently,

$$392 : 8 = 980{\cdot}59 : x\,;\ x = 20{\cdot}012.$$

186 parts of uric acid, therefore, take 20·012 parts of oxygen, which is so little more than 20, that we can, without hesitation, assume the latter figure as correct. 20 parts are two and a half equivalents of oxygen, which would be taken by one equivalent of uric acid, or two equivalents of uric acid would take five equivalents of oxygen. If from 20 backwards we attempt the correction of the empirical figure 0·18968, we find

$$8 : 20 = 392 : 980, \text{ and } \frac{186}{980} = 0{\cdot}1897958,$$

which is very nearly = 0·19, instead of the empirical value 0·18968, which is also very nearly = 0·19.

Uric acid, in the form of a precipitate, is only slowly oxydized by solution of chamæleon. It is best to dissolve it in caustic potash, and after dilution to mix it with an excess of sulphuric acid. In that way uric acid is precipitated so slowly that it remains in solution during the experiment.

If 300 c.c. of urine are mixed with 5 c.c. of sulphuric acid, and allowed to stand for a few days, the uric acid is precipitated. We know already that this precipitate contains extraneous matters, uræmatine, which very nearly makes up for the loss of uric acid, from its imperfect insolubility in the acidified urine. The following experiments show these different relations quantitatively:

0·165 grammes of uric acid were dissolved in 300 c.c. of water by the aid of some caustic potash, and then precipitated by means of sulphuric acid and standing in the cold. 200 c.c. of the fluid were removed from over the precipitate and tested by means of chamæleon. They required 0·9 c.c. of chamæleon, which is equal to 0·00778 grammes of uric acid. This indicates that one part of uric acid is soluble in 25,707 parts of the acid fluid.

The precipitate of uric acid obtained was again dissolved

in caustic potash, the solution diluted to 300 c.c., and acidulated by means of 5 c.c. of sulphuric acid. 200 c.c. of the fluid, supernatant to the precipitate, again required 0·9 c.c. of chamæleon. In another experiment, 300 c.c. of the supernatant fluid saturated 1·4 c.c. of chamæleon. These results are sufficiently uniform.

In order to ascertain the amount of colouring matter which is inclosed in the crystals of a precipitate of uric acid from urine, 300 c.c. of urine were treated with 5 c.c. of sulphuric acid, and allowed to stand for twenty-four hours; the entire deposit required 36·3 c.c. of chamæleon. An equal quantity of urine was precipitated by sulphuric acid, the precipitate dissolved in caustic potash, diluted to 300 c.c., precipitated with sulphuric acid, and 200 c.c. of the supernatant fluid were tested with chamæleon. Of the latter there were required 2·6 c.c.; the entire 300 c.c. of fluid, therefore, would have required 3·9 c.c. of chamæleon. If we deduct of this 1·4 c.c., which were required for 300 c.c. of fluid, from a precipitation of pure uric acid, there remain 2·5 c.c. of chamæleon for the matters not being uric acid contained in the first uric acid precipitate from urine.

The second precipitate of uric acid was yet somewhat coloured, and, on repetition of the analysis, the chamæleon indicated foreign matters, not being uric acid, to the value of 1 c.c. of the solution. The supernatant fluid, from a fourth resolution and precipitation of the same uric acid only required as much chamæleon as the supernatant fluid from pure uric acid.

The total quantity of matters, not being uric acid, contained in the uric acid precipitate, amounted to about one tenth part of the whole. Put against this the loss from the imperfect insolubility, the excess becomes so very much reduced, that it is unnecessary to make any correction of the rough result found, and we may assume the two errors balancing each other, as we have done in the analysis of uric acid by weight.

In some cases the amount of foreign matter precipitated with uric acid may amount to one fifth of the entire precipitate. In this direction further researches are necessary.

Salts of Uric Acid—Urates.[1]

As uric acid is a bibasic acid, there are two different kinds of urates, the neutral and the acid salts. Of these, only the latter occur in urine, one equivalent of base being replaced by

[1] A. Bensch, 'Ann. d. Chem. und Pharm.,' liv, p. 189. Allen and Bensch, ibid., lxv, p. 181.

one equivalent of water, according to the following formula. M = metal.

$$C_{10}H_2N_4O_4\begin{matrix}MO\\HO\end{matrix}\} = C_{10}H_3MN_4O_6 \text{ (Gerhardt).}$$

All urates are either insoluble or only slightly soluble in water.

Urate of ammonia. $C_{10}H_3(NH_4)N_4O_6$.—This salt is always produced when uric acid and ammonia are allowed to act upon each other. When pure and dry it is a white amorphous mass, perfectly soluble in water, one part, however, requiring for solution 1608 parts of water at 77° F. (25° C.)

Some authors state that urate of ammonia requires 2789 parts of urine for solution, and that the solubility is increased by the presence of a moderate quantity of saline matter. The solvent power of urine for urate of ammonia should be equal to that of pure water. But as no urine is quite free from urate of ammonia, and the latter cannot be separated without destroying the character of the former, it is very difficult, nay impossible, to determine the solvent power of urine for urate of ammonia, the more so as it is next to impossible, for practical purposes at least, to separate urate of ammonia from urate of soda. To saturate urine with urate of ammonia, and afterwards find the amount dissolved, is as yet an unsafe proceeding, because various causes may tend to increase the amount of ammonia found, which would have to be placed to the account of uric acid.

It may be obtained in small delicate needles by treating uric acid in boiling water with an excess of ammonia, or by dissolving uric acid in a warm solution of ammonio-phosphate of soda, and allowing the crystals to separate by rest. In the latter case, the needles are united in groups, irregular or regular, presenting a star-like arrangement round a globule. The presence of urine prevents this form of crystallization. When crystallizing out of a solution in ammonia, it forms roundish, oval, or dumb-bell-like masses of a radiated structure and polarizing. This form is met with in the urine of birds. When appearing as a precipitate in alkaline (ammoniacal) urine, it forms very slender dumb-bells.[1] This form I have met with in perfectly black alkaline urine from a child suffering from dropsy after scarlatina. It was mixed with

[1] Prout, 'On Stomach and Urinary Diseases,' 3d ed., pl. i, fig. 4. Ibid., i, figures of urate of NH_3, as it occurs in the alkaline urine of hemiplegic, or paraplegic patients. v. Funke, 'Atlas,' taf. xiii, figs. 5 and 6.

rosettes and hexagonal plates of urate of soda, the deposit being perfectly black after filtration.

Urate of ammonia has, in a few instances of albuminous urine in dropsy after scarlatina, been observed in the form of spherules, with crystals of uric acid adhering to their surface. This appearance is illustrated in fig. 25 of Dr. G. Bird's work. I have succeeded in producing this deposit artificially. A patient having contracted a severe cold by exposure to rain and cold in one of our fashionable public gardens, discharged a large amount of perfectly white urate of ammonia in her urine, which was acid and of yellow colour. I allowed the deposit to subside towards the bottom of the vessel, and after having decanted the supernatant urine, redissolved the deposit by the application of heat. A concentrated solution of urate of ammonia in urine being so procured, some hydrochloric acid was added, and the mixture allowed to cool. A copious precipitate of spherules and granules of urate of ammonia soon formed, from the surface of most of which prisms and needles of uric acid began to crystallize. Under the continued influence of the acid, however, all the globules and granules of urate of ammonia were transformed into crystallized uric acid, the crystallization beginning with the formation of minute prisms, which gradually became larger and longer. The round and irregular bodies of urate of ammonia polarized faintly.

As a general rule, urate of ammonia, when occurring as a deposit, forms a dark, granular, perfectly amorphous precipitate. (Pl. III, fig. 2.) The granules may adhere to linear masses, or appear to form sausage-like bodies; the latter appearance is easily produced by rolling the thin glass cover of the object a few times to and fro, and has been erroneously described as a peculiar agglomeration of the urate.

To the naked eye these deposits of urate of ammonia appear as a subtle powder, varying in colour from absolute whiteness, through rose-colour, pink, brick-red, purple, and brownish-red. These colours are best observed after the deposit is collected on a filter.

The colour of urate of ammonia and of urates generally is caused by the adhesion to its particles of an abnormal colouring matter, urerythrine, Dr. G. Bird's purpurine. For this it has so great an attraction, that it may be used for separating urerythrine by dissolving, with the assistance of heat, repeated quantities of urate of ammonia, which, on cooling, will precipitate, carrying the urerythrine with them.

In diseases most commonly met with, the brick-red or pale fawn-coloured, so-called lateritious sediment is almost

always mixed with the urate of soda, or uric acid, or urate of lime and magnesia. When burnt on platinum foil, there remains a white ash, containing soda and lime; the former demonstrated by imparting a yellow colour to the flame of the blowpipe, the latter by being soluble in acetic acid and precipitated by oxalic acid.

The chemical characters of this substance are not less marked than the microscopic. It is rarely observed in urine until after it has cooled, a circumstance which makes it very difficult to explain how urate of ammonia can possibly form the nucleus of a concretion. It readily disappears when the urine is raised to the temperature at which it left the body, or when the urine is diluted with water. It is soluble in liquor ammoniæ and liquor potassæ, from which solutions uric acid is precipitated by the addition of acetic acid. When the sediment is brought into contact with acetic acid or hydrochloric acid, it is slowly transformed into uric acid crystals, ammonia entering into combination with the acid and forming a soluble salt. The dry deposit gives with nitric acid the characteristic reaction of murexide.

Urate of soda. $C_{10}H_3NaN_4O_6$.—This salt may be obtained artificially, either by dissolving uric acid in caustic soda, and precipitating it by a current of carbonic acid, or by mixing the boiling caustic solution with bicarbonate of soda. In the latter case the urate is formed in delicate needle-shaped crystals. Occurrence: in the urine, dissolved and as sediment; in the blood during gout; in the gouty concretions near the joints.

It is soluble in 123 to 125 parts of boiling water, and requires 1100 to 1200 parts of water of 77° F. (25° C.) The solution is neutral, does not absorb carbonic acid; a precipitate is produced in it by the bicarbonates of the alkalies, and by the salts of baryta, lead, and silver.

Crystallization.—Urate of soda forms short hexagonal prisms, or thick six-sided plates, frequently uniting and forming star-like groups:[1] the two opposite angles of these plates measure 74° 50′, the four angles between these two 142° 35′ (Gorup-Besanez, p. 185). In this form it is met with in urine undergoing the process of alkaline fermentation. The artificial salts, as obtained by the above process, or from the blood, form needles. If obtained by digesting pure uric acid in a hot solution of common phosphate of soda, it crys-

[1] See also Dr. Golding Bird, loc. cit., p. 139, fig. 29. Funke, 'Atlas, taf. iv, fig. 4.

tallizes in needles, tufts, stars, spindle-like figures, and prisms, when it is allowed to separate from the solution on cooling. But if a solution of urate of soda be allowed to evaporate spontaneously, the salt is deposited in simple spherical masses and granules.

Dr. Golding Bird met with the urate of soda in the urine of persons labouring under fever, who were treated with carbonate of soda. It occurred in round, yellowish or white, opaque masses, furnished with projecting, generally curved processes.[1] I have observed the same deposit of an extremely striking character (Pl. II, fig. 3,) in the urine of a child suffering from petechial typhus, who was not treated with the carbonate of soda. The details of this case will be given under the paragraph, *Deposits of Urates occurring in the urinary passages*, p. 101. The same deposit occasionally occurs in the urine of children labouring under measles or scarlet fever.

Urate of lime. $C_{10}H_3CaN_4O_6+2Aq$—This salt occurs occasionally in traces and small quantities in the urine, in sediments, and in concretions, particularly the gouty tumours near joints.

It may be obtained artificially, by mixing a solution of chloride of calcium with a boiling solution of urate of potash or soda. From this mixture it forms as an amorphous precipitate. If the urate employed have been a little alkaline, warty groups of needles are sometimes obtained. It is sparingly soluble in water, requiring 603 parts of cold and 276 parts of boiling water for solution. Its solubility becomes, however, increased by the presence of a small amount of chloride of potassium.

On combustion it leaves carbonate of lime, or caustic lime. On being digested in acetic acid, this salt is destroyed, uric acid being set free; from the acetate of lime, the base may be precipitated by oxalate of ammonia.

Differential diagnosis of urates.—As uric acid is readily set free by stronger acids, its presence is easily enough ascertained. The bases offer little difficulty to analysis, if they occur separately; but if they are mixed, as is mostly the case, the analysis becomes very complicated. It is for this reason that we do not know as yet whether the fixed or the volatile alkali is more commonly combined with uric acid. The question being moreover of no great practical importance, some time will probably elapse before it is finally settled.

[1] See his fig. 28.

Urate of ammonia.	Urate of soda.	Urate of lime.
When heated in a solution of caustic potash or soda, ammonia is evolved. No ash is left on combustion.	When heated in a solution of caustic potash *no* ammonia is evolved. On combustion it leaves a white ash behind, which blues red litmus paper, and effervesces with acids (carbonate of soda). The solution in acetic acid is not precipitated by oxalic acid.	No ammonia with potash. On combustion, leaves a white ash, which may be alkaline and effervescent. Its solution in acetic acid is precipitated by oxalate of ammonia.

If a sediment simply filtered from the urine be taken for analysis, an ash is always obtained on combustion. For the epithelia from the kidneys and urinary passages, and the mucus from the bladder contain alkali and lime; and as they are mixed with the deposit, and burnt with it, they are placed to the account of the uric acid. In all cases, therefore, it is necessary to redissolve the deposit in the urine by the application of heat, and to filter, when all organized particles, with the mucus and uric acid crystals, will remain on the filter. On cooling, the deposit will form again, and may now by filtration be obtained free from admixtures. But colouring matter, containing iron, still adheres to the urate; and however small the amount may be, it would leave a residue on combustion. This colouring matter must therefore be removed by washing the deposit on the filter with boiling alcohol.

If there is more deposit in urine than it will dissolve on the application of heat, which is sometimes the case where the deposit has come ready formed from the bladder, it becomes necessary either to dilute the urine until the deposit is dissolved, to filter it while hot, and to evaporate again to the former bulk, or to filter the urine cold, and then dissolve the urates on the filter by the assistance of hot water. This latter solution may then be kept separate, and on evaporation will leave the urates in a pure state.

Under all circumstances, the deposits of urates may be collected on a filter, washed with alcohol, dissolved in boiling water and filtered; the filtered liquid after evaporation leaves the pure urates.

To determine the urates dissolved in urine, the latter must be evaporated to dryness, and extracted with alcohol; the residue consists of uric acid, urates, and inorganic salts. The urates, which form part of the scum of urine while it is

evaporating, appear as spherical masses, with many spicula protruding from their surfaces. These bodies frequently lie in a film of phosphate of lime and magnesia. When urine is evaporating spontaneously, similar forms are frequently seen. In a concentrated urine from fever, urates formed on spontaneous evaporation which exactly resembled the fig. 28[1] of Dr. G. Bird's work. Hot water dissolves the urates and inorganic salts from the residue obtained after extraction. If the solution be now concentrated, and cooled down, a part of the urates will precipitate, after which they may be collected on a filter, washed, and analysed with regard to their proportions of bases. From the urates in solution with the inorganic salts the uric acid is obtained by the admixture of another acid, and from the composition of the first portion of the urates the amount of the bases which were combined with this uric acid may be calculated.

Amount of Uric Acid discharged during twenty-four hours.

Uric acid being a normal, *i. e.*, a constant ingredient of urine, there is reason to expect that its amount may stand in a certain proportion to the ingesta and the organic changes. But mere reflection on the nature of uric acid, on its relations to urea, uric oxyde, and hypoxanthine, or its occurrence or absence in certain animals and classes of animals, on the mode in which its occurrence and amount in animals is influenced by various conditions, natural or artificial—cannot supply the want of direct observation on this point, however valuable may be the suggestions derived therefrom. The number of direct observations is very small, as compared with the number of attempts to supply this want hypothetically by observations on lower animals. And of the existing observations a great number are entirely useless, because they refer only to 1000 parts of urine, with no regard to the time in which it was discharged. Some otherwise valuable analyses have been executed upon abnormal subjects, as those of Lehmann upon himself. The only really useful series of analyses we possess are those of Becquerel[2] and Neubauer[3]. According to the former, the medium amount of uric acid discharged during twenty-four hours is 0·49 to 0·56 grammes. Neubauer obtained the following results in a series of observations on two healthy individuals—

[1] *Vide* Beale, loc. cit., p. 213.
[2] 'Séméiotique des Urines,' Paris, 1841, p. 44.
[3] Vogel, loc. cit., p. 249.

	Minimum.	Medium.	Maximum.
First Individual.	Grammes	Grammes	Grammes
First series, 5 days. Living usual . .	0·02	0·28	0·61
Second series, 5 days. Ditto, and taking warm bath of thirty minutes' duration, at 82° F. .	0·36	0·44	0·53
Third series, 7 days. Ditto, daily bath, and drinking 500 c.c. of Kochbrunnen, Wiesbaden . . .	0·13	0·27	0·50
Second Individual.			
First series, 8 days. Living usual . .	0·33	0·49	0·67
Second series, 5 days. Living as above (2d ser.)	0·46	0·60	0·81
Third series, 8 days. „ „ (3d ser.)	0·31	0·51	0·67

Lehmann found that he discharged on an average 1·18 grammes of uric acid during twenty-four hours. As he himself supposes this to be an *abnormal* quantity, we must leave the observation out of consideration at present, since we are engaged in determining the *normal* quantity.

Considering the very limited number of observations, the following quantities of uric acid for twenty-four hours may be said to be within the range of perfect health:

Minimum.	Medium.[1]	Maximum.
0·02 grammes.	0·5 grammes.	1·0 grammes.

The fluctuations of uric acid in health are therefore more considerable than those of any other constituent of urine, not only in the same individual during so short a period as five days, as shown by Neubauer's first series of observations on the first individual, but the averages of different individuals show considerable variations, for which an ample allowance must be made, before in any given case the amount discharged can be said to be abnormal; viz., below or above the average. The 1·18 grammes of Lehmann is clearly abnormal, as is also his average amount of urea.[2] The idiosyncrasy of this experimenter is most probably a large appetite.

The relations of urea to uric acid are intimate; their quantities are in certain proportions. For 35·0 grammes of

[1] Dr. G. Bird's medium is 8·1 grains of uric acid during twenty-four hours, which is very nearly the above medium, which is 7·72 grains.

[2] *Vide* Dr. G. Bird, loc. cit., p. 7, and Simon's 'Beiträge zur Physiol. und Pathol. Chemie und Microscopie,' Berlin, 1843, B. i, p. 190.

urea secreted in twenty-four hours, 0·5 grammes of uric acid are on an average discharged in the same period. Whether the fluctuations in the quantities of both are parallel or not, has yet to be ascertained. In disease this seems to be the case, as will presently be shown.

Pathological changes in the quantity of Uric Acid discharged during twenty-four hours.

As a question clearly put is half the answer, we may be permitted here to consider what proximate conditions of the system a rise or fall in the quantity of uric acid beyond the normal limits is likely to indicate. A deficiency may be due to a diminished production in the system, as in anæmia, or to retention, as in certain stages of gout[1] and rheumatism. It is at least questionable whether the retention is *always* due to diseased action of the kidney. Any disease, however, which interferes with the secreting power of the kidney by changing its structure, such as Bright's disease, is certain to cause retention of uric acid in the blood, in proportion to the retention of the other constituents of urine. (Scarlatina seems to make an exception. I have certainly found that, in some cases of this disease, where uric acid is frequently present in excess from the beginning, so as to be precipitated in a cloud by the addition of an acid, the amount of uric acid does not decrease parallel to the fall of urea, when, with albuminous urine, dropsy appears; but it seems to be the normal amount, nay even more, at a time when the amount of urea is about half the normal average. Hundreds of observations will, however, be necessary to establish whether such a process is the rule or the exception.)

An excess of uric acid may be due to excessive production in the body, particularly when the increased excretion lasts for a certain time. It may, however, be owing to the discharge of accumulated uric acid, after retention in the blood. In both cases, the symptoms accompanying or preceding the excessive excretion must be our guides in distinguishing between these conditions.

As a general rule, *i. e.*, one liable to exceptions, it may be assumed that an excessive production of uric acid accompanies an excess in the production of urea. In inflammatory diseases, fever, and certain other zymotic diseases, an increased amount of uric acid is met with. The observations, however,

[1] 'Med.-Chir. Transact.,' vol. xxx, p. 186.

require to be reduced to figures, and repeated with special regard to time.[1]

The following observations of Becquerel are entitled to attention, as referring to the total quantities of uric acid discharged in twenty-four hours:

Healthy urine (*B*'s average)	8·1 grains.
Chlorosis, five cases	min. 1·8 max. 6·0 grains.
Pulmonary emphysema, ext. dyspnœa	4·9 grains.
Phthisis, tubercles softened	9·1 „
„ three days before death	9·8 „
Morbus cordis, with icterus	9·82 „
Acute hepatitis, with icterus	11·18 „
Icterus	17·75 „
Milk fever	19·0 „

Deposits of Uric Acid and Urates.

The physical properties of deposits of uric acid and urates having been already described, I will now offer a few remarks on the circumstances and the conditions under which they occur. As the deposits of urates are much more common than all other urinary deposits taken together, it is of particular importance to define their value as a pathological indication. This I shall attempt at the conclusion of this paragraph.

Uric acid itself is not soluble in the blood, at least not more than in water; it is only so in combination with a base —ammonia, soda, or lime. Uric acid, when occurring in the blood, is always met with as urate of soda or urate of ammonia. As venous blood is used for the examination (or mixed blood, if taken by cupping), the urate must have been an acid one, since the free carbonic acid, at the temperature of the body or at that of the common air, would not permit any neutral urate to exist, but would withdraw one equivalent of base. In venous blood, therefore, the urate must always be an acid one; and this is important to bear in mind. The question now arises whether the urate must also be an acid one in arterial blood; whether there is a sufficient amount of carbonic acid still present in arterial blood to keep the urate acid; or whether this cause of its acidity no longer exists in arterial blood, or, if present, is in any way neutralized by the presence of oxygen. Though it is not exactly ascertained how much of its carbonic acid the blood loses in its passage through the lungs, yet the data we possess are quite sufficient

[1] From the omission of this attention, many of the analyses of Becquerel and L'Heritier are useless for our purposes.

to put the question at rest. Magendie[1] found in 100 grammes of venous blood 0·078 grammes of carbonic acid, in 100 grammes of arterial blood 0·066 grammes of carbonic acid. The blood in becoming arterial had, therefore, lost only 15·4 per cent. of its carbonic acid. Considering the small amount of uric acid salts which, under normal circumstances, is at any time present in the blood, we are quite justified in the conclusion that the 0·066 grammes of carbonic acid present in 100 grammes of arterial blood are sufficient to keep the urate acid. If it should be urged that there is some ammonia in the blood, which might make the urate neutral, I refer the objector to putrefying urine, in which, notwithstanding a large amount of free ammonia, the urates still remain acid. The urates, wherever we meet with them, are acid salts, and from the very property of the neutral urates to be converted into acid salts by the mere influence of carbonic acid, their occurrence in the economy is impossible. If, therefore, Vogel[2] assumes that neutral urates may occur in the urine (and, as he believes, by the supervening of an acid in the urinary passages, may be transformed into acid salts, which being less soluble form a deposit), he thereby contracts a theoretical debt, which we are sorry to say he will never be able to pay.

Granting therefore that uric acid is already formed in the arterial blood on reaching the kidney; that it can only remain in solution as a urate, and that an acid one; and that after having passed the kidneys it still continues to be an acid urate; where, I ask, are now the difficulties surrounding the explanation of the secretion of uric acid in the form of urates?

Do we require such theories as that of Dr. Golding Bird, which begins with an impossibility, and, founded upon an opinion of Liebig, long since abandoned, is merely made for the purpose of explaining the acid reaction of urine by the formation of acid phosphates? But it is best to quote his words, which, at p. 84 of his fourth edition, are thus printed in italics:

"Uric acid, at the moment of separation from the blood, comes in contact with the double phosphate of soda and ammonia, derived from the food, forms urate of ammonia, evolving phosphoric acid, which thus produces the natural acid reaction of urine."

Of course, if uric acid itself is insoluble in the blood, and

[1] *Vide* Gay-Lussac, 'Ann. de Chimie et de Physique,' 1844, t. ii. Also, F. C. Donders, 'Physiologie des Menschen,' Deutsch von F. W. Theile, 1856, vol. i, p. 369.

[2] Loc. cit., p. 198. Lehmann has the same opinion.

is only kept dissolved as a urate, mostly the urate of soda, how can it be separated from the blood, except as a urate? And being secreted as a urate, how can it take ammonia from the supposed phosphate? I will even go further back and ask, how could the uric acid, even if it were free, and as such contained in the blood, remain so, if it were throughout the whole course of the circulation in contact with the very phosphate with whose ammonia it is to combine after separation from the blood? These questions I hand over to the further consideration of the reader. Dr. Bird continues—"If the whole bulk of the urine be to the urate of ammonia formed, not less than about 2701 to 1, the secretion will, at the ordinary temperature of the air, remain clear; but if the bulk of fluid be less, an amorphous deposit of the urate will occur."

This is the simple expression of the fact, as we meet it every day, that urates are more soluble in warm than in cold water or urine. But whether they require about 2701 (Dr. Bird), or 2789 (Dr. B. Jones), or 1608 times (*vide* under urate of ammonia), or even less, namely, only 1100 to 1200 times (*vide* urate of soda), their amount of water or urine for solution at a temperature of 77° F. (25° C.) is a matter to be decided only by direct experiment.

The theory just quoted is incorrect in one more respect; namely, because it assumes that the common deposits of urates are made up of urate of ammonia *only*, since the fact is that they mostly are mixtures of the urates of ammonia, soda, and lime; the urate of soda having in almost all cases the decided preponderance.

The conclusion of Dr. G. Bird's "probable explanation of the mode in which uric acid exists in healthy urine," of which I have quoted two passages, is a reiteration of the theory of Liebig on the acid reaction of urine being produced by the solution of uric acid in the solution of the common or tribasic phosphate of soda, whereby urate of soda is formed on the one hand, and an acid phosphate on the other. The passage runs thus:

"On the other hand, if an excess of uric acid be separated by the kidneys, it will act on the phosphate of soda of the doublesalt, and hence, on cooling, the urine will deposit a crystalline sediment of acid sand, very probably mixed with amorphous urate of ammonia, the latter usually forming a layer above the crystals, which always sink to the bottom of the vessel."

Here again we are met by the difficulty, that uric acid, being secreted in the soluble form of a urate, cannot act on

the phosphate of soda in the manner suggested. If the action were to take place in the blood, the phosphate could not remain acid, and therefore could exert no influence on the urate after secretion. But the most remarkable part of the matter is, that an explanation has been attempted of a fact which does not exist. If any one has ever seen uric acid fall down in any urine on mere cooling, as it does fall down from its artificial solution in the phosphate, he should not omit to publish the fact. I for one never have met with it, nor have any such facts been brought forward by the originator and propagator of that theory, nor by any one else, as far as I am aware. If uric acid is ever formed in that way, it must redissolve on restoring the temperature of the body to the urine. Thus Dr. Golding Bird has defeated his own theory, in unmistakeable words, in § 120, p. 122:

"*Diagnosis of uric acid deposits.*—When heated in the urine, the uric acid deposit does not dissolve; the crystals merely become opaque.[1] They generally become more distinct from the solution of the urate of ammonia, which is frequently mixed with them, and sometimes completely conceals them from view. Hence the best mode of discovering this deposit, is to warm the urine, when turbid from excess of urate of ammonia, in a watch-glass; the acid becomes visible at the bottom of the glass, as soon as the urate dissolves."

Thus an imaginary fact, linked to reality by mere analogy to an artificial chemical process, has been the subject of explanations, which in improbability were only surpassed by what they were intended to explain, and which found their strongest contradiction in the very fact, the misconceived occurrence of which was the problem to be solved.

Deposits of Urates occurring after emission.

The deposits of mixed urates are so very common in the most varied conditions of health and disease, that it would be an endless and useless labour to name those conditions. The attempt to define the characters of urine depositing urates must be futile, because there is almost no description of urine that may not deposit them. Whether acid or alkaline, of high or of low specific gravity, containing much or little urea and colouring matter, urine will, under certain circumstances, deposit urates. Whether occurring in the system (bladder), or out of the body after emission, the conditions of the deposit are identical; there is not a sufficient quantity of water present to hold all the urates in solution at a certain

[1] By losing water.— Thudichum.

temperature. The urine, therefore, after being saturated with the urates, deposits the excess; by the addition of water, or urine not saturated with urates, this excess may, under all circumstances, be dissolved. By concentration of urine, a deposit of urates may be produced.

As the only indication of a deposit of urates is, therefore, that the urine containing it is, at that temperature, saturated with them; and as this may occur after a dance, after abstinence from liquids, or in a fever, this indication in itself amounts to nothing. The amount of the urates may be the ordinary one, though there be a deposit. The indication of a deposit of urates becomes of importance only when considered with relation to the total quantity of urine and dissolved urates discharged in twenty-four hours; with this view we have to distinguish two different cases.

a. If the bulk of the urine for twenty-four hours is the normal average, and if a sediment of urates continues to exist in that urine, it is tolerably certain that an absolute excess of urates is present. (See the indications of an excess of uric acid.)

b. If, on the other hand, the urine for twenty-four hours is below the average, a deposit may possibly be, and in most cases is, due to saturation only. The easiest process of ascertaining this, for ordinary practical purposes at least, is to dilute the urine with water to its average bulk, and to shake it well. If the deposit does not entirely dissolve, an excess of urates is present. The safest proceeding, however, is to ascertain the whole amount of uric acid secreted in twenty-four hours.

If the presence of a deposit of urates be taken as an indication of the saturation of urine by these salts, and if the latter be assumed ordinarily to be of the usual amount, deposits of that kind become more valuable as signs of a diminished secretion of water by the kidneys than of any other symptom. As the appearance of a deposit of urates is always accompanied by morbid sensations and objective symptoms, in the healthy by thirst at least, if by nothing more, the conclusion is simple enough. *The individual whose urine has deposited the urates does not drink water enough, and must drink more, and must drink so much that the urine, at the ordinary temperature of the air, shall remain clear.* Of course, in some cases this will be neither possible nor advisable; but in most cases of acute and febrile disease, it should be a plan of treatment. I have certainly seen it attended by beneficial results in many cases; I have also observed the

contrary,—want of water in the system to be a source of disease.

Deposits of Urates occurring in the urinary passages.

In speaking of the concretions and calculi, I shall have to show in detail the practical importance of this class of deposits; here it may suffice to state that on an average 20 calculi out of 230, or 8·69 per cent., present nuclei of urates, and 37 more out of 230, or 16·08 per cent., contain a certain amount of urates in the form of layers or crusts. The urates, therefore, somehow or other, enter into the composition of 24·78 per cent., or almost one quarter of all calculi existing.

Practically it is important to distinguish two modes in which deposits of urates may be produced in the urinary passages.

a. A urine nearly or just saturated with the urates is secreted by the kidneys, and collected in the bladder. By the endosmotic activity of the veins and absorbents of the bladder, a further concentration of the urine is brought about, in consequence of which a certain amount of the urates passes out of solution, and forms a precipitate. These cases may be of rare occurrence, as is generally believed;[1] or they may be overlooked, and the deposit may be taken for an ordinary deposit by cooling. It is just possible that the following case might have escaped my observation, but for the retention of urine accompanying the deposit in the bladder, making necessary the use of the catheter. The turbid urine, which escaped by the instrument, afforded ocular proof that the deposit (already alluded to on p. 91) had been formed in the bladder.

Observation.—*Typhus petechialis.*—R. G—, æt. 2, a delicate girl, had been some time "out of condition,"[2] had got thin, and been infested with thread-worms, which being removed for a time by the aid of santonine in oil, reappeared again after a time.

On the 7th of September, 1856, I was requested to see the child. For the last fortnight, her parents had perceived her to be unusually quick of perception ("sharp"). Some days since she began to complain, and on the 5th, felt so ill, that she wanted to lie down. On the 6th a rash, resembling flea-bites, made its appearance.

7th.—The child is giddy, and wants to lie down. She is light-headed, almost

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[1] Vogel, loc. cit., p. 198.

[2] The reader will pardon the transference of this popular term to man from its application to our most useful quadruped, the horse. The phrase is equivalent to undefinable ailment.

fainting when raised, and complains of severe headache, frequently taking her head between her hands, and uttering exclamations expressive of the pain. She sleeps very little, being awake the greater part of the night till two or three o'clock in the morning. She has no appetite, but is very thirsty; her lips are dry and peeling; her tongue is covered with a thick fur in the middle, red at the sides and point, but moist all over. Since the last motion, two days ago, which contained many worms, the bowels have been confined. The abdomen is soft, not tympanitic. The pulse is very violent and hard. The skin is hot, generally pale, but covered with petechiæ of the exact form of flea-bites, namely, a purple spot, of the size of the circumference of a pin's head, surrounded with a halo of a fainter purple colour. The spots do not disappear on pressure. I gave her a scruple of the syrup of iodide of iron, three times a day. Of a mixture of two ounces of olive oil, half an ounce of castor oil, and six grains of santonine, she took two teaspoonfuls at once, and one teaspoonful every hour. It required half the oil to produce a dark, moulded motion.

8th.—Continues much the same. The spots have in some degree lost their halo. In the evening, the girl being sleepless and wandering, she began to squint.

9th.—The exanthema stands nicely, and the spots have got larger. The child is very feverish. The urine passed yesterday is acid, reddish-yellow, contains much mucus, some epithelial casts from the tubuli of the kidneys, and deposits a granular sediment of urate of soda. A drop of the urine placed between two slips of glass soon crystallizes into a mass of beautifully defined crystals of urea. After deposition of the small amount of surplus urates, the specific gravity of the urine is 1025, very high for a child of that age.

10th.—The spots get smaller, and lose their halo. They now do disappear by pressure, and return after it. The tongue is getting cleaner from the sides. She only passed a small quantity of urine once in the course of that day, with a motion of the bowels. She squints when excited.

11th.—The spots continue to get paler. The tongue is cleaning. The condition of the abdomen, contrasted with its soft, nay flabby state, five days ago, shows distension. Ocular inspection and percussion show the collection of urine in the bladder, from which nothing had passed since yesterday. A warm poultice put over the abdomen and vulva, and a warm bath, not being of any avail in relaxing the sphincter of the bladder, the catheter was applied, and about eight ounces (perhaps nine, with the unavoidable loss) of urine, mixed with a white deposit, in flakes, escaped by the instrument.

It was the urine of two days, mixed with a copious deposit, which, on standing, settled to the bottom of the vessel. The urine now appeared of a reddish-yellow colour, and of acid reaction. In a specimen, mixed with half its bulk of nitric acid, nitrate of urea crystallized on standing. The colour then became deep red. Hydrochloric acid, when added in sufficient quantity, at first coloured the urine dark blue, nearly black; but this colour after two or three hours transformed into dark cherry-red. A deposit of cyanourine did not therefore take place, though the reaction was indicative of the presence of an excess of uroxanthine. The urine became black and dirty on the admixture of sulphuric acid. The specific gravity of the urine was 1025.

The deposit was white, and consisted of the urate of soda in dumb-bells, globules, and irregular agglomerations, mostly covered with spinous masses of the most varied, fanciful, and irregular description. Some of the globular masses were so large that they could be distinguished with the naked eye; and under the microscope, bristled with spinous masses. That the spines were urate of soda was evidenced by their solubility in water; a deposit when washed on the filter with water, dissolved entirely, leaving no residue. By the influence of an acid, the urate was transformed into ovoid crystals of uric acid.

12th.—The catheterism of yesterday was followed by great relief, and the child passed a little urine spontaneously soon after. But the retention continued; and on this day the catheter discharged four ounces of the same description of urine, with the same amount and quality of sediment as on the day before.

On three following days the urine had to be drawn with the catheter, showing each time the same characters and the same sediment.

On the 16th, the child passed urine spontaneously, still mixed with a deposit; but it consisted of granules and dumb-bells only, with short indications of spinous masses only. This lasted for two or three days, after which the urine became clear, and after standing twenty-four hours deposited ovoid crystals of uric acid. From this time the child recovered her strength rapidly; and, with the assistance of some quinine and iron, was soon much stronger and better looking than at any time before her illness.

I must not omit to state that from the 10th to the 20th the child had taken no medicine whatever, owing to the absence of any indication. This is, perhaps, in favour of the observation, and shows that a discharge of urate of soda in the form of sediment is not necessarily connected with the patient's taking carbonate of soda, a connection which seems to have been assumed by Dr. G. Bird.[1]

The practical considerations on this case are many in number; but most important are the questions on the causes of the deposit and of the retention. That the deposit is due to concentration of the urine in the bladder after secretion from the kidneys cannot be doubted. Urine nearly or perfectly saturated with the urates arrived in the bladder; there it was deprived of a certain amount of water, and a deposit of the nature described fell down. Now it is just possible, and very probable, that the spinous hedgehog-like masses so irritated the mucous membrane of the urethra at the infundibulum as to cause spasmodic contraction of the sphincter. I have seen strangury caused by the passage of almost microscopical crystals of uric acid, and yet they were ovoid round bodies.[2] This confirms my opinion on the cause of the retention. I will not, however, deny the influence which the nervous system may have had in the spasmodic action, seeing that there was spasm in other parts as well, namely, in the muscles of the eye. Those of my readers, however, who should be inclined to ignore altogether the nature of the deposit as a mechanical cause of the irritation producing the spasmodic retention, I will only remind that the spinous deposit appeared and disappeared simultaneously with the retention; and that a deposit of a much less irritating shape was discharged before the retention set in and after it ceased. Undoubtedly, we must be very cautious in these conclusions, because accurate observation is so very difficult in these cases. Conscious of this, I yet hope that I have taken the common-sense view of the observation.

[1] Loc. cit., § 135, p. 138.

[2] See also Prout, 'Stomach and Urinary Diseases,' 3d edit., 1840, p. 202.

It may not be out of place here to quote the following passage from Dr. Prout,[1] which, referring to actual observations similar to the one just now related, suggests the probability that in some cases the urate of soda deposit may close the urethra by forming a simple plug, and without any spasmodic action being perceptible.

"About this period of life (viz., the age of forty) or later, we occasionally see in certain modifications of gouty constitution large quantities of the lithate of soda, perfectly white, deposited in the urine. This compound sometimes assumes the form of amorphous sediment, and renders the urine quite milky when passed; but I have seen it copiously secreted of the consistence of mortar, especially during the night; and in this case it is apt to collect into masses and block up the urethra, so as to occasion considerable difficulty in passing the urine. Such instances are very rare, and appear to be associated with organic disease of the kidneys, and perhaps other organs." Of this association, however, Dr. Prout has not given any proof in observation.

b. The second mode in which deposits of urates may be produced in the urinary passages is by the urine in the bladder undergoing alkaline fermentation. The urates in this case are precipitated in the same manner as in urine putrefying in the open air or in a carefully stoppered glass bottle. The urates are less soluble in a solution of carbonate of ammonia than in fresh acid urine; urea, therefore, after transformation into carbonate of ammonia, precipitates part of the urates. The fixed alkalies, on the other hand, do not interfere with the solubility of the urates.

Deposits of Uric Acid occurring after emission.

As uric acid cannot be secreted by the kidney from the blood in any other form than that of a soluble acid urate, it must always arrive as such in the pelvis of the kidneys. The intervention of a stronger acid is now required to separate uric acid from its base. That the ordinary acidity of the urine should not be sufficient to effect this, nature has taken care to arrange. Whence, therefore, does the acid come which in urine of average description after some hours or days of standing produces a precipitate of uric acid? Scherer[2] has shown that this acid is the product of a peculiar kind of decomposition or fermentation of the urine, which he called the *acid fermentation* just because its main feature is the

[1] Loc. cit., p. 203.
[2] 'Annal. d. Chemie und Pharmacie,' Band xlii, p. 171.

production of one or several acids. The ferment he considers to be the mucus, which causes the colouring matter of the urine to ferment, and to give off among other substances lactic and acetic acid. Under the influence of these acids, uric acid is precipitated sooner or later, according to the time at which the decomposition of urea begins to neutralize the acid formed. The decomposition of urea constitutes the *alkaline fermentation*, a process which we have already described in the chapter on alkaline urine. An important fact is, that if the alkaline fermentation succeeds the acid one, any uric acid precipitated is transformed into urate of ammonia. Of the alkaline fermentation, I shall have to treat more at length under the section on triple phosphates.

Deposits of Uric Acid occurring in the urinary organs.

As the alkaline fermentation of urine after emission may already take place in the body under certain circumstances, it has by analogy been thought possible that the acid fermentation may also occur in the urinary organs. It is true that the direct proof of such a process has not yet been given; yet many facts have been adduced in support of this view, which at least make it much more probable than any other theory hitherto advanced. And even should it afterwards turn out that uric acid in the urinary passages is not exclusively precipitated by acids generated by fermentation, yet in so many instances this seems to be the case, that we can have no hesitation in adopting this theory.

We know that different pathological conditions of the system may so influence the mucus of the urinary passages, as to cause it to ferment the urine in sixteen or twenty-four hours after emission. If the urine be kept at the temperature of the body, the fermentation will frequently precipitate uric acid, even in so short a time as six hours. The mucus in this case was evidently predisposed to undergo the changes necessary to become a ferment; and changes which ordinarily occur out of the body had already taken place in the body.

On the other hand, we know that in cases where uric acid is set free in the urinary organs, pathological conditions are present in the system, which are analogous to, or identical with, those conditions under the influence of which an early acid fermentation of the urine takes place. Nay, we know even that the early fermentation and production of uric acid in the urine after emission is very frequently a forerunner of the deposition of uric acid in the urinary organs.

Of course the effect produced by the acids created by fermentation will be materially influenced by the degree of acidity which the urine possesses on leaving the kidneys. We here suppose that no urine can possibly be secreted, which by itself is so acid as to precipitate uric acid. This substance would, if that was the case, have to be looked for in the substance of the kidney, where we scarcely ever find it.

The circumstances, therefore, which precipitate uric acid in the urinary organs, seem to be the flow of an acid urine over a (mucous) membrane, the secretion of which is in a condition to act as a ferment of the colouring matter of the urine. It seems reasonable to suppose that a certain time is required for this fermentation to set in. The sojourn of the urine in the bladder seems long enough for the induction of this process; it is more difficult to explain its occurrence in the kidney, and yet it is just there where uric acid is most frequently deposited in an insoluble form. That urine may collect in the calyces of the kidneys, we have every reason to believe. The contractile powers of the pelves and infundibula become less with age; the lower part of the pelvis may not be quite emptied of its contents, particularly in the erect position. I have even observed that in certain atrophic conditions of the kidneys, accompanied by the formation of uric acid gravel, the pelvis of the kidneys and sacs of the infundibula become so wide, as to contain urine after death: a sure proof that they could not expel their contents during life, though there was no obstruction in the ureters. This condition only occurs in later life, to which renal concretions almost exclusively are proper. In children and young persons this affection is very rare.

Observation.—A man, æt. 65, died of cancer of the stomach. He had been a drunkard during the latter part of his life. I made the *post-mortem* examination of his body, and found a hard cancerous tumour involving the larger curvature of the stomach. There were also two large cancerous masses in the liver, whither the cancer had progressed by means of infesting the clot in the gastric veins, and in the portal vein. The cancerous juice most probably coagulated the blood; and the coagula became the beds of cancerous cell-development. Of this process all stages could be observed.

The kidneys were in a state of contractive atrophy, their upper halves more than the lower, which gave them a very peculiar shape. Their calyces contained several drachms of turbid urine. In the lowest part of the right calyx there lay a number of uric acid concretions, true red gravel. The ureters were quite pervious. The bladder contained no concretions of any kind. I could not ascertain whether the man had had any symptoms of gravel during life. If this was the case during the development of the cancer, the symptoms probably merged in the suffering attending this disease.

Crystallized Sediments.

The formation of uric acid deposits in the bladder, by means of the acid fermentation, is not of very rare occurrence. It is frequently ascribed, together with the formation of deposits in the kidneys, to the so-called uric acid diathesis; a term intended to comprise all diseases which have a tendency towards the development of a symptom, namely, the precipitation of uric acid. Except this symptom, irregular as it is, these diseases have, however, nothing in common. In fact, the term "uric acid diathesis" has been made the lumber-room into which to throw a number of ill-defined pathological conditions. Uric acid has been made the sinner, where it has taken a most neutral or passive part only. Not even has the proof been given that uric acid plays any part in these cases at all; not even has the proof been given that uric acid really has been in excess in cases where the existence of the deposit has been taken as a proof of the excess. In fact, the uric acid diathesis is one of the few survivors of the number of diatheses that served bygone generations as the *quid pro quo* of an explanation.

The following observations serve to show the difference that may exist between cases in which a precipitate of uric acid formed in the bladder is one of the symptoms:

Observation.—Mrs. T—, æt. 75, had undergone great mental anxiety; and, in consequence apparently, lost her bodily health. There were loss of appetite, indigestion, and increase of the habitual constipation. There was headache over the eyebrows, with flushing of the face, and heat and dryness of the surface of the body. The urine, on being passed, was turbid, being mixed with a dark-brown—almost black—sediment, appearing like fine coffee-grounds. The sediment seemed to increase somewhat after cooling. Under the microscope it exhibited itself to be composed of rhombs of uric acid, mixed with an equal amount of granular urates. A pill of a grain of powdered ipecacuanha, with four grains of rhubarb, taken before every meal, seemed to exert a very beneficial influence upon the digestive organs. An alkaline mixture, taken three hours after the principal meals, counteracted the heartburn. Under this treatment the deposit gradually disappeared.

June 12th, 1856.—After three weeks of apparently good health, another attack of gravel came on. The symptoms were—pain in the loins and chest and around the stomach, great flatulency, great want of appetite, prostration of strength, and headache. The bowels had been kept open by the rhubarb and ipecacuanha pills taken before meals; they even had been relaxed, a very unusual thing with this patient. The alkaline mixture soon restored her to health, as I believe. The uric acid crystals were small, with double outline, dark brown, and were mixed with very light hexagonal plates of what may have been urate of soda.

28th.—There was a single discharge of gravel after some heat in the face, pain in the stomach, and great flatulency. The deposit was most copious. The crystals were hour-glass shaped and ovoid. I did not prescribe any medicine on this occasion, but merely enjoined the patient to empty the bladder frequently.

A tonic plan of treatment was now adopted, which comprised quinine and iron as the pharmaceutical elements; cold sponging bath and exercise as the hygienic part; and rich diet, with a larger amount of spring water taken between meal-times, as the dietetic régime. As no deposit has occurred since, I suppose the treatment was successful.

This case being one where the deposit was formed in the urinary organs, is a good illustration of a certain class of circumstances under which this may occur. The danger of the formation of a concretion is great in these cases. The best preventive measure is the free use of drink-water, and the frequent discharge of the urine from the bladder. In this manner the urinary passages are freed from ferment, and the urine is not allowed time to undergo fermentative decomposition.

The following case is very different from the former, as regards age and condition of the patient, and the symptoms under which the deposit occurred:

Observation.—Master B—, a fine strong boy, nineteen months old, had suffered from severe bronchitis during the winter 1855-56, with congestion of the lungs, at one time bordering on pneumonia. He had a second severe attack in the early part of the spring of 1856, when at Boulogne. From both attacks he had perfectly recovered, when, at the beginning of May, his mother, then staying with him at Gravesend, noticed him to suffer from irritation of the bladder, the child being obliged to pass urine at least twelve or fifteen times in the course of the day. Immediately after the water had been passed, a red sand subsided to the bottom of the vessel. The child was well again next day, without any treatment having been had recourse to.

On June 14th, 1856, another attack of red sand came on, causing symptoms similar to those on the first occasion. The urine on passing contained a large amount of a light-brown sediment of uric acid. The crystals were distinguished by their containing very little colouring matter, so that in strong light some almost escaped observation. They were all flat rhombic plates of different angles. The urine was highly concentrated; urea crystallizing spontaneously from a drop on a slip of glass.

In this case the disorder seemed to have some connection with the diet of the child, to which he either restricted himself or was restricted, namely, milk diet, taking for three meals nothing but milk, with bread and butter or biscuits. Whether the child got well spontaneously, as on the former occasion, or whether the change to a more mixed diet, with light vegetables and meat, had any share in the disappearance of the deposit, I do not dare to decide. The deposit, however, has not reappeared since. This case seems worth noticing, as the uric acid deposit and the strangury caused thereby were the only disorders that could be discovered, the child being all the time as well and blooming as one could wish any child to be. It is possible and probable that the strangury

set up by the uric acid crystals in this and many similar cases of crystallized deposit, is the means of preventing the formation of concretions, and their retention in the urinary passages.

The urine of this boy, in which another sediment occurred after filtration, yielded some few crystals of uric acid on addition of acetic acid. But the case of the aged lady bore out the statement of Dr. Prout,[1] that the urine is so completely divested of lithic acid by this peculiar arrangement of the urinary principles (which we now believe to be acid fermentation), that on adding to it an excess of mineral acid, not another particle of lithic acid is usually deposited.

Another illustrative case of crystallized deposit formed in the urinary organs is recorded by Dr. G. Bird.[2]

In children who are liable to the formation of crystallized uric acid deposits in the bladder, "symptoms of irritation about the urinary organs may," according to Dr. Prout,[3] "be always more or less observed, if the child be attended to. Thus there will be found frequent desire to pass urine, which is voided in very small quantities, and with manifest uneasiness. The irritation about the urinary organs also sometimes induces the child to wet the bed by night," &c. This irritation from the presence of crystallized deposits does not seem to exist in adult persons. It is not mentioned in Dr. Bird's case just quoted, and was not present in my first case.

Uric Acid Concretions.

1. *Sand and gravel.—Crystalline sediments.*—There seems at first sight to be no great reason for drawing any particular distinction between common uric acid deposits, on the one hand, and sand and gravel on the other. Indeed, the common deposits of pulverulent uric acid are frequently called gravel and sand by medical men and by laymen. This practice, however, is not quite correct, and should therefore not be generally adopted. What we call "the common pulverulent deposit of uric acid" is made up of single crystals of that substance. The occurrence in such a deposit of twin crystals, crossed crystals, of crystals simply hanging together in a variety of ways, is an exception, and does not constitute a deposit of sand or gravel. To fall under the latter denomination, a deposit must exhibit a tendency towards a zeolithic arrangement of the crystals—that is, the crystals must group

[1] Loc. cit., p. 198. [2] Loc. cit., p. 158, § 156. [3] Loc. cit., p. 202.

themselves, with their predominant axis, round a common centre, like the rays round the luminous body from which they emanate. Mostly one or two large crystals form the basis of, or are mixed up with, these globular masses. What I should like to call "sand," therefore, would be masses of uric acid, mostly globular, or irregularly roundish, or oblong, of very uniform size, from $\frac{1}{40}$th to $\frac{1}{20}$th of an inch in diameter, and answering to the above definition. Viewed by transmitted light under the microscope, the globules are perfectly impervious to light; and the uric acid crystals on the surface are faintly transparent, of a dark-brown colour. To the naked eye, the deposit is red, with a tinge of brown. When disturbed, the sediment mixes with the clear urine, but rapidly subsides to the bottom when the fluid comes to rest. Generally, no small or well-defined crystals of the ordinary kind are mixed with this sand.

This description of sand is sometimes met with in the pale and watery urine of early infancy.

Under the name of "gravel," I would comprise concretions varying in size from $\frac{1}{20}$th of an inch diameter upwards, until, by their size, they become incapable of passing either the ureters or the urethra. These concretions are generally rough; and if many are discharged at one time are of variable size, from that of a pin's head to that of an almond (Prout). A variety of these crystalline concretions are the "*pisiform*," "the formation of which is attended by a remarkable feature, namely, *the great number* in which they are usually generated, a circumstance which may be said to be characteristic of them. Their great number occasions them to accumulate occasionally in the pelvis of the kidney; or in the lower portion of the ureters, where they terminate in the cavity of the bladder; and on such occasions severe nephritic attacks are sometimes the consequence. These concretions vary in size, from that of a pin's head to that of a pea or marble. Their form is always more or less globular; though they sometimes present flattened or facetted surfaces, produced by their contact or attrition with each other. Their surface is usually smooth, sometimes even porcelainous or polished; and their internal texture is almost invariably crystallized, and usually lamellated. Their colour ranges through all the shades of yellow; and occasionally, though more rarely, they assume a dark-brown or reddish colour." (Prout.[1]) These pisiform concretions are mostly deposited after the age of forty.

[1] Loc. cit., p. 200.

2. *Uric acid calculi.*—The number of calculi, of which uric acid forms either the nucleus or the entire substance is very great, standing to the number of all other calculi in the proportion of two to three. They are found of all sizes, from the largest pisiform concretions to stones of five or six ounces, or more, in weight. If formed in the pelvis of the kidney, a uric acid stone may have a very irregular rough shape and surface. If, however, the body and crust of the stone have been formed in the bladder, as is mostly the case, the shape will, in general, be that of a flattened ovoid, the flattening, in many cases, being so trifling as to escape notice. The exterior of the uric acid calculus is slightly tuberculated; but in many cases the tubercles are so water-worn, that the surface is smooth. In colour, uric acid calculi vary from reddish-yellow or fawn-colour to brownish-red, or brown with an admixture of red, like old mahogany. On being divided by a saw, they are seen to be composed of concentric layers, which are of variable thickness when compared with each other. But every layer preserves its own thickness pretty regularly all round the calculus. The texture of the stone is best seen on the surface of a fracture. In hard and pure stones it is crystalline, fibrous, the fibres of each layer verging like radii towards the centre of the stone. On breaking a stone, the fracture will mostly be parallel with these crystalline fibres. Stones, however, which are less dense and less pure are earthy, and amorphous in fracture. Some few stones are so hard that they give a ringing noise on percussion, a sharp sound like a pebble, and on being chipped exhibit a conchoid fracture. These stones are very dangerous, when they become the subjects of the process of lithotrity, for their fragments are so sharp, that they wound the bladder, and cause infiltration of the urine into the adjacent cellular tissue; the consequences of which are mostly extensive mortification and death. It is, therefore, of high practical importance to ascertain the circumstances under which these hard stones may be formed.

The laminated structure of the uric acid calculi (and of all other laminated calculi) shows that they are formed by the gradual precipitation of uric acid from the urine, the precipitated substance being deposited in an equal layer all over the surface of the concretion, which forms the nucleus, and also over the surface of all subsequent layers; a circumstance which is the condition of the parallelism of the rings seen on section. The layers, however, show something more; namely, that the formation of the stone has been interrupted, or has taken place at different intervals. Of this circumstance there

could not be given so good a description as that of Dr. Prout:[1] "Between the different intervals at which the different laminæ have been formed, periods have intervened during which no deposition has taken place. This remark not only applies to the different laminæ of a heterogeneous calculus, but to the different laminæ of calculi composed of the same substance; as for instance to the different laminæ of which lithic acid concretions usually consist. This explanation is in perfect accordance with the circumstances attending the formation of calculi, which often, as is well known, remain in the bladder for a great number of years, without attaining any remarkable size. Moreover, the constant state of change alone to which the urine in all individuals is liable, almost precludes the notion of homogeneity in a calculus. We may suppose, therefore, that certain changes take place in the urine, during which the law of continuity of deposition is suspended, and the surface of the concretion becomes, as it were, *water-worn* and less apt for future accretion; in short, assumes all the properties of a heterogeneous substance. Under these circumstances, when a tendency to deposition occurs, it will have to commence *de novo*, and, as it were, upon the surface of a foreign body. The consequence will be that the adhesion between the new and the old coats, or laminæ, will be less firm than in the intermediate parts, and that a calculus thus formed will be disposed, when broken, to separate into concentric laminæ." To this we have only to add that one great cause of the formation of layers is the periodicity with which the bladder is emptied of its contents. If uric acid is really precipitated by acid fermentation, and if for this fermentation to produce a sufficient amount of acid a certain time is required, during which the ferment must be in contact with the substance to be fermented, then no uric acid can be deposited immediately after the bladder has discharged its contents; and no uric acid can be deposited if the bladder is so irritable as to discharge its contents at frequent and short intervals, a condition which, as I have already stated, I believe to be the main safeguard against the more frequent occurrence of stone in the bladder. If, on the other hand, the calculus does not irritate the bladder at ordinary times, or is the mechanical cause of a retention of part or the whole of the urine, so that the urine has time to be collected and to be fermented, a deposition upon the calculus will take place.

Chemical characters of uric acid concretions.—The chemical

[1] Loc. cit., p. 361.

characters are those of uric acid. But as the concretions may be more or less pure, it is advisable to follow a method in analysing. The blowpipe decides whether the stone leaves any residue on combustion. A piece of the stone is then reduced to a powder, a weighed portion of which is extracted with ether, then with alcohol, and, at last, repeatedly with boiling water. The ether dissolves any fat; the alcohol takes up colouring matter; the boiling water removes urates and soluble inorganic salts, and a trace of the acid. If it is not necessary to be very accurate, the extraction with ether and alcohol may be omitted. The powder which is not soluble in water may now be dissolved in a dilute and warm solution of caustic potash or soda, and precipitated by carbonic acid, when snowy-white urate of soda will be mostly obtained. Or the solution in potash may be precipitated with acetic acid, when all the uric acid falls down in a very pure state, and is obtained by filtration, washing, and drying. The combined weights of the extracts and of the pure uric acid must be nearly equal to the weight of the powder taken for analysis.

Concretions of Urate of Ammonia, Soda, and Lime.

Calculi composed essentially of urates are of rather rare occurrence, and seem confined to children under puberty.[1] They are of small size, and have a smooth or slightly tuberculated surface, and a pale slate or clay colour, sometimes with an admixture of red or brown. In rare instances their colour is fawn, and in such stones pink layers occur towards the centre. They are composed of concentric layers, but the layers are much less distinct and much thinner than those of uric acid calculi. They have a fine earthy fracture, and are easily broken.

The *chemical diagnosis* rests upon the solubility of the urates in boiling water, by which they are distinguished from all other calculi. After the urates have been obtained in a pure state by dissolving and filtering, the uric acid may be precipitated by acetic acid, collected on a filter, washed, dried, and weighed. The filtered fluid contains the acetates of the bases with which uric acid was combined. We evaporate to dryness, and expose the residue to a red heat, when soda and lime remain, the former combined with carbonic acid, the latter partly as carbonate, partly as caustic lime. The residue is now dissolved in a little acid, muriatic or acetic; the lime is precipitated as oxalate by the addition of oxalate

[1] *Vide* Prout, loc. cit., p. 106, and 'Med.-Chir. Trans.,' vol. x, p. 389.

of ammonia, filtered, dried, and weighed. The filtered liquid contains the soda, which may be determined either as muriate or acetate, or better, after heating, as carbonate. If for every equivalent of base an equivalent of uric acid be taken, we find by the excess of uric acid the amount of ammonia which was present and combined with it.

The calculi composed of lithates frequently contain oxalate of lime and small quantities of the phosphates in intimate mixture with the lithates. They are then called *mixed calculi.*

Layers of Uric Acid and Urates in alternating and mixed Calculi.

These layers are due to the same causes as the massive concretions. But there seems to be one cause of the occurrence of urates to which it is necessary to advert, before concluding the chapter on uric acid. Ammonia at the temperature of the body very quickly changes uric acid into urate of ammonia. Let us apply this to a uric acid stone. The urine in calculous disorders very frequently becomes alkaline; nay, if the disorder last long enough, alkaline decomposition of the urine in the bladder is almost always present. In evidence of this, almost one half of all calculi possesses a cortical layer of mixed phosphates, the consequences exclusively of alkaline urine. Now there can be no doubt, that if a uric acid stone become the cause of such disorders of the urinary passages as will induce alkaline fermentation in the urine, the outer layers of this stone must be transformed into urate of ammonia, and this urate of ammonia (or soda) would undoubtedly be dissolved and carried away, unless the carbonic acid present diminished its solubility, and if the urine were dilute enough to act as a solvent, *i. e.*, were not itself too much saturated with the urates. A stone with a uric acid nucleus, a body of urates, and a cortical portion of mixed phosphates, is to my understanding the type of this process, and suggests to me the following history: In the beginning there was a renal uric acid concretion, which increased by the acid fermentation in the bladder. Then the calculus caused disorder of the bladder, or of the urine (as by excessive treatment with alkaline remedies), which ended in the establishment of alkaline fermentation in the bladder, by which the outer layers of the uric acid concretion were first transformed into urate of ammonia, and afterwards encased in a crust of mixed phosphates.

CHAPTER V.

CREATINE AND CREATININE.

History.

The juice of flesh contains a crystallizable substance, which was in 1835 discovered by Chevreul[1] in beef-tea of the Dutch Company, and by him termed creatine. Creatine and creatinine (in the form of chloride of zinc salt) were subsequently, in 1844, found in the urine contemporaneously by Heintz[2] and Pettenkofer,[3] but their identity with the crystallizable substance of the juice of flesh was not then recognised. In 1847 creatine and creatinine were demonstrated by Liebig[4] to be constant ingredients of the juices of the flesh of almost all the classes of vertebrate animals and of the urine of man. Verdeil and Marcet[5] found creatine in the blood of the ox.

CREATINE.

The *composition* of creatine is as follows:

8 equivalents of	carbon . . .	48	36·64
3 „	nitrogen . .	42	32·06
9 „	hydrogen . .	9	6·87
4 „	oxygen . . .	32	24·43
Atomic weight of dry creatine		131	100·00

Crystallized creatine, therefore, corresponds to the formula

$C_8H_9N_3O_4 + 2Aq.$	1 atom of dry creatine .	131	87·92
	2 atoms of water . . .	18	12·08
		149	100·00

Occurrence.

Creatinine is present in the flesh of man and the mammalia, of birds, amphibia, and fishes. The flesh of fowl yields the

[1] 'Journal de Pharm.,' t. xxi, p. 236.

[2] (Heintz) 'Poggendorf's Annal.,' lxii, p. 602; lxx, p. 460; lxxiii, p. 696; lxxiv, p. 125.

[3] 'Annal. d. Chem. und Pharm.,' Bd. lii, S. 97.

[4] 'Chemische Untersuchung über das Fleisch und seine Zubereitung zum Nahrungsmittel,' Heidelberg, 1847, p. 47.

[5] Journ. de Pharm.,' (3) xx, p. 89. Liebig and Kopp's 'Jahresbericht,' 1851, p. 586.

largest proportion (3·2 per mille); next the ox's heart (1·3 per mille); and the flesh of the cod-fish (0·9 to 1·7 per mille). The quantity of creatine obtained from the flesh of man is 0·67 per mille, about the same proportion as from beef. Creatine is present in the blood and urine of man and all animals hitherto examined.

Liebig's method of obtaining Creatine.

In order to obtain creatine pure, a quantity, say ten pounds, of flesh of a recently killed animal is freed of fat and finely chopped; five pounds are then mixed with an equal amount of cold distilled water, carefully kneaded through by means of the hands, and then pressed carefully in a bag of coarse linen. The residue is now again carefully mixed with another five pounds of water, and again subjected to pressure. The fluid from the first pressing is put aside for further treatment to be described; the fluid from the second pressing serves towards the extraction of the second portion of the flesh. The first portion of flesh is a third time treated in a similar way with five pounds of water, and the fluid obtained by pressing is used for the second extraction of the second portion of flesh; the latter is treated a third time with pure water, and pressed.

The united fluids are filtered through a clean cloth, and filled into a large balloon of glass; the latter is placed in a kettle with water, which is gradually heated to the boiling point, and kept at that temperature until the extract has lost its colour, and albumen and colouring matter have separated in the form of a coagulum. If a portion of the fluid in a test-tube heated to boiling remains clear, this operation is completed.

The fluid is now separated from the coagula by filtration through a cloth, and subsequent pressing. The united fluids are then filtered through paper.

The colour of the fluid so obtained is reddish, if extracted from the flesh of the ox, doe, hare, or fox; but the fluid from the flesh of the calf, fowl, or fish, is scarcely coloured. The extracts from the flesh of all animals are acid, from the presence of free acid, which must be removed before evaporating the fluid, as it would cause a dark brown colour of the concentrated fluid, and not permit the crystallization of creatine. In order to remove this acid, a concentrated solution of caustic baryta is added to the extract as long as a white precipitate is thereby produced. Neutrality or alkalinity should not deter the operator from adding the baryta solution as long as it produces any turbidity.

After separation from the precipitate, which contains all the phosphoric acid of the juice of flesh in the form of phosphate of baryta and magnesia, the fluid is evaporated in shallow china dishes on the water- or sand-bath, taking care never to allow it to be heated to ebullition; the upper part of the dish must never get more hot than the fluid, as a ring of dry substance is formed thereby, which afterwards, on the addition of new portions of fluid, dissolves, and on further concentration imparts a brown colour to the fluid. The extracts from the flesh of fowl or fish remain colourless and clear to the last. If an excess of baryta have been added, a pellicle of carbonate of baryta is formed on the surface. The extract from the flesh of the ox, calf, or horse, at certain stages of its concentration, forms pellicles of organic matter on its surface, which must be removed as often as they are formed.

When the extract has been evaporated to about $\frac{1}{20}$th part of its volume, and has assumed a syrupy consistence, it is put into a moderately warm place, and evaporation slowly allowed to go on; very soon there appear on its surface small, short, colourless needles, which increase in numbers by standing and cooling of the fluid, so that the walls of the vessel gradually become covered by them. These crystals are creatine. They are freed from the mother-liquor by filtration, washed with water, lastly with alcohol, and dissolved in boiling water. Should this solution be coloured, it is boiled with a little animal charcoal, and, after filtration, will be as clear as water. On cooling, it deposits creatine in perfectly pure crystals.

According to Gregory,[1] creatine is obtained cheaply from cod, which, when chopped, well mixed with little more than its own weight of water, and pressed out, yields a fluid which, when neutralized (after the coagulation of albumen) by baryta, filtered to separate the phosphate of baryta, and gently evaporated till, on cooling, it forms a thin jelly, deposits, on standing, creatine in large crystals, nearly pure.

The heart of the ox is another convenient material, rich in creatine. The cheapest material from which to obtain creatine is urine. The method of obtaining creatine from urine I shall describe under creatinine.

Physical properties.

Creatine crystallizes in the clinorhombic system: all axes

[1] 'Quarterly Journ. of the Chem. Soc.,' i, p. 25. 'Handbook of Organ. Chemistry,' 3rd edit., 1852, p. 444.

unequal, two at right angles to each other in a horizontal plane, the third axis inclined in a plane cutting either of the other two axes. The clinodiagonal inclined to the principal axis in an angle of 70° 20′; inclination of the planes ∞ P : ∞ P in the orthodiagonal principal section = about 133° 2′. Specific gravity of the crystals = 1·35 to 1·34.[1] The crystals are colourless, perfectly transparent, and lustrous. They are connected with each other in tufts and groups, and then resemble acetate of lead (vide plate ii, fig. 5).

Chemical properties.

Creatine is easily soluble in boiling water; a solution saturated at that temperature becomes on cooling a mass of fine lustrous needles. From a dilute solution, however, creatine crystallizes very slowly in rather large crystals, which may attain a length of from one fourth to three eighths of an inch, and a thickness of one eighth of an inch, and will further increase in size if left in the mother-liquor for some time.

1000 parts of water at 64°4 F (18°C.) dissolve 13·44 creatine, or one part of creatine dissolves in 74·4 water.

In cold alcohol creatine is almost insoluble, one part requiring 9410 parts of alcohol for solution. It is more soluble in spirits of wine containing some water.

The watery cold solution of creatine, which contains a very small amount of that substance, possesses for that reason a weak, bitterish taste, and causes a sensation of irritation in the pharynx. If the solution contains a trace of a foreign organic substance, it changes very easily, mouldy vegetations form in it, and it assumes a disgusting odour.

Creatine even in the largest quantity does not neutralize the acid reaction of the weakest acid; it does not possess a basic character; it is soluble in baryta water at a higher temperature, but crystallizes out of the cooling solution without having undergone any change. The crystals so obtained contain no baryta, and from the solution the whole of the baryta may be precipitated by carbonic acid.

Decompositions.—On being boiled with baryta water, creatine is decomposed, ammonia being evolved on the one hand, and carbonate of baryta in crystalline granules formed on the other. This decomposition will take place even though the air be entirely excluded from influencing the substance.

[1] Heintz, 'Poggend. Ann.,' lxxiii, p. 595.

In solution there remains an organic base of the composition $C_6H_7NO_4$, sarcosine. This formula, when deducted from the elements of creatine, leaves a formula which exactly corresponds to the composition of urea.

1 equiv. creatine . . .	$C_8H_{11}N_3O_6$ less
1 equiv. sarcosine . . .	$C_6H_7\ N\ O_4$
Remain urea . . .	$C_2H_4\ N_2O_2$

It is, therefore, evident that ammonia and carbonic acid are products of a secondary decomposition and derived from the urea.

A solution of permanganate of potash in which creatine is dissolved loses its red colour only after standing some length of time in a higher temperature. No gas is evolved during this process. The fluid after decoloration does not any longer contain creatine, but yields white crystals on evaporation, and the potash is in part combined with carbonic acid.

The influence of strong mineral acids is very remarkable. A solution of creatine, to which at the ordinary temperature hydrochloric acid has been added, gives on spontaneous evaporation crystals consisting of unchanged creatine. If, however, the solution is heated with strong hydrochloric acid, creatine cannot be obtained any longer from the solution. The same effect is obtained by either sulphuric, phosphoric, or nitric acid. If creatine is dissolved in one of these acids, and the solution is evaporated at a gentle heat, crystals are obtained which are easily soluble in alcohol, a property which does not belong to creatine. These crystals contain a portion of the acid in chemical combination; they are, in fact, the salts of the acid with an organic base, creatinine. This transformation of creatine into creatinine under the influence of mineral acids consists essentially in the elimination from the former of four equivalents of water.

1 equiv. creatine	$= C_8H_{11}N_3O_6$ less
4 equiv. water	$= H_4\ O_4$
1 equiv. creatinine	$= C_8H_7\ N_3O_2$

Physiology of Creatine.

Creatine being present in the muscles, striated and organic,[1]

[1] Gorup-Besanez, loc. cit., p. 121.

of all classes of vertebrate animals, and being absent from the brain, liver, and kidneys of the same animals, it becomes highly probable that it stands in a certain relation to the chemical changes in these organs in which it is found. It seems to be a product of the chemical action induced in the muscle by the influence of motion. For in wild and hunted animals, such as foxes and game, the quantity of creatine contained in the muscles is much larger than in domesticated animals. This difference in the amount of creatine produced in the muscular tissue is very strikingly exhibited in the same class of animals.

A fox which had been fed on meat for two hundred days, at the Anatomical Institution in Giessen, did not yield one tenth part of the quantity of creatine which was obtained from an equal weight of the flesh of foxes which were caught by hunting.

The amount of creatine contained in the muscles of an animal stands in a close relation to the quantity of fat deposited in the animal, or to the causes which determine the deposition of fat. From fat meat there are frequently obtained only traces of creatine, and under all circumstances a much smaller quantity than from lean meat with an equal amount of fibrous matter. The above-mentioned fox, which had been fed on meat, yielded above one pound of fat from the peritoneal folds, while in hunted or otherwise chased foxes no fat was perceptible to the eye. The heart of the ox, a never-resting muscle, contains a large amount of creatine, and is therefore frequently used for producing it in quantities.

Creatine is present in the blood, by which it makes its way to the kidneys. It occurs in the urine as a regular ingredient, though present in small quantities only. It is partly transformed into creatinine, most probably somewhere between the muscle and the urinary residue out of which the zinc salt crystallizes. For, in the muscle, creatine has by far the preponderance over creatinine; in the urine, creatinine over creatine.

Creatine is, therefore, truly excrementitious: its relation to urea proves this beyond doubt. Its exclusive occurrence in the muscles shows the seat of its formation; it is, with other matters, a product of the chemical changes in the muscles.

Quantity discharged in twenty-four hours.

This question seems of sufficient importance; but few observations have been made on it. My own experiments, detailed at the end of this chapter, yield 0·305 grammes of creatine

discharged in the urine during twenty-four hours, as the average of twenty-six days of two individuals. In disease the quantity of creatine, together with that of creatinine, might serve to indicate the intensity of any spasmodic or convulsive action. The question as to its quantity in tetanic and epileptic disease is one of high interest. Cases of paralysis agitans, in which the spasmodic action ceases with sleep, may perhaps afford good opportunities for demonstrating the influence of rest and motion; though the different nutrition in the muscle may, perhaps, vary the chemical changes in some degree.

These suggestions for future researches must not be mistaken for theories or suppositions.

CREATININE.

The *composition* of creatinine in 100 parts is as follows:

8 equivalents of carbon	48	42·48
7 „ hydrogen	7	6·19
3 „ nitrogen	42	37·17
2 „ oxygen	16	14·16
Atomic weight of creatinine	113	100·00

The formula is $C_8H_7N_3O_2$.

Occurrence.

Creatinine is found in the muscles of the vertebrate animals in small quantities, and in the urine of man in larger quantities than in the muscles. It is the product of the natural or artificial decomposition of creatine, as already described.

Mode of obtaining Creatinine and Creatine from Urine.

The urine is neutralized with some milk of lime, and a solution of chloride of calcium is then added, so long as a precipitate of phosphate of lime is produced. The fluid is then filtered and evaporated until the salts are deposited. The mother-liquor is then separated from the salts (without the use of alcohol), and mixed with one twenty-fourth of its weight of a syrupy solution of neutral chloride of zinc. After the lapse of three or four days, a great part of the chloride of creatinine and zinc, with some creatine, has crystallized in yellow, roundish, warty granules. The deposit is washed with water, then dissolved in boiling water, and to this solu-

tion hydrated oxyde of lead is added, until the fluid gives an alkaline reaction to test-paper. The threefold amount of the oxyde of lead used up to this point is now added, and the fluid kept boiling, until it appears to coagulate into a light yellow magma. The decomposition is now completed. Zinc, hydrochloric acid, and lead in the form of the basic oxychloride are thus transformed into an insoluble condition; the substance combined with them before the addition of the lead remains in solution. The latter is now treated with some animal charcoal, which removes a yellow colouring matter and a trace of oxyde of lead, and is then evaporated to dryness. There remains now a white crystalline body—a mixture of two substances, which may easily be separated by alcohol, as the one dissolves easily in boiling alcohol, in which the other is almost insoluble. A portion of the crystalline residue, when heated with eight or ten times its weight of alcohol, either leaves a residue, or dissolves completely; and the solution deposits crystals on cooling: these crystals are identical in their properties with the residue, if any was left. If these crystals are removed from the mother-liquor, and the latter is evaporated, a new crystallization of a different form and different properties is obtained. The body remaining as a residue, or crystallizing first, contains water of crystallization, and is without reaction upon vegetable colours; the other in its watery solution is strongly alkaline, its crystals do not disintegrate by losing water, and the chemical analysis shows that the body which crystallizes first is creatine, and the other creatinine.

Mode of obtaining Creatinine from putrid Urine.

If putrid urine, in which the whole of urea is transformed into carbonate of ammonia, be boiled with milk of lime, until ammonia is not any longer evolved, the fluid then filtered, evaporated to a syrupy consistence, and treated with one twenty-fourth part of its weight of a syrupy solution of neutral chloride of zinc, there will, in the course of a few days, be deposited a considerable quantity of a yellow granular body, which contains chlorine and zinc, and, under the microscope, cannot be distinguished from the zinc salt obtained from fresh urine in the manner above described. When dissolved in boiling water, and freed from the chloride of zinc and colouring matter by means of hydrated oxyde of lead and animal charcoal, the organic substance, which was combined with the zinc, appears as pure creatinine without any admixture of creatine.

During putrefaction of the urine, therefore, creatine is decomposed, while creatinine undergoes no change.

Creatine is an accidental and variable admixture of the salt of creatinine with chloride of zinc. A warm—not boiling—solution of creatine is not precipitated by chloride of zinc, and the crystals deposited from it are free from chlorine and zinc, and have the characters of pure creatine.

It is evident that when fresh urine contains creatinine in combination with an acid, and free creatine, the creatinine will be set free by neutralization with an alkali; and if this fluid be now concentrated and evaporated to about one twentieth of its original volume, a combination of creatinine will be precipitated by the addition of chloride of zinc, the crystals of which will, however, be mixed with crystals of creatine, as soon as the latter is present in a larger quantity than the fluid can retain in solution at the ordinary temperature of the air.

Mode of obtaining Creatinine from Creatine.

If creatine be treated with concentrated hydrochloric acid, the solution evaporated, and the dry mass heated in the water-bath until all free hydrochloric acid has been driven out, the residue consists of pure chloride of creatinine. From this salt the creatinine is obtained by boiling its solution in water with hydrated oxyde of lead.

In a similar manner creatinine is obtained from the sulphate, by adding to the boiling watery solution carbonate of baryta, until the fluid shows an alkaline reaction, and no more carbonic acid is evolved. Sulphate of baryta is precipitated, and pure creatinine remains in solution.

Physical properties.

Creatinine, according to Kopp,[1] crystallizes in the monoclinometric (clinorhombic) system. The crystals are formed by the prism ∞ P, the basic terminal plane 0P, and the clinodiagonal terminal plane ∞ P ∞. The orthodiagonal is shorter than the clinodiagonal. The angle 0P : ∞ P ∞ (the angle, namely, at which the principal axis is inclined to the clinodiagonal) was found $= 69° 24'$. The angle at which the lateral planes ∞ P coincide in the orthodiagonal section is $= 98° 20'$: and accordingly the angle formed by ∞ P ∞ with ∞ P is $= 130° 50'$. (vide plate ii, fig. 6.)

[1] Liebig, loc. cit., p. 44.

Chemical properties.

Creatinine is much more soluble in cold water than creatine. 1000 parts of water dissolve 87 parts of creatinine, or one part dissolves in 11·5 parts of water at 60° F. (15° C.) In hot water it is much easier soluble.

The watery solution restores the blue colour to reddened litmus paper. A crystal of creatinine, placed upon a piece of wet turmeric paper, produces a brown stain on the spot where it lies. In concentrated solutions it has a caustic taste, like dilute liquor of ammonia.

Creatinine dissolves in boiling alcohol, and crystallizes from the solution on cooling. 1000 parts of alcohol at 60° F. (15° C.) dissolve 9·8 parts of creatinine, 102 parts dissolve one part.

The chemical character of creatinine is quite that of ammonia.

A moderately concentrated solution of nitrate of silver, to which a solution of creatinine is added, coagulates immediately into a mass of delicate white needles, which are easily soluble in hot water, but crystallize out of it on cooling, without having undergone any change. They consist of a basic combination of creatinine with nitrate of silver.

In a solution of corrosive sublimate, creatinine produces immediately a white curdy precipitate, which, in the course of a few minutes, transforms into a heap of delicate, transparent, colourless needles.

In a watery neutral solution of chloride of zinc, creatinine produces immediately a crystalline precipitate, in the form of roundish, warty granules, which, under the microscope, are seen to consist of delicate needles in zeolithic arrangement. (vide plate iii, fig. 1.)

Creatinine expels ammonia from its salts, and forms blue crystallizable double-salts with the salts of oxyde of copper.

Chloride of platinum produces no precipitate in solutions of chloride of creatinine. If the mixture of the two solutions is, however, evaporated at a gentle heat, dark-yellow, transparent, rather large crystals are formed, which are pretty easily soluble in water, less soluble in alcohol. This salt has a composition similar to the double-salt of chloride of platinum and ammonium.

Combinations.

Chloride of creatinine.—On exposing crystallized creatine

in Liebig's drying apparatus, at a temperature of 240° F. (100° C.), to a current of dry hydrochloric acid gas, the weight of the apparatus increases at first; on continuing, however, the high temperature and current of hydrochloric acid gas for some time, very nearly the original weight of the apparatus is at last obtained. During the experiment water is constantly seen to leave the apparatus, until the weight of the apparatus remains stationary. If dried creatine be taken for the experiment, the apparatus shows an increase in weight. The body produced under these circumstances is neutral chloride of creatinine.

In the same manner, chloride of creatinine is obtained by dissolving creatine in concentrated hydrochloric acid, in a china dish, evaporating the solution, and heating the residue in the water-bath until all free hydrochloric acid has disappeared.

This salt contains one equivalent of hydrochloric acid and one equivalent of creatinine. It is easily soluble in boiling alcohol, and crystallizes from this solution in short, transparent, colourless prisms, which are easily soluble in water. On evaporation, it is obtained in large transparent laminæ of an acid reaction.

Chloride of creatinine + chloride of platinum.—A solution of chloride of creatinine, when mixed with chloride of platinum, and gently evaporated, yields rosy crystals, prisms of the double-salt. On rapid formation, this salt is obtained in yellowish-red, transparent granules. It contains 30·95 per cent. of platinum.

Sulphate of creatinine.—On adding to one part of creatine an equal weight of dilute sulphuric acid (composed of 27 parts of concentrated sulphuric acid and 73 parts of water), evaporating to dryness, and heating until all moisture is volatilized, neutral sulphate of creatinine is obtained. It may also be produced by adding to a boiling saturated solution of creatinine dilute sulphuric acid, until a strongly acid reaction is perceived, and evaporating to dryness. A white crystalline mass is thus obtained, easily soluble in hot alcohol. On cooling, the solution becomes milky, and, on becoming clear, deposits transparent, concentric, quadratic plates of neutral sulphate of creatinine. They remain transparent and clear at a temperature of 240° F. (100° C.)

Chloride of zinc + creatinine.—On adding a syrupy solution of neutral chloride of zinc to a concentrated solution of creatinine, a white granular precipitate is immediately pro-

duced, the microscopical appearances of which I have already described. This may be filtered from the mother-liquid after twenty-four hours, washed with cold water, in which it is very little soluble. It is much more soluble in boiling water, and crystallizes from a saturated solution, on slow evaporation in large granules, warts, and groups of needles. This salt, mixed with creatine, constitutes the substance originally obtained by Pettenkofer, and produced from urine by the first method.

From this salt and from the chloride creatinine may be separated by boiling with hydrated oxyde of lead, in the manner described for the first method. From the sulphate, creatinine may be obtained by adding to its boiling watery solution carbonate of baryta, until effervescence is not any longer produced, and the fluid has got an alkaline reaction. Sulphate of baryta being thus formed, pure creatinine remains in solution.

Observations on the quantity of Creatinine and Creatine discharged in given times by healthy individuals.

Observation 1.—Five days' urine from *A*, 28 years of age, weight of body 70 kilogrammes, was treated for creatinine and creatine by Liebig's process. The zinc salt was decomposed by hydrated oxyde of lead. The mixture of the two substances obtained was separated by alcohol, the alcoholic solution of creatinine was evaporated to dryness in a water-bath. The drying process was completed with a chloride-of-calcium-tube and an air-pump. There was obtained, creatinine, 3·1292 grammes.

The creatine which constituted the residue from the alcoholic extraction was washed into a silver capsule with boiling water, and evaporated to dryness. Its weight was creatine, 2·0475 grammes.

This gives 0·6258 grammes of creatinine per day, and 0·4095 grammes of creatine per day.

Observation 2.—Four days' urine from *A*, treated as usual, the zinc salt decomposed with lead, no charcoal used.

There were obtained, creatinine, 1·4532 grammes, equal to 0·3633 grammes for twenty-four hours.

The alcoholic extraction left creatine, 1·2120 grammes, equal to 0·3030 grammes for twenty-four hours.

Observation 3.—Two days' urine from *B*, aged 28, weight of body 72 kilogrammes. There were obtained two portions

of chloride of zinc creatinine, the second portion not quite pure. It was, therefore, recrystallized, and, together with the first, dissolved in boiling water. The zinc was then precipitated by sulphuretted hydrogen, after a little ammonia had been added to the solution. The mixture stood for several days to allow of perfect precipitation of the sulphuret of zinc. But when the filtrate was evaporated, redissolved, and, after a new filtration, re-evaporated, there was always again sufficient sulphuret of zinc formed to constitute an impurity. During these proceedings it was found that the ammonia which had been added, and which must have formed chloride of ammonium with the hydrochloric acid from the zinc salt, was gradually driven out by the creatinine, and the last portions of it disappeared with the alcohol which evaporated from the creatinine. The hydrochloric acid was removed with oxyde of lead and charcoal, the filtrate evaporated, the mixture of the residue obtained was separated by alcohol, and the quantities of substances obtained were as follows:

2 days' creatinine . . .	0·8182	grammes.
2 days' creatine	0·6185	do.

The creatine contained yet a very slight amount of creatinine; the figures for creatinine are, therefore, somewhat below the actual amount, those of creatine a little higher.

1 day's creatinine . . .	0·4091	grammes.
1 day's creatine	0·3092	do.

Observation 4.—Five days' urine from *B*, yielded 4·363 grammes of chloride of zinc creatinine (and creatine, as an admixture). After having been dissolved in boiling water, and made alkaline with ammonia, a current of sulphuretted hydrogen was passed through the solution for several days; the yellowish-white sulphuret of zinc was thereby precipitated. The filtrate was boiled for a length of time to drive the ammonia out of its combination, it was then evaporated, and the dried residue was treated with alcohol. There were obtained, chloride of creatinine, 2·4072 grammes, which is equal to 2·93 grammes chloride of zinc creatinine, which, deducted from the above 4·363 grammes of zinc salt, leaves 1·433 grammes for the creatine contained in the zinc salt as an admixture.

The creatine obtained weighed 1·1201 grammes.

Creatine calculated . . .	1·433	grammes.
Creatine found	1·1201	do.
Loss	0·3129	do.

This loss, when distributed over the different operations, and in part accounted for by the abstraction of colouring matter by the lead and the charcoal used for the purpose, cannot be called excessive, though it is still considerable. The experiment illustrates the proportions between the creatine on the one hand, and the creatinine zinc salt on the other, contained in the crystallized substance obtained from the urine.

Secreted in five days,	creatinine	1·8322	grammes.
Do. do.	creatine	1·1201	do.
Secreted in one day,	creatinine	0·3664	do.
Do. do.	creatine	0·2240	do.

Observation 5.—Five days' urine from *B*, yielded 6·7663 grammes of crystallized substance (chloride of zinc creatine and creatine mixed), washed and dried. From this the amount of creatinine and creatine was ascertained by calculation, upon the basis of the parts found in the fourth observation.

If 4·3630 grammes of crystallized zinc salt yielded 1·8322 grammes of creatinine, how much would be obtained from 6·7663 grammes of zinc salt?

$$4{\cdot}3630 : 1{\cdot}8322 = 6{\cdot}7663 : x$$

$$\frac{1{\cdot}8322 \times 6{\cdot}7663}{4{\cdot}3630} \quad 2{\cdot}8373 \text{ grammes}$$

of creatinine secreted during five days.

$$4{\cdot}3630 : 1{\cdot}1201 \text{ (creatine)} = 6{\cdot}7663 : x$$

$$\frac{1{\cdot}1201 \times 6{\cdot}7763}{4{\cdot}3630} = 1{\cdot}7370 \text{ grammes}$$

of creatine secreted during five days.

Secreted in one day,	creatinine	0·5674	grammes.
Do. do.	creatine	0·3474	do.

Observation 6.—Five days' urine from *A*, yielded a quantity of crystallized zinc salt, which was washed, redissolved in boiling water, filtered, evaporated, and dried. When dry, it was a powder-like mass of a light-yellow colour, a sample of which, when burned on platinum foil, left pure oxyde of zinc on the foil. When exposed to the air, it attracted very little moisture. Its weight, when perfectly dry, was 4·6324

grammes. The amount of creatinine and creatine was calculated upon the basis of observation 4.

$$4{\cdot}3630 : 1{\cdot}8322 = 4{\cdot}6324 : x$$

$$\frac{1{\cdot}8322 \times 4{\cdot}6324}{4{\cdot}3630} = 1{\cdot}9453 \text{ grammes}$$

of creatinine contained in the zinc salt.

$$4{\cdot}3630 : 1{\cdot}1201 = 4{\cdot}6324 : x$$

$$\frac{1{\cdot}1201 \times 4{\cdot}6324}{4{\cdot}3630} = 1{\cdot}1892 \text{ grammes}$$

of creatine contained as an admixture in the zinc salt.

There was a second portion of crystallized substance obtained from the mother-liquor. It was, however, impossible to free it from impurities, and it could, therefore, not be approached by quantitative analysis. The above values are, therefore, only expressive of a minimum, since there was certainly more creatine and creatinine present in the urine than could be obtained pure.

The above observations of the quantity of creatinine and creatine discharged by healthy individuals in a given time, have been arranged in the following tables :

Individual.	Number of Observation.	Number of days observed.	Grammes of					Remarks.
			Zinc salt obtained from urine.	Creatinine of relative days.	Creatine of relative days.	Average of Creatinine in 24 hours.	Average of Creatine in 24 hours.	
A, man, 28 years of age, weighs 70 kilogrammes.	1	5	—	3·1292	2·0475	0·6258	0·4095	Obtained direct.
	2	4	—	1·4532	1·2120	0·3633	0·3030	
	6	5	4·6324	1·9453	1·1892	0·3890	0·2378	By calculation from zinc salt.
B, man, 28 years of age, weighs 72 kilogrammes.	3	2	—	0·8182	0·6185	0·4091	0·3092	Obtained direct.
	4	5	4·3630	1·8322	1·1201	0·3664	0·2240	
	5	5	6·7663	2·8373	1·7370	0·5674	0·3474	By calculation from zinc salt.

Individual.	Number of Observation.	Number of days observed.	Grains of		Remarks.
			Average of Creatinine in twenty-four hours.	Average of Creatine in twenty-four hours.	
A.	1	5	9·66	6·32	Obtained direct.
	2	4	5·61	4·68	
	6	5	6·00	3·67	By calculation from zinc salt.
B.	3	2	6·31	4·77	Obtained direct.
	4	5	5·66	3·45	
	5	5	8·76	4·36	By calculation from zinc salt.

CHAPTER VI.

COLOURING MATTER—URÆMATINE.

In treating of the colour of urine as one of its physical characters, we have already made the distinction between the colouring matter of the urine proper, and those colouring principles which are accidental admixtures. Starting from the probability, in support of which we must give a few facts hereafter, that the normal colouring principle of urine is derived from the pigment of the blood or hæmatine, we have adopted the name of uræmatine; this denomination may be considered as corresponding to Heller's urophæine, and to a series of terms which were never generally introduced, and which it will therefore not be difficult to relinquish.

The *elementary composition* of uræmatine is not yet ascertained, principally because no substance has as yet been found with which it would combine in unvariable proportions. But there are certain tests at present which promise to lead ultimately to a satisfactory analysis of this substance.

The principal *physical property* of uræmatine is its colour. In a pure and dry state it is dark red; but when dissolved in alcohol and ether it is of a bright red, like port wine. To the urine it imparts all the varieties of colour with which we are acquainted; its presence in larger quantities will cause the deep tints, in small quantities the light tints, of that fluid, provided that the presence of abnormal pigments be out of the question.

Chemical properties.

Uræmatine combines with lime in uncertain proportions, and is separated from this combination by a mixture of alcohol and hydrochloric acid.

It has a greater affinity for ether than for either alcohol or water.

It is insoluble in nitric, hydrochloric, sulphuric, tartaric, and oxalic acids; soluble in ammonia, solutions of soda and of potash, and in chloroform.

On combustion it leaves a small residue, consisting exclusively of oxyde of iron. By this fact its relation to hæmatine is satisfactorily established.

It adheres with remarkable obstinacy to the salts of the urine, and therefore Berzelius applied to it the name of halophile.

The following is Scherer's[1] plan for isolating the uræmatine:

By adding a solution of basic acetate of lead to urine, a precipitate is obtained, which consists of lead, several acids of the urine, and a certain amount of colouring matter. The whole of the colouring matter cannot, however, be precipitated by the basic acetate, a circumstance which leads to the conclusion, that either the substance uræmatine consists in fact of two distinct bodies, or is decomposed by the influence of the basic acetate.

The precipitate of the basic acetate of lead, when digested in alcohol acidulated by hydrochloric acid, yields lead to the acid and colouring matter to the alcohol, which latter on evaporation leaves the colouring matter as a blackish mass. The latter is freed from any acids by careful washing with water, in which it is insoluble. This insolubility shows that the substance must have undergone a change during the several operations for obtaining it in an isolated state.

Another smaller quantity of colouring matter is precipitated by neutral acetate of lead.

These precipitates, both with basic and neutral acetate of lead, contain from 6·25 to 8·83 per cent. of nitrogen, from 56 to 66 per cent. of carbon, and from 4·10 to 7·45 per cent. of hydrogen.

These experiments of Scherer have been continued under his superintendence by Dr. G. Harley,[2] who found that the precipitate of colouring matter with the basic acetate of lead could be separated into three or four constituents. But none of these matters have been obtained either crystallized, or in a certain combination with other known substances. They may therefore be the products of decomposition, and have at present no claim to be considered either as normal ingredients of the urine or as defined chemical entities.

[1] 'Med. Gazette,' 1845, pp. 363, 410.

[2] 'Verhandl. des Würzburger Physic. Vereins,' Band v, 1854.

Dr. Harley's method of obtaining uræmatine is as follows: A large quantity of urine is evaporated to the consistence of molasses, the salts being removed from the fluid whenever crystallized. The residue is then extracted by alcohol. The latter is brought to a boiling heat, when milk of lime is added until all the colour has disappeared. The mixture is now filtered, when the combination of uræmatine with lime remains on the filter, and is washed out by means of ether and water. This compound, after having been dried, is digested in alcohol acidulated by hydrochloric acid; the alcoholic solution is filtered off, mixed with its volume of ether, and put aside for several days, during which time it must, however, be frequently shaken, in order to make the alcohol yield as much uræmatine to the ether as possible. The ether and alcohol are then separated by the addition of water. The etherial solution, which has a fine colour of red wine, must now be washed with water, in order to free it from the traces of acid, salts, and resinous substances that may be dissolved in it. This washing must not be continued too long, because a little uræmatine is precipitated with every fresh quantity of water. The substance so obtained shows the properties above described.

It is quite evident that such a method of analysis is not available for clinical purposes, or for quantitative researches. And as we have no other direct chemical analysis for uræmatine which would at all come up to the modern requirements of chemistry, the indications of this ingredient of the urine are not easily to be determined.

Happily, however, we possess a method, for which we are indebted to Professor Vogel,[1] which enables us to estimate the quantity of uræmatine present in any urine with a tolerable degree of accuracy, and permits us to draw valuable conclusions regarding the diagnosis and prognosis of disease, and its therapeutical indications.

It has been ascertained that a deeply coloured urine, when diluted wth various quantities of water, will produce all the lighter tints of more frequent occurrence. From this it was reasonable to conclude that the various tints are only dilutions of one and the same description of colouring principle. Taking certain colours as starting points, a scale of tints was produced by mixing urine of the former colour with its equal volume of water. By this a tint was produced which was the next fixed point in the scale, and so on. These colours had to be expressed in material substances, for the purpose of

[1] 'Archiv des Vereins für gemeinschaftliche Arbeiten,' Bd. i, p. 137, 1853.

procuring a standard which everybody might ascertain. The scale and its material representatives were therefore arranged as follows, and as is represented in the table affixed to the volume:

I. First Group. *Yellowish Urines.*

The colour is yellow (gamboge), mixed with a greater or lesser amount of water. Starting with the perfectly colourless urine, this group has three gradations or nuances:

1. Pale yellow (gamboge with much water).
2. Light yellow (gamboge with less water).
3. Yellow (gamboge with very little water).

II. Second Group. *Reddish Urines.*

With the yellow there is mixed a greater or lesser amount of red (gamboge with crimson lake). These urines are generally termed "highly coloured." There are again three varieties of this group:

4. Reddish-yellow. An admixture of some red to the prevailing yellow (gamboge with a little crimson lake).
5. Yellowish-red. The red colour becomes more prominent in the yellow body of the fluid (gamboge with more crimson lake).
6. Red. The red colour is prevalent, but there is still a slight admixture of yellow (crimson lake with little gamboge).

III. Third Group. *Brown (dark) Urines.*

The red colour passes through brown to almost black tints (gamboge, crimson lake, and more or less Prussian blue).

7. Brownish-red. Red with an admixture of a little brown.
8. Reddish-brown. There is more of the brown colour than in the last.
9. Brownish-black. Almost black, but with a touch of the reddish-brown.

Though a delicate eye may yet distinguish several varieties of intermediate colours, yet the nine tints just described are all that are useful to be distinguished at the bedside.

We now come to the determination of the unit in the corresponding varieties of urine. As the absolute quantity of uræmatine is not known which is required in a given bulk of urine to produce a certain colour, our unit must be a

philosophical one; that is, it must be comparatively correct to coincide with the scale in such a manner, that every urine of any given colour of the scale, by dilution with its equal amount of water, may produce the next following dilution, and that the darkest urine, on being diluted the necessary number of times, will produce all the colours of the scale in succession; in other words, that the gradations of the unit are simple multiplications by two.

The unit, then, is the amount of uræmatine, or colouring matter, contained in 1000 c.c. of the first variety, or pale-yellowish urine. This amount, no matter to how much it may amount in real weight, is put down as = 1. 1000 c.c. of yellow urine (III) therefore contain four times as much uræmatine as 1000 c.c. of the first variety; and 1000 c.c. of yellow urine will require three times their own bulk of water for becoming of the pale-yellow colour of variety 1. The following table is intended to represent these relations more perspicuously:

I.	II.	III.	IV.	V.	VI.	VII.	VIII.	IX.	
1	2	4	8	16	32	64	128	256	Pale yellow = I.
	1	2	4	8	16	32	64	128	Light yellow = II.
		1	2	4	8	16	32	64	Yellow = III.
			1	2	4	8	16	32	Reddish-yellow = IV.
				1	2	4	8	16	Yellowish-red = V.
					1	2	4	8	Red = VI.
						1	2	4	Brownish-red = VII.
							1	2	Reddish-brown = VIII.
								1	Brownish-black = IX.

This table shows how much uræmatine is contained in equal parts of urine of different colours. To illustrate it with another example; if a certain volume of pale-yellow urine contains 1 part of uræmatine, the same volume of reddish-yellow urine contains 8 parts, and the same volume of reddish-brown urine 128 parts of uræmatine. One volume of yellow urine, on the other hand, contains just as much colouring matter as 4 volumes of pale yellow; 1 volume of red urine the same quantity as 4 volumes of reddish-yellow urine. If, therefore, an individual discharge 1000 c.c. urine of yellow colour in twenty-four hours, and another, during the same period of time, 4000 c.c. of pale-yellow urine, both discharge equal quantities of uræmatine during the same time. And if an individual discharge any number of c.c. of urine of a certain colour during a given time, the amount of colour-

ing matter thereby discharged is ascertained by simple equation. For example, in twenty-four hours there were discharged 1800 c.c. of urine of yellow colour; 1000 c.c. contain 4 parts, how much do 1800 contain?

$$1000 : 4 = 1800 : x$$

$x = 7{\cdot}2$ = the amount of uræmatine contained in 1800 c.c. of yellow urine.

In order to obtain uniform results by this method, it is essential that the urine be absolutely clear. It has, therefore, to be filtered in most instances. Its colour must be ascertained by transmitted light, and for this purpose the body of urine should be of a diameter of not less than four or five inches.

Several objections have been raised against this method, which have been answered satisfactorily by its originator. It is quite clear that in cases where the colour of the urine depends on any other substance than uræmatine, it would give erroneous results. But these cases can, in the first instance, easily be detected by the tests given when treating of the colour of urine; and, in the second instance, they are of rare occurrence as compared with the great number of instances in which the urine is coloured by the ordinary uræmatine only.

In some rare cases the urine on dilution will not yield the colours which would correspond to the scale. In these cases it may be doubtful whether a red urine contains 32 times, or a brownish-red urine 64 times the amount of uræmatine contained in the same quantity of pale-yellow urine. It may well be admitted that modifications of the uræmatine occur, which have a different colouring power from that of the ordinary substance. Admitting all this, we may still coincide with Vogel in the opinion that, for approximative determinations of the quantity of uræmatine discharged in a given time, the method is useful. An error is not so dangerous, if we know the extent to which it can be committed, and the sources from which it may arise. Of the sources we have spoken; we can say less of the extent, as we do not know to what quantity of uræmatine a certain colour corresponds. The highest amount of error to which, in the opinion of Vogel, his method might be liable, is one third or one fourth of the figures found. Fluctuations, therefore, within these limits might be left out of the question; but when they surmount certain boundaries, they may with safety be used for the comparison of the quantity of uræmatine contained in two different descriptions of urine. Thus, if the quantity

of uræmatine which is discharged in the urine by a healthy individual in twenty-four hours amounts to 4, and we find that in the urine of a patient, for twenty-four hours, it amounts to 16 or 20, there can be no doubt that the quantity of uræmatine discharged by the latter is double or three times the amount of that discharged in the same time by the healthy individual. If, on the other hand, we find in the urine of a patient the amount of uræmatine to be 1 for twenty-four hours, its quantity is clearly diminished. If, however, we find 3·5, or 4·5, as the amount of uræmatine in the urine of a sick person, we could not say with certainty whether the amount of uræmatine was diminished or increased in this case.

Physiology of Uræmatine.

It is very probable that a number of blood-corpuscles are constantly undergoing the process of disintegration in the blood, and that the hæmatine which is thus set free, however changed from its original character, finds its way out of the body in the form of colouring matter of bile (cholæmatine) and uræmatine. We know the indestructible nature of hæmatine, how obstinately it retains its colour under the most varied circumstances, whether in extravasations within the body, or during artificial or natural processes of decomposition out of the body. We know, moreover, that the changes of colour which hæmatine undergoes under certain circumstances in the body—for example, when effused into a bruise under the skin or epidermis—correspond with the destructive changes in the blood; so that hæmatine thus effused will go through all the stages of colour from red to green, yellow, and pale yellow—the colours which are found in the cholæmatine and uræmatine. From this property of retaining its colour under the most varied circumstances, it is highly improbable that hæmatine, after having served the economy, should leave the body as a colourless substance. And if it, therefore, is probable that effete hæmatine is discharged as a coloured substance, the only excreta which are coloured, namely, fæces and urine, most probably owe their colour to effete hæmatine. If we, moreover, take into consideration that the purest uræmatine always contains some iron in chemical combination, it can scarcely be doubted that it is the offspring of the colouring matter of the blood-corpuscles.

The *quantity of uræmatine* which, according to Vogel, is discharged by an adult healthy person in twenty-four hours,

amounts to from 3 to 6 of the above units, and, on an average, to about 4·8, which, calculated upon the hour, gives 0·2.

Quantity of Uræmatine in Disease.—Pathological Indications.

According to the observations of Professor Vogel, which may be verified by daily observation at the bedside, the amount of uræmatine discharged during acute febrile diseases is considerably increased, and, notwithstanding a considerable decrease in the total quantity of urine, amounts to 16, 20, and more. This amount becomes even much higher in typhoid and septical fevers, which are combined with dissolution of the blood. In accordance with this we observe, that in the course of all these diseases the amount of blood-corpuscles in the blood becomes so considerably diminished as to cause an anæmic, or better oligocythæmic, condition. In a number of pneumonic patients the daily amount of uræmatine fluctuated during the acme of the disease between 16 and 24. During the acme of a case of acute rheumatism it was 30 to 32. In a case of typhus in a man it was for some days 80 to 100. In a case of lead colic I found it 64 for three days. In a case of scarlatinous nephritis I found it on two occasions 256 for twenty-four hours.

In cases where the disintegration of the blood-corpuscles is diminished, as in chlorosis and anæmia, in hysterical and nervous diseases, and in the convalescence from severe diseases, the quantity of uræmatine discharged during a given time is generally diminished. In these cases the condition of the urine affords valuable therapeutic indications, as pointing to the exhibition of tonics, in particular iron.

In chlorotic patients the daily quantity of uræmatine is frequently below 1; in the convalescence from severe diseases it is frequently, for some length of time, not above 1 or 2 (Vogel). In a case of ovarian tumour I found it below 1 (*vide* p. 75). This urine resembles that of young children who are growing fast, but has of course a different significance.

CHAPTER VII.

HIPPURIC ACID.

Composition.

Symbol: $\overline{H}$.

Composition in 100 parts:		
	Carbon	60·335
	Hydrogen . . .	4·469
	Nitrogen . . .	7·821
	Oxygen. . . .	22·347
	Water	5·028
		100·000

From this composition the following formula is derived: $C_{18}H_8NO_5 + HO$, or $C_{18}H_9NO_6$.

History and Literature.

Rouelle (1784), *Fourcroy* and *Vauquelin* (1799) 'Journ. d. Pharm.,' von S. B. Trommsdorff, v, p. 197; vii, p. 199, found it in the urine of graminivorous animals, but mistook it for benzoic acid.

Scheele, Fourcroy, and *Reynard* demonstrated its existence in the urine of young infants.

Proust, 'Ann. de Chim. et de Phys.,' xiv, 260 (1820), found it as benzoic acid in the distillate from putrid urine.

Liebig, 'Poggend. Ann.,' xvii, p. 389 (1830), demonstrated hippuric acid to be a peculiar substance, distinct from benzoic acid, with which it had been confounded.

Ure, 'Med.-Chir. Transact.,' vol. xxiv, and *Keller,* 'Ann. d. Chem. und Pharm.,' xliii, p. 198, proved that benzoic acid is transformed in the body into hippuric acid.

Liebig, 'Ann. d. Chem. und Pharm.,' l, p. 161, proved its existence as a normal ingredient in the urine of man.

Dessaignes, 'Compt. rend.,' xxi, p. 1224, found that glycocoll combines with benzoic acid to form hippuric acid.

In the course of his researches on putrefied urine, Proust made the observation that during the distillation of such

urine, to which some sulphuric or hydrochloric acid had been added, acetic acid and benzoic acid were evolved, the latter of which was deposited in crystals in the neck of the retort. Liebig, in repeating these experiments, found that after neutralization of the acetic acid so obtained by the addition of oxyde of lead, there was formed in the fluid a considerable amount of a white precipitate, which consisted of pure benzoate of lead. The presence of benzoic acid in putrefied urine could, moreover, be proved by concentrating the urine, adding some sulphuric acid, and letting it stand for several days, after the lapse of which benzoic acid was found to have formed in brown glistening scales. No urine which was subjected to this test by Liebig during a period of three months was found to be void of this acid.

There could be no doubt that benzoic acid was not contained as such in the fresh urine, inasmuch as it had been proved to certainty by the experiments of Ure and Keller, that crystallized benzoic acid is transformed in the body into hippuric acid, and appears in the urine as hippurate of soda. As it was furthermore known that the hippuric acid in the urine of graminivorous animals is decomposed during the putrefaction of this urine, and that benzoic acid is one of the products of that decomposition, it was to be supposed with certainty that the benzoic acid discovered in the putrefied urine of man had the same origin, and in the fresh urine was present in the form of hippuric acid. On a closer examination, Liebig found this to be the fact. All urine of individuals taking mixed food was found to contain hippuric acid in about equal proportions with uric acid.

Occurrence and Methods of obtaining it pure.

Hippuric acid is a regular ingredient of the urine of man[1] and the graminivorous animals—the horse, (from which it derives its name) horned cattle, camels,[2] and elephants. It is found in guano,[3] as hippurate of ammonia, and has been observed in the excreta of a tortoise (*Testudo Græca*), and in the excreta of the larvæ of butterflies, and of butterflies themselves.[4] It has been found in the blood of calves and oxen by Verdeil and Dollfus.[5] It is absent from the urine of

[1] Liebig, 'Ann. d. Pharm.,' xxxvii, p. 82.
[2] Schwarz, ibid., liv, p. 31.
[3] Marchand, 'N. Journ. d. Pharm.,' vii, p. 134.
[4] T. Davy, 'Edinb. New Philos. Journ.,' xlv, p. 17.
[5] 'Ann. d. Chem. und Pharm.,' lxxiv, p. 215; also Lehmann's 'Physiolog. Chemistry,' Cavend. Soc. Edit., vol. ii, p. 212.

animals exclusively carnivorous. It may, however, be made to appear in their urine by giving them, with their food, hippuric acid, or any substance capable of forming it. When Schwarz[1] had given to a dog some hippuric acid, it made its reappearance in the urine. Buchheim[2] found that when free hippuric acid, hippurate of soda, or acid hippurate of ammonia were taken, a quantity of hippuric acid was obtained from the urine, which was so large that scarcely any acid could have been lost in its passage through the organism.

The amount of hippuric acid in the urine may be considerably increased by the ingestion with the food of benzoic or cinnamic acids, or essential oil of bitter almonds. Any amount up to 10 grammes of benzoic acid, whether taken as such, or in combination with bases, soda, ammonia, magnesia, iron, will in the course of a few hours or over night, appear in the urine as hippuric acid. The hippuric acid in each case corresponds in quantity to that of the benzoic acid taken (Buchheim). Dr. Garrod[3] obtained, however, only 15 to 29 grains of hippuric acid, after having taken from 20 to 30 grains of benzoic acid. Marchand[4] obtained 39·2 grains of hippuric acid from the urine after having taken 30·0 grains of benzoic acid. The consumption of a large amount of fruit, such as apples (Pettenkofer) or plums (*Prune Claude, Prunus domestica chlorocarpa*, Duchek), will cause a considerable quantity of hippuric acid to appear in the urine. Duchek[5] examined the greengage, and found benzoic acid in it, but not in sufficient quantity to account for the whole of the hippuric acid found in the urine after the use of a certain quantity of that fruit. He accordingly is of opinion that the greengage might contain some other compound of benzoyle capable of being transformed into hippuric acid. Duchek did not find hippuric acid to be a constant constituent of human urine. Hoefle[6] could never find it in his urine.

Pathologically an increased amount of hippuric acid is met with in the acid urine of fever-patients (Lehmann), in the urine of diabetic patients (Lehmann's[7] and Hünefeld's[8] observations both confirmed by Duchek). In one instance hippuric acid was observed in the scales from ichthyosis

[1] Loc. cit., p. 32.
[2] 'Archiv für Physiol. Heilk.,' 1857, vol. i, p. 122.
[3] 'Philos. Magaz,' xx, p. 501.
[4] 'Journ. of Pract. Chem.,' lxxv, p. 309.
[5] 'Prager Vierteljahrschrift,' 1854, vol. iii, p. 25. See also the 'Lancet,' July 26, 1856, p. 114.
[6] 'Chemie und Microscop am Krankenbette.'
[7] 'Journ. d. Pract. Chem.,' vi, p. 112.
[8] Ibid., viii, p 552.

(Schlossberger). Sometimes it occurs together with uric acid as a sediment.

By the following method hippuric acid can be obtained from comparatively small quantities of fresh human urine:

Fresh urine is evaporated in the water-bath to a syrupy consistence, and, after the addition of some hydrochloric acid, is shaken with its equal volume of ether, which dissolves the hippuric acid. In most cases the mixture does not separate, because the ether is inclosed by the fluid in a sort of lather; but the separation of the ether takes place immediately, if, after the mixture has stood for an hour, one twentieth of its volume of alcohol be added. In that case the lather disappears and the fluid separates into two layers, of which the upper and lighter one contains the hippuric acid; but, at the same time, there is some urea dissolved in it, by means of the alcohol which has been added. This layer is now carefully removed by means of a pipette and shaken with small portions of water; the alcohol and urea combine with the water, and the hippuric acid alone remains dissolved in the ether. By evaporation it is obtained in crystals, which generally are of a yellowish or brown colour, from a resinous substance, which may be easily and perfectly removed by animal charcoal.

From the urine of horses or cows the acid may sometimes be obtained in the form of a yellowish-brown powder, by the addition of hydrochloric acid. It is, however, preferable to concentrate the urine to one sixth or one eighth of its original volume before adding hydrochloric acid. The hippuric acid thereby obtained is very much coloured. It is therefore advisable to remove as much colouring matter as possible from the urine before concentration. For this purpose it is mixed with an excess of milk of lime, and boiled for some minutes; the decanted fluid is evaporated to one sixth or one twelfth of its volume, and after cooling mixed with an excess of hydrochloric acid. After the lapse of about twelve hours the crystallization of hippuric acid is completed.

The crystals so obtained have yet a brownish colour and a disagreeable urinous odour, which must be removed by a purifying process. The solution in water is boiled with some caustic lime and filtered; to the filtrate chloride of lime is added until the urinous odour has disappeared; animal charcoal is now mixed with the fluid until the filtrate is colourless; the filtrate is mixed with hydrochloric acid, and, on cooling, deposits hippuric acid perfectly white and pure (Liebig). In this proceeding some hippuric acid is perhaps transformed into benzoic acid, and therefore some chemists

prefer the following proceeding, by Bensch.[1] The impure acid is mixed with ten parts of boiling water and an excess of milk of lime; the fluid is decanted, and the deposit pressed in a bag of calico; the united solutions are now treated with solution of alum until the alkaline reaction has disappeared, cooled down to 104° F. (40° C.), treated with solution of carbonate of soda as long as a precipitate is being produced, and again freed from the deposit by decantation and filtration through calico by the aid of pressure. From this solution hippuric acid is precipitated by means of hydrochloric acid. The precipitate, after washing with water, is pressed, dissolved in boiling water, and the solution treated with one part of animal charcoal upon sixteen parts of hippuric acid; and, after filtration through paper when boiling hot, is allowed to crystallize.

Physical properties.

Pure hippuric acid, prepared from human or animal urine, appears in long, glistening, transparent prisms, four-sided parallel to the longest axis, the ends acuminated by two or four planes, being planes of prisms parallel to the brachy- and macro-diagonal. The primary form is a vertical rhombic prism, whose planes are inclined at an angle of 94° 50′. The planes of the brachy-diagonal (horizontal) prism are inclined at an angle of 94° 50,′ those of the macro-diagonal (also horizontal) prism at an angle of 85° 14.′[2] Some microscopical crystals from human urine are represented on Pl. II, fig. 4.

Chemical properties.

This acid is destitute of odour, and is of a bitterish taste. It requires for solution 600 parts of water 32° F. (0° C.) temperature, and 400 parts of water at the ordinary temperature of the air; but is much more soluble in hot and boiling water and in alcohol. Its solubility in ether is somewhat less than in alcohol. The solutions redden litmus paper.

Decompositions.

Hippuric acid is not volatile at the temperature at which benzoic acid sublimes. At a higher temperature it deliquesces, forming a brownish-red liquid, which on cooling becomes

[1] 'Ann. d. Chem. und Pharm.,' lviii, p. 267.
[2] Gorup-Besanez, loc. cit., p. 191.

a milk-white crystalline mass. By dry distillation it yields a red oil, which has the odour of the Tonka bean ("the pride and flower of the snuff-box"), ammonia, and benzoic acid (the latter two, perhaps, in part as benzoate of ammonia) and a large residue of charcoal. Sometimes the acid before charring evolves a cyanogen compound, having the odour of hydrocyanic acid. If the temperature during dry distillation be not raised above 482° F. (250° C.), benzoic acid is obtained, slightly reddened, a trace of hydrocyanic acid, and benzonitrile is collected in the receiver.

Hippuric acid is soluble in warm nitric acid, and hot hydrochloric acid, and from both solutions crystallizes on cooling; but when boiled for some time in either of these solutions it undergoes a decomposition, by which benzoic acid crystallizes out of the solution on cooling. Combined with the nitric acid there remains glycine, or glycocoll, or sugar of gelatine. This decomposition may also be produced by sulphuric and oxalic acids, and by boiling with caustic soda or potash. From this mode of decomposition Dessaignes concluded that hippuric acid was a combination of benzoic acid and glycine, and that by the artificial combination of these two bodies hippuric acid might be produced. He succeeded in producing hippuric acid by exposing a combination of glycine with oxyde of zinc to the influence of chlorine-benzoyle.

Under the influence of a ferment, in the presence of an alkali, hippuric acid undergoes the same decomposition into benzoic acid and glycocoll.[1] The disintegration of hippuric acid in putrefying urine is thus satisfactorily explained.

Hippuric acid is the amide of a new acid, benzoglycolic acid,[2] which is free from nitrogen, and has the composition $C_{18}H_8O_8$. It is formed when hippuric acid is acted on by hyponitrous acid, and is obtained by conducting a current of oxyde of nitrogen through a solution of hippuric acid in nitric acid.

$$\underbrace{C_{18}H_9NO_6}_{\text{Hippuric acid.}} + NO_3 = \underbrace{C_{18}H_8O_8}_{\text{Benzoglycolic acid.}} + 2N + HO.$$

Benzoglycolic acid crystallizes from the solution in colourless prisms, which are easily soluble in alcohol and ether, but sparingly soluble in water. It forms neutral salts with one equivalent of base, which are mostly crystallizable. The lime-salt, $CaO, C_{18}H_7O_7$, crystallizes in colourless needles, and has a tendency to form oversaturated solutions.

[1] Buchner, 'Ann. d. Chem. und Pharm.' lxxviii, p. 203.
[2] Socoloff and Strecker, 'Ann. d. Chem. und Pharm.,' lxxx, p. 17.

When benzoglycolic acid is treated with dilute acids it is decomposed to benzoic and glycolic acid after the formula

$$\underbrace{C_{18}H_8O_8}_{\text{Benzoglycolic acid.}} + 2HO = \underbrace{C_{14}H_6O_4}_{\text{Benzoic acid.}} + \underbrace{C_4H_4O_6}_{\text{Glycolic acid.}}.$$

This decomposition explains why hippuric acid, although it be the amide of benzoglycolic acid, does not yield that acid and ammonia when boiled with acids, but benzoic acid and glycocoll. The benzoglycolic acid is at first formed along with ammonia, but is immediately decomposed into benzoic and glycolic acid, and the latter, with the ammonia, forms its amide, glycocoll, and water.

Hippuric acid, when treated with oxydizing agents,[1] *e. g.*, peroxyde of lead in water, yields benzamide, carbonic acid, and water, according to the following formula.

$$\underbrace{C_{18}H_9NO_6}_{\text{Hippuric acid.}} = \underbrace{C_{14}H_7NO_2}_{\text{Benzamide.}} + 4CO_2 + 2HO.$$

Compounds of Hippuric Acid.

Nitrohippuric acid.[2] $C_{18}H_8N_2O_{10}$.—To a solution of hippuric acid in cold fuming nitric acid, an equal volume of oil of vitriol is gradually added, care being taken not to let the mixture get hot. After two hours the reaction is completed. The fluid is now mixed with three times its volume of water, being continually kept at a low temperature. The mixture, after twelve hours, has deposited about one half of the hippuric acid employed in the form of nitrohippuric acid in needle-shaped crystals. The mother-liquor, when neutralized by carbonate of soda until it begins to get turbid, deposits another quantity of the acid. The impure acid is washed with cold water, combined with lime, and the solution of the lime-salt in lukewarm water is precipitated by hydrochloric acid.

Nitrobenzoic acid may be taken internally, in quantities amounting to 6 grammes per diem, without injury to the system. It reappears as nitrohippuric acid in the urine, from which it may be obtained by the following proceeding. The acid urine is evaporated to a small bulk. It remains clear on the addition of hydrochloric acid; the fluid is now shaken

[1] Fehling, 'Ann. d. Chem. und Pharm.,' xxviii, p. 48.
[2] Bertagnini, 'Compt. Rend.,' xxxi, p. 490.

with ether and some alcohol, which take up nitrohippuric acid, and, on spontaneous evaporation, deposit it in brown warty crystals, which, when removed from the mother-liquor, dried on a brick, and recrystallized from hot water, appear as brownish needles. When boiled for five minutes with excess of milk of lime, colouring matter is removed, and the filtrate, on decomposition by hydrochloric acid, yields pure nitrohippuric acid, which is obtained in fine crystals by recrystallization from hot water.

Hippuric Acid Salts—Hippurates.

The alkaline and earthy hippurates are soluble in water. Hippurate of soda seems to be a combination which occurs in human urine. But as hippuric acid in human urine, when present in larger quantities, crystallizes on simple evaporation on the surface of the fluid, there is, *à priori*, great probability that it may also be present in a free state. But as it cannot easily have existed as such in the blood, an explanation would be required of the agency by which, in the moment of secretion, or afterwards, it was deprived of its base. This must at present remain a subject for future inquiry. In the urine of the horse hippuric acid is combined with lime. Metallic hippurates are sparingly soluble. All hippurates yield their bases to hydrochloric acid, hippuric acid crystallizing from the solution in delicate silky needles.

The hippurates may be basic, neutral, or acid salts; that is, containing either one half, or one or two equivalents of acid to one of base.

Hippurate of baryta, neutral. $C_{18}BaH_8NO_6+HO$ (crystals).—By dissolving hippuric acid in excess of baryta water, and precipitating the excess of baryta by a current of carbonic acid, or by boiling an excess of carbonate of baryta in a solution of hippuric acid, a solution of neutral hippurate of baryta is obtained after filtration, which on evaporation yields the salt in crusts, consisting of microscopic quadratic prisms.

Hippurate of lime. $C_{18}CaH_8NO_6+3\ HO$.—By boiling an excess of carbonate of lime in a solution of hippuric acid, a filtrate is obtained, which on evaporation deposits this salt in rhombic prisms, or glistening scales. It is also obtained by boiling a solution of hippuric acid with excess of milk of lime, filtering, and passing a current of carbonic acid gas through the solution. The filtrate contains the salt. This compound is said to occur in the urine of the horse and cow. It is soluble in 18 parts of cold, and 6 parts of boiling water.

Hippurate of lead, neutral, $C_{18}PbH_8NO_6+3HO$, is obtained by mixing the hot solution of an hippurate with solution of acetate of lead; on cooling the salt is deposited in laminæ of the lustre of mother of pearl. If cold solutions of lead and hippurate are mixed, the salt precipitates at once in cheesy flakes, which are with difficulty soluble in boiling water. The precipitate may be washed on a filter, dissolved in boiling water, and after filtration while boiling hot, on a funnel, kept hot, is obtained from the cooling solution in silky groups of fine needles. These needles contain only two equivalents of water of crystallization, but frequently transform into the salt with three equivalents of water, by suddenly taking up one equivalent of water under circumstances not yet accurately known. A basic hippurate of lead is obtained by boiling hydrated oxide of lead in a solution of hippuric acid.

Hippurate of iron.—The soluble hippurates cause a rusty brown precipitate in salts of the oxyde of iron. Neutral sesqui-chloride of iron produces a light isabell yellow voluminous precipitate in a cold solution of hippurate of potash, which in hot water, or by drying at a temperature of 30° C., looses water, and forms a brown mass like Canada balsam. It is insoluble in water, easily soluble in spirits of wine, particularly in hot spirits, and from the solution separates on cooling, partly in amorphous masses, partly in groups of red oblique rhombic prisms.

The salts with cobalt, nickel, copper, mercury, and silver, present no peculiarities.

Deposits of Hippuric Acid.

As the type of hippuric acid deposits we may consider the crystals which form, on evaporation, in urine containing the acid in solution. They are the long needle-like rhombic prisms in a variety of combinations, the crystals forming in groups of a stellar arrangement. The characters which, I may say, distinguish the hippuric acid deposit at first sight from the uric, are the small amount of colouring matter it contains, the needle-like habitus, and the stellar arrangement. The hippuric acid crystals have a tendency to become club-shaped at their ends. This tendency eventually ends in the apposition of many acicular crystals to the end, or both ends, of a single prism.

Deposits of hippuric acid are by no means common. I have seen only two instances of this kind; and in one of them benzoic acid had been administered as a medicine. The

second case was that of a young married lady, who suffered from a severe attack of colic. The observation is, however, not sufficiently accurate to be recorded at full length. Vogel[1] has observed several times that needle-like crystals of hippuric acid projected like spears from larger crystals of uric acid. In such a case it is best to collect the deposit on a filter, and afterwards to boil it in alcohol. The alcoholic solution leaves the crystals of hippuric acid on evaporation.

The deposits of hippuric acid are by no means due to the same individual causes as those of uric acid, though the same causes may co-operate to produce such deposits. For, hippuric acid being more soluble in water, it follows that the acid must be present in excess before any deposit can take place. This is known to be not requisite for a deposit of uric acid. Any sediment of hippuric acid can therefore only have been produced by the co-operation of two causes: 1, an acid present in the urine, to separate hippuric acid from its base; 2, an excess of hippuric acid over the saturating point of the urine at a certain temperature.

Quantity of Hippuric Acid secreted in twenty-four hours.

Beyond the assertion of Liebig that hippuric acid was present in human urine in about the same proportion as uric acid, we possess no observations on this point. These observations are the more necessary, as Duchek has negatived the opinion of Liebig, now generally received, that hippuric acid is a constant constituent of human urine.

Physiology.

Benzoic acid, introduced into the stomach, appears in the urine as hippuric acid. One or several drachms of benzoic acid in a glass of grog may thus be taken; and, after the slight irritation of the glottis has passed away, not the least inconvenience is experienced by the individual subjected to the experiment. I observed, however, that a strong feeling of sickness followed the ingestion of a dose of one drachm in a glass of grog. It disappeared in the course of half an hour. Benzoic acid appropriates to itself glycine. The question now arises, where that combination takes place, whether in the intestinal canal, in the portal blood, in the liver, or in any other part of the system? This question must be

[1] Loc. cit., p. 201.

answered by experiment; and we must take care not to be biassed by the presence of glycine in the bile, combined with choleic acid as glycocholic acid.

So far the observations are clear that, if benzoic, cinnamic, nitrobenzoic acids, or any substances containing them, are taken internally, they appear in the urine as hippuric and nitrohippuric acids. But, as the food of most people does not contain any benzoic acid as far as we know, the regular appearance of hippuric acid cannot be the consequence of diet only. Even Duchek found that his greengages did not contain a sufficient quantity of benzoic acid to account for the whole amount of hippuric acid found in his urine after eating them; and he therefore takes refuge in a supposition, that there was another compound of benzoyle present in the fruit, which was capable of forming hippuric acid. The strongest argument has been brought by Liebig.[1] The urine of cows is always equally rich in hippuric acid, no matter whether they feed on hay or on mangel wurzel. Now, as the latter has been found by direct analysis, and by experience in the manufacture of sugar, not to contain any benzoic acid, we cannot draw any other conclusion from the presence of hippuric acid in the urine of herbivora and of man, than that it is a product of the organism, to the formation of which the elements of the food give the materials. Proust[2] and Guckelberger[3] both observed the formation of bitter oil of almonds, and, secondarily, of benzoic acid, as one of the products of oxydation of albuminous substances. We may, therefore, by analogy, think it possible that the oxydation of albuminous substances in the body may yield some benzoic acid, as a collateral product, in small quantity. These considerations point to a difference between the oxydation of albuminous substances in herbivorous animals and in carnivora. The urine of the latter has not been observed to contain any hippuric acid, and the urine of cows always contains this acid, even when their food is decidedly free from benzoic acid. The explanation of this difference, if it really exist, will have to be sought by further experiments.

Regarding the physiological bearing of hippuric acid in animals, the observations seem to show that rest and activity, as well as different descriptions of food, have a considerable influence upon the quantity in which it is found in the urine. According to Liebig,[4] rest seems to favour the production of

[1] Loc. cit., p. 171.
[2] Gehlen's 'Neues Journ. d. Chem.,' ii, p. 241.
[3] 'Ann. d. Chem. und Pharm., lxiv, p. 39.
[4] 'Thierchemie,' 3te Aufl., p. 86.

hippuric acid, and the urine of horses contains a larger amount of it when they are not overworked. In accordance with this statement, Erdmann and Marchand[1] found the urine of horses kept for private use to contain much hippuric acid; that of horses used for ploughing, however, contained only benzoic acid. Hutstein[2] also observed that the urine of private horses, which had yielded hippuric acid exclusively, contained only benzoic acid after they were used for hard work. Dr. G. Bird[3] says that both hippuric and benzoic acids will disappear from the urine of over-driven animals. He could not detect a trace of either in the urine of an ox which had been driven up from the country to Smithfield, and killed a few hours after.

The influence of some descriptions of food has been investigated by Landerer,[4] who found that the urine of horses would only yield hippuric acid while they were fed on oats and hay, and did not yield any while fed on barley and straw. Riley[5] also found the urine of calves to yield hippuric acid only while feeding on grass or hay; and Schwartz[6] observed that the urine of cows contained only traces of hippuric acid when fed on the residue from the distillation of spirits.

The occurrence of benzoic acid in the fresh urine of animals is at least problematical.[7] Much more problematical, however, is rendered the influence of either work or rest upon the quantity of hippuric acid secreted by animals, through the following statements of Roussin.[8] He found that horses fatigued produce much hippuric acid, and little urea. Horses well fed and quiet produce little or no hippuric acid; urea, on the contrary, is found in their urine in very large proportions. The limpidity of the liquid may be the index. If it be clear, and deposit little carbonate of lime, it has much urea and little hippuric acid; if it be muddy, it is certain that there is much hippuric acid. Upon this fact Roussin builds a speculation on the transformation of hippuric acid into urea, and *vice versâ*, the very nature of which, however, makes the character of his analyses still more doubtful than they appear at first sight, from the fact of their being in direct opposition to the results of the analyses enu-

[1] 'Journ. d. Pract. Chem.,' xxvi, p. 492.
[2] 'Brande's 'Neues Archiv d. Pharm.,' lxvi.
[3] Loc. cit., p. 201.
[4] 'N. Journ. d. Pharm.,' xx, p. 288.
[5] Ibid., xxii, p. 354.
[6] 'Ann. d. Chem. und Pharm.,' liv, p. 31.
[7] Gorup-Besanez, loc. cit., p. 171.
[8] I have taken this from an extract in the 'American Journal of Science and Art,' July, 1856, No. 64, p. 102.

merated above. In the following analyses he determined the urea in the form of the dry nitrate:

	Description of Horse.	Grammes of Hippuric acid in one litre.	Grammes of Urea in one litre.
1	Omnibus-horses . . .	7·8	
2	,, ,, at work . .	10·0	18·0
3	Arabian stallions completely quiet.	0·0	32·0
4	,, ,, ,,	0·0	35·0
5	,, ,, ,,	0·0	33·0
6	,, ,, ,,	0·0	34·0
7	Horses at work	5·0	21·0
8	,, fatigued by a long course.	13·0	12·0
9	Horse after a very long course .	14·0	15·0

These analyses should be repeated with the whole of the urine discharged in twenty-four hours; in other words, with regard to time. The urea is, moreover, to be determined by a more accurate method than that through the antiquated nitrate.

Pathological occurrence.

The case of a girl, suffering from chorea, who lived on apples, bread, and water, and discharged an excess of hippuric acid, has been recorded by Pettenkofer.[1] In a case by Bouchardat, milk diet is blamed as the cause of a discharge of two parts, in a thousand of the urine, of hippuric acid, by a woman suffering from a variety of severe disorders. A case observed by Dr. Garrod[2] relates to a young man who, under certain circumstances, discharged a urine which, on the addition of an acid, yielded crystals of hippuric acid. Half a pint of urine yielded 40 grains of the acid. No information as to the source of the hippuric acid could be obtained from the history of the patient. It is denied that he had ever taken any benzoic acid, so that, if no imposition was practised by the patient, there is at all events some mystery about his case.

A large quantity of hippuric acid is present in the acid urine of fever patients, of which it is said to cause, in part at least, the acid reaction. The observer of this fact, Lehmann, has also found hippuric acid in diabetic urine, in every instance in which he has sought for it. In one instance 100 parts of urine yielded 0·025 parts of crystallized hippuric acid. I

[1] 'Ann. d. Chem. und Pharm.,' lii, p. 86.

[2] Originally communicated in Dr. G. Bird's work, p. 303. The first two cases may also be consulted there in detail.

have already mentioned that Hünefeld and Duchek have confirmed Lehman's observations.

The last observation is that of Schlossberger, already mentioned. He found hippuric acid in the scales of ichthyosis. We have not yet been informed whether it was accidentally present in a single case, or whether it is of frequent or constant occurrence in that disease.

The reader will think this a very unsatisfactory chapter, and so indeed it is. We want observations, for which there is a large field open. But undoubtedly some technical difficulties will have to be overcome first, before the analysis of hippuric acid can be made with sufficient accuracy.

CHAPTER VIII.

CHLORINE AND CHLORIDES.

Remarks on the Incineration of Urine.

The solid residue of the evaporation of urine, when exposed to a red heat for the necessary length of time after the complete combustion of all organic ingredients, leaves an ash, which is made up of the so-called incombustible salts. Accurate analysis has shown that this ash does not contain the inorganic salts in the same condition in which they were dissolved in the urine; from which we must conclude that, under the united influences of heat, the oxygen of the air, and the reducing quality of the charred animal matter, they have undergone certain considerable changes. The acid phosphate of soda, for example, when intimately mixed with carbon, will, under the influence of red heat, give off a part of its acid, which is reduced at the same time, and volatilized in the form of phosphorus and carbonic acid. But the most considerable loss which the fixed salts incur by the process of incineration is that of chlorine. Indeed so considerable is this loss, that Becquerel found, as the average quantity of chlorine discharged by healthy adult persons in twenty-four hours, only 0·66 grammes, which is scarcely one tenth of the average of chlorine actually removed by the urine. From this it is evident that the mode of determining the fixed salts by incineration of the residue of the urine after evaporation is quite useless for analytical purposes, as are also the whole of the analyses made by that method. But even were the analyses by incineration approximatively correct, yet evaporation and incineration take so much trouble and time, that the process is entirely unavailable for practical purposes. These reasons are

quite sufficient for us altogether to abandon the proceeding in determining the acids, and without regret, as we possess volumetrical and other methods of the highest accuracy, by means of which the amount of any of the acids in combination with the fixed bases in the urine may be determined.

CHLORIDE OF SODIUM. NaCl.

Composition and Occurrence.

Sodium . .	23·3
Chlorine . .	35·5
NaCl . . .	58·8 = equiv. chloride of sodium.

A physiological law makes this substance the common accompaniment of our food. Salt is a necessary to man and animal, and nature finds means and ways to supply it to both. Like oxygen, which composes two thirds of our globe, salt is found everywhere. Its solubility in water equals the diffusibility of oxygen; and thus it penetrates the masses. There is probably no water on the globe which does not contain it, and consequently it pervades the vegetable and the animal kingdoms. Of all waters, sea and mineral water contain the greatest abundance of it. It occurs, moreover, in a solid crystalline state, mostly imbedded in layers of gypsum, and then is termed rock-salt. Of this we have to make an important use in the quantitative analysis of the chloride of sodium of the urine. For, no salt being so pure as rock-salt, a solution of it in water serves as the basis for the preparation of all the tests which are required for the volumetrical method.

Crystallography.

Chloride of sodium crystallizes in the cubic system. The cleavage of rock-salt leads to a cube, and crystallizations of salt from pure solutions always assume this form. If, however, certain organic substances are mixed with the solution, the crystallization will ensue in the form of the regular octahedron. Chloride of sodium, therefore, when crystallizing out of the urine or other animal fluids, always appears in octahedra. The latter are best obtained by evaporating a large amount of (one day's) urine to a thin syrupy consistence, and letting it stand over night. The crystals will be found in the sediment on decanting the supernatant fluid, and are good objects for microscopical observation.

Chemical properties.

Chloride of sodium dissolves in water of from 54° to 75° F. (12° to 24° C.), invariably at the rate of 31·84 parts in 100 parts of the saturated solution. For procuring the latter clear rock-salt is best used, as already described under Urea (p. 57).

In solutions of chloride of sodium, nitrate of silver produces a white precipitate, which is insoluble in nitric and hydrochloric acids. We make use of this test for removing chlorides from the urine when we wish to ascertain accurately the amount of urea by the volumetrical method. In the same solutions the nitrate of the suboxyde of mercury produces a precipitate of calomel (subchloride of mercury).

If a concentrated solution of chloride of sodium is mixed with a similar solution of nitrate of protoxyde of mercury, nitrate of soda and bichloride of mercury (corrosive sublimate) are formed, the latter transforming the fluid into a white magma of crystals. The same juxtaposition takes place in dilute solutions, with the difference, however, that the fluid remains clear, because the sublimate is kept in solution. In solutions which contain chloride of sodium and urea at the same time, no precipitation of urea by nitrate of protoxyde of mercury will take place, as long as any chloride of sodium is yet present untransformed into nitre and corrosive sublimate. Upon this test is based the volumetrical analysis of chloride of sodium by Professor Liebig.

Diagnosis in Urine.

As it is, in some cases, of interest to know whether chloride of sodium be present in the urine or not, it is useful to have a short qualitative test at hand for ascertaining the fact. This test is nitrate of silver. One caution only is required, namely, to strongly acidulate the urine to be tested with nitric acid, in order to prevent the precipitation of phosphate of silver. Or the nitric acid may be added after the nitrate of silver, when any phosphate of silver will be immediately dissolved.

Liebig's Method of determining the quantity of Chlorine in neutral fluids by means of Nitrate of Protoxyde of Mercury.

From the analysis of urea we are already acquainted with the fact, that nitrate of protoxyde of mercury produces a

copious white precipitate in a solution of urea. This precipitate is not produced with corrosive sublimate.

On mixing a chloride of any of the alkali metals with nitrate of protoxyde of mercury, a transmutation of the two salts into corrosive sublimate and a nitrate of the alkaline base takes place. We have already seen the result of this process as regards chloride of sodium.

If a solution of urea is mixed with some chloride of sodium, and a dilute solution of nitrate of protoxyde of mercury is then added in small portions, a white turbidity occurs on the spot where the two fluids mix with each other; but this turbidity immediately disappears if the fluid is shaken a little, and the latter remains as clear and transparent as before the addition of the nitrate; without the chloride of sodium it would have remained permanently thick. On the addition of the nitrate being continued, the precipitate will disappear until the whole of the chloride has been transformed into corrosive sublimate. Beyond this limit a single drop of the mercurial solution produces a permanent turbidity of the fluid.

From this it is evident that, if we know the amount of mercury contained in the solution of the nitrate of the protoxyde of mercury, which has been added to the solution of urea containing an unknown amount of chloride of sodium, until the permanent turbidity was produced, the amount of chlorine, or chloride of sodium, contained in that solution may be also known. One equivalent of mercury of the mercurial solution consumed, exactly corresponds to one equivalent of chlorine or chloride of sodium.

On the contrary, if the amount of chloride of sodium contained in the solution of urea be known, and the amount of mercury contained in the mercurial solution be unknown, it is easy to calculate the amount of mercury contained in the mercurial solution used.

This proceeding for ascertaining the amount of chloride of sodium is particularly applicable to the urine, because the addition of urea is here not required. It may, of course, be used with advantage for ascertaining the amount of chlorine contained in brine or sea-water, and, generally speaking, in all cases where a large number of analyses have to be made in the shortest possible time. If, however, the amount of chlorine in fluids not being urine is to be determined, the proceeding has to undergo some modification.

I have already described (pp. 54, 55) the simplest modes of obtaining solutions of the nitrate of the protoxyde of mercury. Care must be taken not to use the common mercury

of commerce, because it always contains lead and bismuth, which render the analysis of chloride of sodium uncertain. If either lead or bismuth be present in a solution of mercury, it will, on the latter being mixed with a solution of urea containing chloride of sodium, immediately cause a white turbidity or opalescence, which makes it impossible to see distinctly the point at which the combination of urea and oxyde of mercury begins to be precipitated.

If, therefore, it is the intention of the operator to use the common mercury of commerce, it will be best for him to transform it into crystallized protonitrate or nitrate of suboxyde of mercury, by boiling an excess of the metal in dilute nitric acid, concentrating and cooling the solution. The crystals of this salt are then separated from the mother-liquor, which contains the foreign metals; they are washed with dilute nitric acid, afterwards with a little water, by which process a part is transformed into basic salt. If the commercial nitrate of the suboxyde be used, this process of washing must always be gone through, because the manufacturers simply remove the crystals from the mother-liquor without washing them. Small pieces of the crystallized salt should not be used at all, because the yellowish mother-liquor adheres to them with such pertinacity, that it is difficult to remove it by washing without dissolving the greater part of the salt also.

The crystals of nitrate of suboxyde of mercury are now dissolved in nitric acid, and heated until the evolution of vapours of nitrous acid has entirely ceased, and a drop of the solution is no longer precipitated by chloride of sodium. The solution, after evaporation on the water-bath to a syrupy consistence, is diluted with ten times its own volume of water. If, after the lapse of twenty-four hours, any basic salt of the protoxyde has been precipitated, it may be removed by filtration.

In order to make this solution serviceable for the quantitative analysis of chloride of sodium it must be graduated, so as to contain a definite amount of nitrate of protoxyde of mercury in a given volume. This may be effected in two ways. It is either graduated directly by means of a solution of chloride of sodium of known strength, or, after the amount of protoxyde it contains has been determined, it may be diluted with as much water as is necessary, in order to make one cubic centimètre of this dilute mercurial solution indicate exactly 10 milligrammes of chloride of sodium. For both proceedings a solution of chloride of sodium is required, containing a known amount of this salt. The prepa-

ration of the standard saturated solution has already been described at p. 56. Of this saturated solution we take with a pipette, observing the usual caution, 20 c.c., and add 298·4 c.c. of water, whereby we obtain 318·4 c.c. of dilute solution of chloride of sodium, containing in all 2×3184 milligrammes of chloride of sodium; 10 c.c. of this solution contain, therefore, 200 milligrammes of chloride of sodium.

Preparation of mercurial solution graduated for chloride of sodium.—Ten cubic centimètres are measured by means of a small pipette delivering exactly that amount of fluid after having been filled up to the mark on the narrow tube. These 10 c.c. are poured into a small beaker; to this are added 3 c.c. of a solution of urea, containing in 100 c.c. 4 grammes of urea, in 1 c.c. therefore 40 milligrammes of urea. For measuring this latter solution a narrow test-tube is very serviceable, when marked with a file at the point to which it will be filled by any 3 c.c. of fluid. It does not matter whether a few drops more or less are taken.

The dilute solution of mercury to be graduated is now filled into a dropping glass or burette, and from this, and after noting down the level, it is added in drops to the solution of chloride of sodium containing urea, which is kept in a rotatory motion. The formation of a distinct and permanent precipitate indicates the completion of the test. An opalescence of the fluid must not be mistaken for the precipitate of urea and protoxyde of mercury. It is caused by a trace of foreign metal; it may easily be recognised as not proceeding from the completion of the test by the circumstance, that after its appearance the turbidity is not increased by the addition of a few more drops of the mercurial solution. If the precipitate has been caused by the compound of urea, every additional drop of the mercurial fluid produces an increase of the precipitate, and therefore makes the fluid thicker than it was before.

In graduating these fluids, I generally take the following caution. I measure 10 c.c. of water into a beaker, add 3 c.c. of the solution of urea, and then one or two drops of the mercurial solution to be graduated. The amount of precipitate thus produced shows the limit to which the addition of mercurial solution to the fluid containing a known amount of chloride of sodium must be carried, in order to be safe against the error from the opalescence of the mixture.

Suppose that there have been used for the production of the precipitate, in 10 c.c. of the solution of chloride of sodium, 7·8 c.c. of the mercurial fluid, the latter is too concentrated to

admit of accurate graduation; it is therefore diluted with its equal volume of water, and then tested a second time. Suppose that there have now been used, for 10 c.c. of the solution of chloride of sodium mixed with urea, 15·5 c.c. of the mercurial solution for the production of a permanent precipitate, then we add, to every 155 volumes of this mercurial solution, 45 volumes of water, whereby we obtain 200 volumes of a mercurial solution, of which 200 c.c. exactly indicate 200 milligrammes of chloride of sodium, or one cubic centimètre 10 milligrammes of chloride of sodium.

If, in the first test, we use 2·7 c.c. for 10 c.c. of solution of chloride of sodium, we then add five or six times the amount of water to it. The mercurial solution, which is to be graduated, must not be too different in concentration from the fluid required for the test, and which we are desirous of producing.

We finally ascertain the correctness of the measurements by an experiment. The degree of permanent precipitate produced by the addition of 20 c.c. to 10 c.c. of the solution of chloride of sodium and urea, must be borne in mind when performing the actual analysis for practical purposes. The only source of error connected with this quantitative analysis of chloride of sodium, is that an excess of the mercurial solution may be added, so that the precipitate is formed in excess; or that too little of the solution may be added, so that the turbidity is insufficient. But a little practice, and the caution recommended above, will soon teach us how to avoid this error.

The test-fluid, the preparation of which has just been described, is calculated for those cases in which, besides chlorides, there are no other salts and no excess of urea in solution. It is liable to lead to a small error, when used for the determination of chloride of sodium in the urine, which makes its apparent amount in urine smaller than in reality it is. This error is occasioned by the earlier appearance of the critical precipitate at the completion of the test, in cases where much urea and other salts are present, because the precipitate is less soluble in the more concentrated fluids. A deposit of nitrate of urea and protoxyde of mercury is of course not formed in the fluid, before the latter is saturated with the former. The mercurial solution always contains free nitric acid, which dissolves more of the nitrate of urea and protoxyde of mercury than water, and the latter more than a solution of nitrate of urea.

But as urine generally contains more urea than has been added to the solution of chloride of sodium for the purpose of its graduation, this urea takes a part of the free nitric acid of

the mercurial solution, forming nitrate of urea, which diminishes the solubility of the precipitate in the fluid. As the precipitate in that case appears earlier, less test-fluid is used, for producing the critical test. This error may be completely avoided by adding to the 10 c.c. of solution of chloride of sodium, to which 3 c.c. of the solution of urea have been added, 5 c.c. of a solution of sulphate of soda, saturated at the ordinary temperature of the air, and then graduating the fluid.

Nitrate of protoxyde of mercury, when added to a solution of sulphate of soda, produces a yellow pulverulent precipitate of turpeth mineral. If the sulphate of soda contain chloride of sodium, the addition of the nitrate of protoxyde of mercury will not form a precipitate of turpethum before the whole of the chloride of sodium has been transformed into sublimate, and the addition of the sulphate of soda modifies the experiment only in one way, namely, by the combination of the free acid of the mercurial solution with the sulphate of soda an acid salt is formed, which has the same effect as an excess of urea.

On adding urea, and afterwards nitrate of protoxyde of mercury, to a solution of sulphate of soda which does not contain any chloride of sodium, and may be tolerably dilute, the mixture becomes a gelatinous magma of a snowy-white combination, which contains sulphuric acid, urea, and protoxyde of mercury, and is a little less soluble in water than the corresponding nitrate.

The quantitative analysis of chlorine by means of a salt of silver is so accurate, that we cannot say that there is a more accurate one in existence. The method just described of finding the amount of chlorine or chloride of sodium by means of the nitrate of protoxyde of mercury is, however, by no means inferior as regards accuracy to the method which employs nitrate of silver. But the former is only suitable for neutral, very slightly acid, or alkaline fluids, because an excess of acid prevents the precipitation of the urea compound.

The only advantage of the nitrate of protoxyde of mercury over the silver salts consists in the circumstance, that the end of the experiment is indicated by the beginning of the reaction. In testing with the solution of silver the test is completed when no precipitate is any longer formed, and no reaction is perceived. In this case the thickness of the fluid, and the difficulty of making it clear, stand in the way of rapid execution. But, with the mercurial solution, some dozen analyses may be made in an hour; and it is, therefore, particularly applicable to technical proceedings;

for example, ascertaining the amount of chloride of sodium in sulphate of soda, and, after previous neutralization, in commercial soda.

The fluid applied to the urine.—Special proceedings.— Before the fluid can be applied to the urine, it is necessary to remove the phosphoric acid from the latter. This is done by the solution of baryta in the manner described at p. 61. The fluid filtered from the precipitate is alkaline from an excess of baryta. This alkaline reaction must be removed by the addition of nitric acid. The correctness of the analyses to be made mainly depends upon the caution not to add more nitric acid to the filtered liquid from the baryta precipitate, than is just necessary to produce a faint acid reaction. For this reason it is advisable to acidulate the whole filtered liquid before taking any part from it by means of dilute nitric acid; an excess of one drop of acid in 100 c.c. of fluid is of no consequence, while it would interfere with the accuracy of the analysis when added to the smaller quantity used for analysis.

For the test we take 15 c.c. of the acidulated fluid, corresponding to 10 c.c. of urine. This is done by means of a small pipette which exactly delivers 15 c.c. when filled to the mark in the narrow tube. The measured quantity is delivered into a small beaker, and being kept in a rotatory motion the mercurial solution is made to flow into it. After the turbidity has appeared, the amount of test-fluid used is read off the scale of the burette; every cubic centimètre used corresponds to 10 milligrammes of chloride of sodium.

The presence of chloride of sodium in the urine requires some modifications of the analysis for urea, which has already been described at p. 62, *et seq.* There it has been stated that, for very accurate analyses, the removal of the chlorine from the urine before the addition of the fluid graduated for urea became essential, and a graduated solution of nitrate of silver to be used for that purpose was described. In this case the analysis of chloride of sodium, by means of the mercurial solution, serves to indicate exactly the amount of solution of silver (graduated for the same amount of chloride of sodium as the mercurial solution) which has to be added to the urine for precipitating the whole of the chlorine contained in it.

Daily average amount of Chlorine discharged during health.

As the amount of chloride of sodium found in the urine by different observers is, in many instances, expressed by the amount of chlorine only, which has been found by analysis,

the reader will do well to take care not to confound figures expressing the amount of chlorine with those expressing the amount of chloride of sodium.

The first observations of the daily average amount of chlorine discharged by persons of different sexes and ages were made by Bischoff.[1] His results are as follows :

	Chlorine.	Chloride of Sodium.		
		Min.	Med.	Max.
	Grammes.	Gram.	Gram.	Gram.
Adult man, living well . . discharged	8·7	8·64	14·73	24·84
Woman, 43 years of age	5·5	—	—	—
Girl, 18 years „	4·5	—	—	—
Boy of 16 years „	5·3	—	—	—
Boy of 3 years „	0·8	—	—	—

Before Bischoff, Hegar[2] published a series of very accurate observations made upon eight young gentlemen, students at the University of Giessen. The daily average of chlorine discharged he found to vary in different individuals, and to fluctuate between 7·4 and 13·9 grammes. This gives for one individual of that class a daily average of 10 grammes of chlorine, corresponding to 16·5 grammes of chloride of sodium, and calculated for one hour it gives 0·44 grammes of chlorine, corresponding to 0·73 grammes of chloride of sodium. For the average of adult persons, however, the medium amount of chlorine discharged during twenty-four hours is not quite so high, and accordingly Vogel assumes for the majority of adult individuals 6 to 8 grammes as the average of chlorine discharged during twenty-four hours, corresponding to 10 and 13 grammes of chloride of sodium, which, calculated for one hour, gives 0·25 to 0·33 grammes of chlorine, equal to from 0·41 to 0·54 grammes of chloride of sodium. The figures given by Bischoff show some relative quantities in women and children.

That the amount of chlorine discharged during twenty-four hours varies in different individuals, undoubtedly depends mainly upon the fact that unequal amounts of chloride of sodium are ingested with the food by different persons. Sailors, who have lived on salt rations for the greater part of

[1] Loc. cit., p. 23, 1853.

[2] Hegar, Alfred, 'Ueber Ausscheidung der Chlorverbindungen durch den Harn,' Giessen, 1852.

their life spent afloat, will discharge an extraordinary amount of chlorine in their urine, because the ordinary food of our kitchen is insipid to them without the addition of an amount of salt that would make any ordinary person ill. These men may frequently be seen dipping sweet cake into the salt-cellar, and this inclination generally lasts for the remainder of their life on land. Common life shows how different are the tastes of individuals relative to the amount of salt in their food, and leads us to expect the differences which indeed we find.

The amount of chlorine discharged by an individual varies on different days, according to and corresponding with the amount of chloride of sodium taken with his food. When Falck ate strongly salt food on three successive days, he discharged the following respective amounts of chlorine, namely, 6·0, 7·8, and 10·3 grammes during twenty-four hours. But when he partook of food containing no addition of salt, he discharged 2·5, 1·6, and 0·9 grammes of chlorine on the three respective days succeeding the experiment. Professor Vogel observed the amount of chlorine discharged per hour by several individuals who had taken kitchen salt in doses not sufficiently large to purge them. In all, the amount of chlorine discharged per hour was increased, and rose from 0·4 grammes to 1·0, nay, even 1·8 grammes. In some, the chlorine which had passed into the blood was discharged again by the urine rapidly and in large quantities; while in others the discharge lasted longer, and the quantities for equal times were smaller.

The largest amount of chlorine per hour is secreted a few hours after the largest meal of the day, the smallest amount is invariably secreted during the night (*sleep*). In eight individuals examined by Hegar the average amount of chlorine discharged per hour was, in the afternoon, 0·57; in the night, 0·28; in the forenoon, 0·48 grammes. In one and the same person the average amount of chlorine per hour would vary between 0·20 as minimum and 1·32 grammes as maximum per hour, so that the maximum was more than six times as large as the minimum. From this we must conclude that *the secretory activity of the kidneys, as regards chlorine, is diminished during rest and sleep.* Though the blood be rich in chlorine taken with the food in the evening, yet the lowest amount of chlorine is discharged during the night. *Mental and bodily activity, on the other hand, will increase the secretory activity for chlorine of the kidneys at any time during the day or night.* This is particularly striking in the morning. For, though a person after a supper

containing plenty of salt may secrete a very small amount of chlorine during the sleep of the night following, and for breakfast may take food containing no addition of salt, or no food at all, or only a tumbler-full of water, yet the amount of chlorine discharged during the hours of the forenoon, when the mind and body are most active, and when the nutritive changes of the body are being rapidly effected, will be double the amount of that during the night. It will of course rise still more, if food containing an addition of salt be taken. The amount of chlorine discharged after a substantial English breakfast, with meat and eggs, is therefore considerably larger than that discharged after the Continental *café au lait*, or the coffee and hot rolls of the German student. Hegar found that a person who used to be given to mental labour discharged more chlorine per hour of the night (0·47 grammes) than during the same time in the morning, when the quantity was only 0·44 grammes. Vogel observed frequently an instantaneous increase in the amount of chlorine secreted by the urine under the influence of increased mental and bodily labour. We have already seen that the same causes exert a similar influence upon the total quantity of urine discharged, and upon the amount of urea secreted with it. There can be no doubt that most of the ingredients of the urine share this fate, as we have seen or shall see more particularly under the history of the single substances. Vogel states, moreover, that by the ingestion into the system of large quantities of water, which stimulate the kidneys, not only the amount of urine and urea, but also of chlorine is increased. After the stimulus has ceased, there follows a period of relaxation; during which the activity of the kidneys becomes lessened, and less chlorine than usual is excreted. A person whose hourly secretion of chlorine during the night was 0·13 grammes, drank four pints of water in the evening. The hourly amount of chlorine rose to 0·60 for several hours, fell then to 0·12 grammes, and somewhat later to 0·10 grammes. In the morning, however, though no breakfast had been taken, the amount of chlorine was raised to 0·51 grammes by horse exercise. Another person drank four pints of water in the afternoon after dinner, whereby the hourly amount of chlorine towards and during the evening rose to 1·89 grammes; during the night it amounted to 0·57 grammes, being 0·19 in excess of the usual average. On the next morning the same individual drank again two pints of water; but, notwithstanding this, the hourly amount of chlorine remained below the normal average during the

entire day, amounting only to 0·42 grammes, sinking in the night following as low as to 0·014, rising a little on the second morning to 0·22 grammes, and falling again to 0·18 grammes, notwithstanding the person had eaten a piece of bread and butter with much salt (*vide* Vogel, p. 257).

Upon the basis of the above facts we are now enabled to explain the opinion of Barral,[1] who by a series of very accurate analyses, the substance of which was first presented to the French Academy, and subsequently published in a separate form, came to the conclusion that chloride of sodium increased the elimination of the nitrogenized ingredients of the urine. In some of his experiments, Barral determined the whole amount of chlorine taken with the food, and, on the other hand, the chlorine and urea excreted. If such a series of analyses were now to be performed by the more accurate methods, there can be no doubt that they would lead to important evidence regarding the causes and influences determining and modifying the amount of chlorine excreted by the kidneys, particularly if the fæces and other excreta were also taken into consideration. There is one way, however, in which chloride of sodium indirectly increases the discharge of urine and its ingredients; namely, by causing thirst when taken in any quantity; the water which is drank in consequence, acting as a stimulant of the kidneys, carries away, not only the salt, but also organic ingredients in solution.

Chlorine of the Urine in disease.

Since Redtenbacher drew the attention of the medical world to the fact of the absence of the chlorides from the urine discharged by patients in certain stages of pneumonia, and to the diminution of these salts in other stages of that disease, many researches have been made in that direction. Though at first they were mainly directed towards pneumonia,[2] of which disease exclusively the absence of the chlorides was for some time thought to be a peculiar feature, yet the extension of the investigations to other diseases showed soon that the bearing of the chlorides in all acute diseases was so very much the same, that the idea of its being a peculiarity of pneumonia had to be abandoned.

The result of many observations of Vogel and others, last of myself, then, is that *in all acute febrile diseases the*

[1] Barral, S. A., 'Statique chimique des Animaux, appliquée specialement à la question du sel,' Paris, 1850.

[2] Beale, Dr. Lionel, 'Med.-Chir. Transact.'

amount of chlorine discharged in the urine sinks rapidly to a minimum, say one hundredth part of the quantity normal to the individual, until at last, in certain cases, it disappears entirely for a short time. When the diseased action is abating, the amount of the chlorides rises during convalescence, sometimes above the normal average. We have already seen that the total quantity of urine has a similar relation to the stages of acute febrile diseases. But it is the reverse with the colouring matter or uræmatine, the amount of which rises and falls in the inverse ratio of the chlorine; so that when the latter is entirely absent, the former is discharged in the largest quantity. Urea, on the other hand, though rising at first in amount inversely to the sinking of the amount of chlorine, afterwards sinks below the healthy average, and during convalescence rises parallel with the amount of chlorine.

In the case of a man suffering from severe pleuro-pneumonia, Vogel found the chlorine sinking rapidly to 0·6 grammes in twenty-four hours on the third day of the disease, to 0·3 grammes on the fourth, on the fifth to almost 0. From this day the diseased action abated, and the appetite improved, when, together with these improvements, the amount of chlorine discharged rose to the normal average, as the following figures show: 0·4, 1·8, 2·6, 5·5, 9·0 grammes. From this time the amount of chlorine fluctuated a little, and sometimes exceeded the normal average. It was, on the respective days, 10·7, 13·5, 9·7, 11·9, 15·9, 10·8 grammes.

The same course has been established by the observations of Beale. He found that the chloride of sodium was totally absent from the urine of pneumonic patients at the period of complete hepatization of the lung, and that it reappeared after the resolution of the inflammation. The fact that the sputa of pneumonic patients contain a very large quantity of the chlorides, must probably be explained by their being in part extravasations and exudations from the blood, which, we now know, always retains a certain amount of the chlorides. These exudations may either have been deposited at the time when the blood yet possessed an excess of chlorine, or they may have appeared after the chlorine had ceased to be discharged in the urine in appreciable quantities. However, that may ultimately be decided by analysis; what I desire to point out is, that the absence of the chlorides in the urine does not necessarily involve the absence of chlorine from exudations. For the latter are produces of diseased action derived directly from stagnant blood, and certainly not subject to the specific laws of secre-

tion. The presence of chlorine in sputa, therefore, at a time when it is absent from the urine, is not sufficient proof of a determination of the chloride towards the inflamed lung; a proposition which, moreover, loses all probability from the partial or total disappearance from the urine of the chloride in all acute diseases. We may mention bronchitis, typhus, acute rheumatism, pyæmia, pleuritis, as diseases in which this diminution of the chlorides has been prominently observed. We have seen the influence which different quantities of chlorine taken with the food exert upon the amount of chlorine discharged by the urine during health. It is therefore easy to believe that the diet of patients has the greatest influence upon the amount of chlorine in pathological urine; and that the chlorine is diminished or absent because these patients take little or no food, and what they take generally contains no salt. One important point, however, must not be lost sight of; namely, that urine containing no appreciable trace of chlorine is secreted from blood containing a certain amount of it; from which it follows that the composition of the blood is such as not to allow any further removal of chlorine, or that the kidneys have lost their secretory activity as regards chlorine, as well as (which has been seen to be the case) with reference to water.

The analysis of the amount of chlorine in the urine of patients may, therefore, afford an insight into the degree of the pathological action taking place in the body. A continuous decrease of chlorine in the urine is an indication of the growing severity of the disease, the intensity of which will be greatest when the chlorine in the urine falls to a minimum, say 0·5 grammes, or disappears altogether. This may be the combined effect of an entire loss of appetite, copious serous diarrhœa, or other serous exudations, of secretions such as perspirations, and of the want of secreting power of the kidneys. A rise in the amount of chlorine, on the other hand, indicates a steady abatement of the acuteness of the disease, and is a good measure of the returning appetite and improved digestive powers of the patient.

In chronic diseases the excretion of chlorine is, according to Vogel, generally diminished, correspondingly with the low state of nutrition and moderate appetite of the patients of that class. To this rule, however, diabetes insipidus makes an exception—a disease, during the entire or partial course of which a considerable excess of chlorine is discharged, parallel to the increased amount of other solids. In a case of that description Vogel found the amount of chlorine dis-

charged by the urine so much increased for a period, that on one day it was 29·0 grammes in weight. The same observer found that dropsical patients, when under the influence of diuretics, discharged an increased amount of chlorine, which evidently had passed into the tissues and cavities dissolved in the exudations and transudations. One of these patients discharged 33·0 grammes of chlorine (equal to 55·0 grammes of chloride of sodium), 28·0 grammes, and 21 grammes of chlorine, on three successive days without having taken any more salt than usual with his food. In these and other chronic cases the amount of chlorine in the urine is a measure of the digestive powers of the patient. A quantity of chlorine, amounting to from 6 to 10 grammes for twenty-four hours, may lead us to infer a good digestion; a quantity of chlorine, however, below 5 grammes for the same time, shows impaired nutrition, provided that the decrease have not been preceded by a diet containing little or no chlorine, or by any of the causes which have been above enumerated as diminishing the amount of chlorine in the blood, such as serous diarrhœa, exudations, and perspirations. An increase in the amount of chlorine, when not caused by an excessive ingestion with the food, is indicative of diabetes insipidus. In dropsical and hydræmic conditions, an increase of the amount of chlorine is a favorable symptom. (*Vide* Vogel, p. 260.)

CHAPTER IX.

SULPHURIC ACID AND SULPHATES.

The chemical characters of sulphuric acid are so well known, that it is scarcely necessary to advert to them here for the purpose of establishing its diagnosis. There is one test which distinguishes sulphuric acid from all other substances that may occur in the urine, namely, that with a common soluble salt of baryta it forms a precipitate, which is not soluble in any acid, and has the good property of being distinctly visible when present in the smallest quantity. But, though we may be able to ascertain the amount of sulphuric acid discharged in the urine, yet we have at present no means of ascertaining the bases with which it is combined. It has been a general practice in analytical chemistry, separately to determine the acids and bases, and afterwards to distribute them according to the principle that the strongest acid takes the strongest base. But since it has been shown that this affinity is not the same under all circumstances, that mixtures and dilutions will materially alter it, we had better discontinue such a mode of arranging the constituting acids and bases according to their ordinary strength of affinity, and express in separate amounts the acids, leaving it undecided with which base, or with what amount of base, they may have been combined.

Formula: $SO_3 + HO$, being the hydrate of sulphuric acid.

Equivalent:	16·0	sulphur.
	24·0	oxygen.
	40·0	sulphuric acid.

Method of determining the amount of Sulphuric Acid in Urine by Volumetrical Analysis.

This proceeding originated with Gay-Lussac, and has for a length of time only been used for testing the alkalies of commerce for their impurities.[1] It has, however, been adapted to the analysis of the urine by different chemists; the adaptation consisting in giving to the test-fluid a sufficient degree of dilution corresponding to the small amount of sulphuric acid contained in urine.

The proceeding consists in adding to a measured quantity of urine a solution of chloride of barium of known strength, until a precipitate is no longer produced.

Preparation of test-fluid.—One equivalent of the test-fluid is to contain just so much barium as is required to neutralize 10 milligrammes of sulphuric acid. For that purpose we pulverize crystallized chloride of barium (of the formula $ClBa+2HO$; equivalent $Cl=35{\cdot}4$, $Ba=68{\cdot}6$, $2Aq=18=122$), and expose it to the air until it no longer loses water. Of this powder, 30·5 grammes are dissolved in so much water that the solution will amount to 1 litre. Of this solution 1 c.c. will precipitate 10 milligrammes of anhydrous sulphuric acid.

Neubauer gives a ten times more dilute solution, for the purpose of finishing the analysis where great accuracy is desired. It is made by mixing 100 c.c. of the solution described with 900 c.c. of water. Of this dilute solution, 1 c.c. is required for precipitating 1 milligramme of sulphuric acid.

Application of the test-fluid to urine.—One hundred cubic centimètres of the urine to be examined are measured into a balloon, acidulated with 20 or 30 drops of hydrochloric or nitric acid, and heated to the boiling point. The balloon best suited for that purpose is a Florence oil flask. The graduated solution of baryta is now added to the boiling urine in small portions; and before every fresh addition of solution, the fluid is allowed to rest, for the subsidence to the bottom of the precipitate formed. When the upper strata of the fluid in the flask have become clear, more of the test-fluid may be added, and so on, as long as a fresh addition of test-fluid produces a turbidity in the clear upper strata. But when it becomes doubtful whether any precipitate is yet formed

[1] Schwarz, 'Die Maassanalysen,' p. 21.

or not, it becomes necessary to filter a small portion of the mixture, and to test it separately with a drop of the test-fluid in a very small test-tube. If a precipitate be still produced, the whole amount filtered must be poured back to the total quantity employed for the analysis, and a new quantity of test-fluid must be added, and so on, until a new filtration shows that there is no more sulphuric acid in solution. We have now to ascertain that no excess of the solution of baryta has been added to the mixture; this is found by adding a drop of a solution of sulphate of potash. If neither solution of chloride of barium, nor of sulphate of potash, produce any precipitate in separate portions of the filtered liquid, the analysis is perfect.

It is, however, very difficult to arrive at this point, because there is no means of preventing the addition of an excess of the solution of baryta. As soon, however, as an excess has been added, a new experiment becomes necessary. In conducting this, we have the advantage of knowing, from the first experiment, that, after the addition of, say 10 c.c., there was yet sulphuric acid uncombined with baryta, and that, after the addition of another cubic centimètre, there was an excess of barium present. The truth therefore lies between 10 and 11 c.c. of test-fluid, and the urine used contains from 100 to 110 milligrammes of sulphuric acid. Such a fact is sufficiently accurate for ordinary medical purposes. If we desire to make the analysis quite correct by a second analysis, we at once add to the 100 c.c. of acidulated boiling urine 10 c.c. of test-fluid, and complete the analysis with the dilute test-fluid in the manner described. For calculation, the quantities of the two test-fluids used are simply added, with the caution of putting the figures for the dilute fluid one decimal further back, and taking it into account as concentrated.

Direct analysis of Sulphuric Acid.

One hundred cubic centimètres, or any measured quantity of filtered urine, are acidulated with some hydrochloric acid, and, by the addition of chloride of barium in excess, the whole amount of sulphuric acid is precipitated. The precipitate is then boiled for some minutes in the acid fluid, filtered, washed, and exposed to a red heat, the filter being incinerated separately on the cover of the platinum crucible. $BaO + SO_3 : SO_3 = 116{\cdot}5$ (116·59, Neubauer) : 40 (Will.)

To prevent the formation of sulphuret of barium by the reducing influence of any animal matter which may have

been intimately mixed with the precipitate, it is advisable to add a little sulphuric acid to the sulphate in the crucible, after it has got cool from the first heating. It is then again heated for a short time, and, after cooling, may now be weighed.

Quantity of Sulphuric Acid discharged by healthy persons during twenty-four hours.

The results of the best observations are put together in the following table :

Observer.	Persons upon whom the observation was made.	Min.	Med.	Max.
		Gramm	Gramm.	Gramm.
Gruner[1] .	7 young gentlemen, at Giessen . .	1·509	2·094	2·485
	1 kilogramme of weight of body therefore discharge	2·04	3·19	3·73
	100 centimètres of length „	0·85	1·18	1·35
Clare[2] .	A young gentleman at Dorpat, medium of 15 days	1·858	2·288	2·973
Neubauer[3]	2 young gentlemen at Wiesbaden: 1st aver. of 17 days	1·9 0	2·48	3·21
	2 young gentlemen at Wiesbaden: 2d „ 22 „	1·7 0	2·27	3·20

From these observations it follows that the average amount of sulphuric acid discharged during twenty-four hours, by healthy young men, fluctuates between 1·5 and 2·5 grammes. Vogel and Gruner have made some direct observations of the quantities of sulphuric acid secreted during every single hour of the day, and have found the average of one hour to be 0·090 grammes.

The average for every single hour of the forenoon they found 0·063 grammes, for one hour of the afternoon 0·108 grammes, for one hour of the night 0·070 grammes. From this Vogel abstracts the general law that *the largest amount per hour of sulphuric acid is discharged a few hours after the principal meal of the day. The quantity then begins to decrease, and continues so with every hour up to the principal meal of the next day, after which it again rises.*

In some individuals the discharge of sulphuric acid is effected more rapidly than in others, in whom the total average

[1] Gruner, Gottlieb, 'Die Ausscheidung der Schwefelsäure durch den Harn,' Giessen, 1852.

[2] Clare, Waldemar, 'Experimenta de excretione acidi sulfurici per urinam, Dorpati Livonorum, 1854.

[3] *Vide* Vogel, 'Semiotic,' p. 261.

for the twenty-four hours is spread more equally over that time. The former may have an hourly average varying between 0·317 grammes and 0·016 grammes, or between 0·165 grammes and so small a quantity that it cannot be determined.

Physiological origin of Sulphuric Acid.

Though the analysis of food has shown that a certain amount of sulphuric acid in the form of sulphates is being taken daily, yet this is not sufficient to account for the whole amount discharged by the urine. This excess of sulphuric acid over the amount ingested as such, is undoubtedly due to the oxydation in the body of the sulphur which, as we know, enters into the constitution of albuminous substances. But as the greater part of our albumen is taken in the form of meat, it is a reasonable supposition that the greater part of the sulphuric acid in the urine of well-living people is due to the oxydation of the sulphur contained in the meat they eat. In accordance with this it has been found that, under a diet consisting principally of meat, the amount of sulphuric acid discharged in the urine may be double or three times the amount of the ordinary average. On the other hand, a purely vegetable diet has been found to make the amount of sulphuric acid sink considerably below the average under ordinary mixed diet. Lehmann, while living on ordinary mixed food, found 7·026 grammes of sulphuric acid in the urine of twenty-four hours. But when, during twelve successive days, he confined himself to animal food exclusively, the sulphuric acid rose to 10·399 grammes per day. Under an exclusively vegetable diet it fell to 5·846 grammes for twenty-four hours. These quantities are very high, and, like the rest of Lehmann's observations upon himself, do not permit any conclusion as to the average quantities of ordinary mortals with a slighter appetite. But in itself the experiment is as conclusive as the following ones. Vogel examined the urine of a person whose ordinary average for twenty-four hours was 2·02 grammes of sulphuric acid. That person took a large supper of meat principally, in consequence of which the discharge of sulphuric acid by the urine rose to 0·50 grammes per hour between midnight and nine o'clock next morning; the ordinary average per hour for that time of the day having been 0·10. During the subsequent twenty-four hours the amount of sulphuric acid rose to 7·3 grammes, being more than three times the ordinary average of 2·02 grammes. It was observed by Vogel that the rise and fall of

the amount of sulphuric acid in the urine of several other persons was mainly dependent upon the amount of sulphur taken with their albuminous food; and that when farinaceous food, containing only a small amount of gluten, such as bread and butter, rice, and similar food, was taken, the amount of sulphuric acid in the urine fell. The same observation was made by Clare, in a series of experiments which he performed upon himself. During three days he lived on meat only, and at the end of those three days he had discharged the respective amounts of sulphuric acid as follows: on the first day, 2·094 grammes; on the second day, 5·130 grammes; on the third day, 3·868 grammes. He then, during two days, ate common mixed diet, and discharged, on the fourth day of the experiment, 3·592 grammes; and on the fifth, 2·262 grammes, of sulphuric acid. The next three days he restricted himself to vegetable diet, and discharged, on the sixth day of the experiment, 2·262 grammes; on the seventh, 1·394 grammes; on the eighth, 1·022 grammes. On the ninth and tenth day he again took his ordinary diet, and secreted 1·979 and 2·859 grammes of sulphuric acid on each day respectively.

Table showing the influence of diet upon the amount of Sulphuric Acid discharged in the Urine (from Clare's experiments).

Day . . .	1	2	3	4	5	6	7	8	9	10
Diet . . .	Meat diet.			Ordinary mixed.		Vegetable exclusively.			Ordinary mixed.	
$SO_3 + HO$.	2·094	5·130	3·868	3·592	2·262	2·262	1·394	1·022	1·979	2·859

This table exhibits quite clearly that the influence of the meat diet showed itself on the second day of the experiment only, in which point the observation differs from that of Vogel, in which the rise in the quantity of sulphuric acid took place already during the night and on the morning following the meat supper. However, this later appearance of the increase is compensated for by its lasting so much longer, that the urine of the fourth day, being the first of the ordinary mixed diet, is yet under the influence of the meat diet of the previous day, the first day of vegetable diet is yet under the influence of the previous day of mixed diet, and the diminution of the sulphuric acid by the vegetable diet lasts yet over the whole ninth day, when ordinary diet was already taken.

We have now sketched the circumstances on which the amount of sulphuric acid in the urine is ordinarily dependent. There may, however, be accidental causes which increase the sulphuric acid, and as these must be assigned the internal use of sulphur, sulphurets, sulphuric acid, and sulphates.

The internal use of sulphur has been found by Krause[1] to increase the amount of sulphuric acid in the urine.

It was observed by Boecker and Clare that large doses of red sulphuret of antimony caused a rise in the amount of sulphuric acid in the urine.

The action of the sulphuretted mineral waters, which is generally ascribed to the formation of sulphuric acid in the body, forms an interesting subject for inquiry in this direction.

As to sulphuric acid, it was observed by Vogel that it increased, in the urine of a patient who had taken it for the cure of hæmoptoe, from 1·2 to 3·0 and 3·28 grammes.

Gruner made some observations regarding the influence of sulphates, and found that sulphate of soda, when taken internally, caused a considerable increase in the amount of sulphuric acid in the urine. In one experiment the hourly quantity rose from 0·049 grammes to 0·122, 0·176, 0·145, and 0·220 grammes. In another experiment the rise was equally well marked, namely, from 0·041 grammes to 0·138, 0·122, and 0·164 grammes. The time required by the organism to discharge the excess of sulphuric acid varied in different experiments.

The influences which different physiological conditions of the body may have upon the amount of sulphuric acid in the urine it has not yet been possible to ascertain. We do not know whether the organism requires a certain amount of the sulphates, below which secretion cannot be carried on, or whether sulphates may be retained and accumulated in the economy. The influences of rest and activity, and of the ingestion of large quantities of water into the stomach, did not appear materially to affect the amount of sulphuric acid in the urine, according to some experiments of Clare and Gruner. Vogel, however, believes it probable that such influences exist, that the secretory activity for sulphuric acid is dependent upon certain individual and cosmic influences; a conclusion to which we are led by the fact that different persons oxydize and discharge (supposing it to be discharged as soon as formed) the sulphur taken with their albuminous food with different degrees of rapidity, and that the secretion

[1] Krause, A., 'De transitu Sulfuris in Urinam,' Dorpati, 1855.

of sulphates in any form in some is spread over a longer period of time than in others. Vogel, also, from observation, is of opinion that the prolonged use of sulphates in digestive doses is decidedly weakening, and believes it probable that this depressing action may be due to an accumulation of the salts in the system. When to this it is added that sulphate of soda in larger doses is an emetic and sulphate of potash a poison, the question into the influence of sulphuric acid and sulphates in the urine becomes one of sufficient importance to fix the attention of future inquirers.

Quantity of Sulphuric Acid in disease.

The observations hitherto made on this point have not yielded any very decided result. Vogel found sulphuric acid considerably diminished in most acute febrile diseases. As patients suffering from these diseases take little food, and that little mostly of a vegetable nature, the diminution is partly accounted for. The same observer found, however, exceptions to his general rule, in three patients affected with violent pneumonia. In these cases the amount of sulphuric acid discharged was considerably above the normal average. The first patient, who was treated with large doses of digitalis, secreted the following quantities of sulphuric acid on nine respective days: 2·4, 3·1, 2·9, 5·7, 4·3, 1·8, 1·1, 1·6, 2·7 grammes. Of the two other cases, which took a rapidly fatal turn, the first showed the amount of sulphuric acid to be 2·9 and 1·4 grammes on two respective days, the other on the day of decease 4·4 grammes. On contrasting these figures with those obtained in cases where the amount of sulphuric acid is less, the difference becomes very striking. In a man with diphtheritis buccalis Vogel found only 0·5 grammes of sulphuric acid for the day. In a patient with febrile catarrh it was 0·29 and 0·38 grammes. A man affected with pleuritis secreted 0·63 grammes. A girl suffering from rheumatic fever discharged 0·8 grammes at the height of the disease, another with erysipelas of the face 0·48 grammes.

In chronic diseases Vogel found the amount of sulphuric acid to be variable, but mostly below the normal average; and it remained so in cases where the secretion of chlorides could be vastly increased by administering diuretics, as in cases of dropsy. An increase in the amount of sulphuric acid discharged by patients affected with chronic disease could only be observed after the ingestion into the stomach of sulphuric acid and sulphates, and in diabetic patients after a liberal meal of meat.

Thus a patient labouring under icterus secreted 1·4 grammes of sulphuric acid; a case of rheumatism of the neck gave 1·11; a case of emphysema of the lungs, 1·2 grammes. A case of amenorrhœa showed 0·5; of fluor albus, 0·7; of habitual hypermenorrhœa, 0·97 and 1·1 grammes. A dropsical patient who, under the influence of diuretics, secreted 33 grammes of chlorine during twenty-four hours, discharged only 1 gramme of sulphuric acid during the same time; and on the day following, with 28 grammes of chlorine, only 0·5 grammes of sulphuric acid. A patient, who took sulphuric acid internally, secreted more than 3·0 grammes of it during twenty-four hours, and a patient affected with diabetes insipidus discharged 5·2 grammes.

Pathological indications.

If there can be no doubt about the origin of sulphuric acid, the determination of its quantity in the urine must be useful for determining the amount of disintegration of albuminous matters in the system, in cases where the ingestion of sulphur in any form or combination is very low or altogether suspended. The amount of sulphuric acid would then, perhaps, correspond in a certain degree with the amount of urea, supposing their inclination to pass the kidneys to be equally great. But upon this point there are yet doubts. Where we find both urea and sulphuric acid in increased quantities, we may be sure that it is due to the oxydation of a large quantity of animal matter introduced into the stomach, to animal or meat diet. A considerable diminution of the quantity of sulphuric acid, on the other hand, indicates that the patient has been taking little or no animal food, little or no vegetable food, or no food at all. Of course, all these features may be constant or accidental. A sudden rise in the amount of sulphuric acid, but of short duration, would, under all circumstances, have to be referred to the ingestion of sulphur in some of its combinations, organic or inorganic.

The relations of sulphuric acid to the processes of the animal economy are by no means simple. Introduced in an organic combination, sulphur becomes oxydized, and in the form of the acid has to join a base. It would, of course, deprive another base of its acid by the right of the stronger. The neutral phosphates are thus most probably deprived of some part of their base.

Sulphuric acid or sulphates are not present in the juices of flesh, as was first ascertained by Berzelius, and afterwards

confirmed by Liebig.[1] For the precipitate which baryta causes in the juice is, in many cases, entirely soluble in nitric acid; and if a precipitate of sulphate of baryta remain undissolved, its quantity is so small, that it cannot be determined by analysis, even from so large a quantity of flesh as that of an entire fowl or an entire fox.

The analyses of the quantity of sulphuric acid in the blood will have to be repeated without incineration, which, as we have seen, destroys the relative proportions of acids and bases in the salts of the alkalies. The production of sulphuric acid then being apparently confined to the blood, it becomes a question of high importance, whether the action of the kidneys does not in part consist in the final oxydation or that stage of disintegration of albuminous matter, in which sulphur, in the form of sulphuric acid, leaves the organic combination, joins a base, and appears in the urine. This influence of sulphuric acid (the produce of the oxydation of the sulphur in albuminous substances) in producing in part the acid reaction of urine was first pointed out by Liebig.[2]

Albumen contains 1·6 per cent. of sulphur and 0·4 per cent. of phosphorus.[3] White of eggs contains more sulphur than albumen from blood.[4] Casein contains 0·84 per cent. of sulphur. We may trust soon to know all intermediate stages of matter from albumen down to urea and sulphuric acid, when the analysis of these substances in the urine will be of still greater value than even at present we anticipate.

1 'Chem. Unters. über das Fleisch,' p. 76.
2 'Ann. d. Chem. und Pharm.,' l. p. 181, et seq.
3 *Vide* Gorup-Besanez, loc. cit., p. 51, et seq.
4 Liebig, loc. cit., p. 21.

CHAPTER X.

PHOSPHORIC ACID AND PHOSPHATES.

It is well known that phosphorus was first obtained from urine by Brandt (1669). This substance occurs naturally only in the form of the tribasic phosphoric acid, and in combination with organic substances. In these two forms it is met with in all organized bodies. It is an invariable ingredient of all food, and enters largely into the composition of all parts of the animal and human body.

In the urine phosphorus occurs only as the acid, and, in combination with soda, lime, and magnesia, forms a regular constituent of that fluid.

Phosphoric Acid. Composition, Equivalent, Formula.

The common or tribasic phosphoric acid has the composition PO_5+3HO. This formula expresses the equivalent of

1 equiv. phosphorus . .	P	= 31·436
8 ditto oxygen . .	O_8	= 64·000
3 ditto hydrogen . .	H_3	= 3·000
1 equivalent of phosphoric acid,		= 98·436

The theory which assumes P to be a double atom, and the single atomic weight = 15·718, uses P_2 as the symbol for the above equivalent of phosphorus. This is an explanation to the reader, should he find himself embarrassed by the formulæ of different authors.

Physical properties.

Phosphoric acid may be obtained in crystals forming quadrangular or hexagonal prisms of a transparency like glass, or

as a syrupy fluid. When heated to 320° F., it begins to lose water, and, at a temperature of 415·4° F., is transformed into pyrophosphoric acid, PO_5+2HO. When heated still more, it loses another equivalent of HO, and is then metaphosphoric acid, $PO_5 + HO$. When exposed to red heat in an open platinum capsule, it is volatilized.

Chemical properties.

Phosphoric acid is easily soluble in water and alcohol or spirits of wine, and its solutions exhibit a strongly acid reaction. Solutions of albumen, chloride of barium or calcium, do not cause any precipitate in solutions of phosphoric acid; the solutions of caustic baryta, strontia, or lime, when added in excess, produce a white precipitate.

With the basic oxydes phosphoric acid has great affinity, and forms with them the phosphates, which may contain one, two, or three equivalents of almost any of the common bases, instead of any of the three equivalents of water. Thus we may have in the urine:

Phosphates of Alkalies.

Phosphate of soda with two equivalents of base and one of water, PO_5, $2NaO+HO$ (alkaline) may occur abnormally in the alkaline urine of chlorosis.

Ammonio-phosphate of soda, $PO_5+NaO+NH_4O+HO+8HO$.

Acid phosphate of soda, $PO_5+NaO+2HO$.

Phosphates of the Alkalies and Earths.

Ammonio-phosphate of magnesia, $PO_5+2MgO+NH_4O+12HO$.

Phosphates of the Alkaline Earths.

Phosphate of lime (acid), $PO_5+2CaO+HO$.
Phosphate of magnesia, $PO_5+2MgO+HO$.

Of these, the phosphates of the alkalies are easily soluble in water; the others are scarcely soluble, or altogether insoluble. They all dissolve in nitric or hydrochloric acid. The phosphates of the alkaline earths, when newly precipitated, are, moreover, soluble in acetic acid. The solution of an earthy phosphate in an acid, when neutralized with an alkali, throws down a precipitate of the original phosphate, which is

insoluble in an excess of the alkali. The insoluble phosphates are, as a rule, soluble in an excess of a solution of any salt from which they have been precipitated by phosphate of soda;[1] *this solution becomes very turbid by heating, and clears again on cooling.*[2]

With the common soluble phosphates, nitrate of silver produces a yellow precipitate (PO_5+3AgO), which is soluble in nitric acid, and in ammonia. Acetate of lead produces a white precipitate (PO_5+3PbO), which is soluble in nitric acid, but insoluble in acetic acid and in ammonia. If chlorides are present, the precipitate contains chloride of lead in chemical combination.

Chloride of barium and chloride of calcium produce white precipitates with the soluble phosphates (PO_5+3BaO and PO_5+3CaO), each readily soluble in hydrochloric, nitric, or acetic acid.

When a solution of phosphate of lime in acetic acid is allowed to stand some time, the phosphate has a great inclination to fall down from this solution in a crystalline state, particularly when the mixture is warmed a little, and when the phosphate is prevalent. Phosphate of lime is somewhat soluble in water containing carbonic acid, and in salts of ammonia, even when free ammonia is present. From its solution in acetic acid, or from its solution in hydrochloric acid when mixed with acetate of soda (which is virtually a solution in acetic acid, because hydrochloric acid, combining with the soda, sets acetic acid free, which is now the solvent for the phosphate of lime), oxalate of ammonia throws down the whole amount of lime as oxalate of lime. From its solution in hydrochloric or nitric acid, the entire amount of lime may be precipitated by means of sulphuric acid and alcohol. These reactions are the bases for the quantitative analysis of lime in ashes and the earth of bones.

A mixture of sulphate of magnesia, or chloride of magnesium, with chloride of ammonium and ammonia, produces a crystalline precipitate in soluble phosphates, which has the composition PO_5+2MgO, $NH_4O+12HO$, is easily soluble in all acids, somewhat soluble in pure water, and perfectly insoluble in water containing ammonia, even if a large amount of any salt of ammonia should be present. This precipitate, after exposure to red heat, is of the composition PO_5+2MgO, and is the qualitative and quantitative test for phosphoric acid (in absence of arsenic acid) in all combinations, which are soluble in water, the watery solution of which does,

[1] Enderlin, 'Ann. d. Chem. und Pharm.,' 1844, p. 320.
[2] Dr. G. Owen Rees, 'Guy's Hospital Rep.,' vol. i, p. 402.

however, not become turbid by admixture of a solution of chloride of ammonium and ammonia. In very dilute solutions the precipitate forms only slowly. When the solution contains tartaric acid and oxyde of iron, some tartrate of magnesia and oxyde of iron may easily be mixed with the precipitate.

Chloride of iron produces in solutions of phosphates a yellowish-white precipitate of $PO_5 + Fe_2O_3$, which is soluble in hydrochloric acid, in an excess of chloride of iron, in acetate of iron, and in ammonia. This precipitate is, however, quite insoluble in acetic acid, and will, for this reason, form even when its solution in hydrochloric acid is mixed with acetate of soda, as already explained, or when the solution in hydrochloric acid of the phosphate of an alkaline earth is mixed with a small quantity of chloride of iron, and with acetate of soda. If the solution of any phosphate in hydrochloric acid, after any excess of the acid has been neutralized by a little ammonia or carbonate of soda, is mixed first with acetate of soda, and then with chloride of iron in slight excess (which may be recognised by the fluid assuming a reddish colour), and is then heated to ebullition, a reddish-brown precipitate is obtained, which contains the whole amount of oxyde of iron and all the phosphoric acid present. It is filtered hot, and the precipitate and filter are washed with hot water. This test forms the basis of the volumetrical analysis of phosphoric acid by Professor Liebig, and of the method for removing all phosphoric acid and iron from solutions in which the quantity of lime and magnesia and isomorphous oxydes has yet to be determined.

On mixing a solution of the nitrate of protoxyde of mercury with a solution of phosphate of soda, a white flocculent precipitate of phosphate of protoxyde of mercury is immediately produced, which on being allowed to stand in the fluid, rapidly becomes crystalline. A solution of corrosive sublimate, however, may be mixed with the alkaline phosphate without any turbidity being produced. If to a mixture of the two first-mentioned salts we add a solution of chloride of sodium before the precipitate has had time to become crystalline, the latter will immediately decompose with the chloride of sodium, corrosive sublimate and phosphate of soda being produced: the precipitate disappears, and the fluid becomes perfectly clear.

This test is the basis of Professor Liebig's method for ascertaining the amount of protoxyde of mercury contained in a solution of its nitrate. (*Vide* p. 59 *et seq.*)

Method of ascertaining the amount of Phosphoric Acid in the Urine.

I have already described the test upon which this method, also by Professor Liebig, is based. By adding to the urine, containing an unknown amount of phosphoric acid, some acetate of soda, and then a nearly neutral solution of chloride of iron of known strength, until the entire amount of phosphoric acid is precipitated, and a trace of the solution of chloride of iron can be discovered to have been added in excess, we ascertain from the amount of iron in the test-fluid the amount of phosphoric acid precipitated in the form of $PO_5 + F_2O_3$. The excess of chloride of iron remaining in solution causes the latter to give a blue precipitate when mixed with some ferrocyanide of potassium. Before this test could be applied, a filtration of the fluid from the precipitate would be required. But this is avoided by the following simple manipulation: a piece of bibulous paper is saturated with a solution of ferrocyanide of potassium, and spread over a white china plate, or a glass disc lying on a piece of white paper. A drop of the solution to be tested is now allowed to fall on a second slip of dry bibulous paper, spread over the one saturated with the ferrocyanide. The solution thus filtered mixes with the ferrocyanide of potassium in the moistened paper, and, when it contains an excess of chloride of iron, causes a blue spot to appear on the paper.

In the performance of this analysis there is, however, one caution to be observed; namely, to take the *first* blue test obtained as the mark of the completion of the analysis. For if any excess of chloride of iron is present in the fluid only for a very short time, the precipitate $PO_5 + Fe_2O_3$ takes up more iron, and the blue spot is now no longer obtained with the fluid. A few drops of the chloride of iron added to the fluid will immediately allow it to reappear. Thus an excess of the test-fluid might be added, which would unduly increase the apparent amount of phosphoric acid. This error is avoided by the observance of the above caution.

Preparation of the solution of Iron of known strength.

15·556 grammes of pure iron (piano-forte string) are dissolved in as much hydrochloric acid as necessary. After addition of a little nitric acid, the solution is evaporated to

dryness on the water-bath. The remaining neutral chloride is then dissolved in water, and diluted with water until amounting to two litres. One cubic centimètre of this solution corresponds to 10 milligrammes of phosphoric acid.

A second method of preparing the fluid, which, according to Neubauer, is preferable to the former, consists in graduating a solution of chloride of iron of unknown strength, by means of a solution of phosphate of soda of known strength, the phosphoric acid in the latter having been determined by the precipitate $PO_5+2MgO+NH_4O+12HO$, or, after heating, $PO_5 + 2MgO$, as described above. Of this solution of phosphate of soda a quantity is to be measured off, containing 0·10 or 0·15 grammes of phosphoric acid, and is to be diluted with about 30 or 40 c.c. of water. To this solution there are to be added 10 c.c. of the solution of acetate of soda to be described hereafter. The solution of chloride of iron which is to be graduated is then to be added in drops, until a drop of the mixture produces a blue spot on the paper described. The amount of solution used contains then the equivalent of the amount of phosphoric acid previously found by analysis to be contained in the solution of soda.

$P = 31·436$	$2Na = 45·946$	$H = 1·000$	$2Fe = 56·000$
$O_5 = 40·000$	$2O = 16·000$	$O = 8·000$	$3Cl = 106·389$
$PO_5 = 71·436$	$2NaO = 61·946$	$HO = 9·000$	$Fe_2Cl_3 = 162·389$

The operator must exactly recollect the amount of blue colour obtained by the test, in order always to add the same excess for which the fluid is graduated. Otherwise his results may be subject to considerable variations.

Solution of Acetate of Soda.

By a series of experiments Neubauer has ascertained, that for every 10 or 15 c.c. of the graduated solution of chloride of iron, when not containing too much free acid, one gramme of acetate of soda must be contained in the urine to be tested. He therefore prepares a solution of 20·0 grammes of crystallised acetate of soda, dilutes it with water until the bulk of the solution is 160·0 c.c., and adds 40·0 c.c. of dilute acetic acid (acetum concentratum). 10·0 c.c. of the 200·0 c.c. thus obtained contain 1·0 gramme of acetate of soda, and 2 grammes of acetic acid.

Application to the urine. Total amount of PO_5.—No preparation of the urine is required except filtering. The quantity to be taken for the test is 50 c.c. After addition of the 10 c.c. of the solution of acetate of soda, the graduated solution is added until the test is obtained as described above. The quantity of the standard solution of iron used for the test indicates the amount of phosphoric acid contained in the 50 c.c. of urine. 1 c.c. = 10 milligrammes of phosphoric acid.

In case the urine should be turbid from alkalinity, the earthy phosphates thereby precipitated must be re-dissolved by a few drops of hydrochloric acid. If a larger amount of the latter acid has been required for effecting solution, the amount of solution of acetate of soda to be added must be increased accordingly.

PO_5 of alkalies and earths separately.—If, on the contrary, we are desirous of determining the separate amounts of phosphoric acid combined with alkalies and earths respectively, it becomes necessary to separate the earthy phosphates from the urine to be analysed. This is best done by adding to the 50 c.c. required for analysis some ammonia, until an alkaline reaction is observed, when all the earthy phosphates will be precipitated. The urine is now filtered, the precipitate, is washed, and the washings are added to the filtered liquid, which latter, after neutralization with acetic acid, is treated with the solution of acetate of soda and chloride of iron, as described above. The number of cubic centimètres of the latter used indicate the amount of phosphoric acid which was in combination with the alkalies. If the total amount of phosphoric acid in 50 c.c. of urine is known, and of that in combination with the alkalies, the difference gives the amount of phosphoric acid which was precipitated with the earthy phosphates.

If the amount of phosphoric acid in urine be small, the above method is liable to give rise to an error amounting, in the hands even of a good operator, to 10 per cent., according to Neubauer. This error, according to Vogel, may amount to 20 or 30 per cent., if a less conscientious operator assumes blue spots of different intensities as the completion of his analyses, or if he allows some time to elapse before trying for the blue spot.

Quantity of Phosphoric Acid discharged by healthy persons during twenty-four hours.

The results of numerous examinations are arranged in the following table, which gives, after the name of the observer, the average quantities of acid found in single individuals and the average of all examinations of each observer at the end.

Table showing the amount of PO_5 *in Urine of twenty-four hours.*

Breed,[1] average of four individuals .	5·180 grammes to 3·765
Winter,[2] first individual, 3·7; second, 4·2; third, 5·2 grammes	average 4·36
Mosler,[3] first series, 2·4; second series, 3·7 in the same individual	average 3·05
Neubauer, first individual, 3·1; second, 1·6	average 2·35
Aubert,[4]	2·8
Average amount of PO_5 discharged by an adult male in twenty-four hours	3·66
Ditto in one hour	0·15

According to the observations of Winter, 100 kilogrammes of man discharge on an average 0·27 gr. and 100 centimètres 0·1 gramme of phosphoric acid.

The maximum and minimum amount of phosphoric acid discharged by single individuals during twenty-four hours is subject to considerable variations, as exhibited by the following observations:

	Maximum.	Minimum.
Neubauer found in one individual daily	2·16 gr.	1·21 gr.
,, found in second individual .	4·88 gr.	2·44 gr.
Mosler, ditto	4·86 gr.	2·40 gr.

The fluctuations in the hourly average are still greater, so that Vogel found by a series of experiments the maximum to be 0·216, while the minimum of the same subject only amounted to 0·085 grammes. Both extremes happened on one and the same day, the whole inquiry extending over ten days.

[1] 'Ann. d. Chem. und Pharm.,' Bd. 78, p. 150.

[2] Winter, A., 'Beiträge zur Kenntniss der Urinabsonderung bei Gesunden,' Giessen, 1852.

[3] Mosler, F., ibid., 1853.

[4] Henle und Pfeufer, 'Zeitschrift für rationelle Medizin,' 1852, ii, 3.

Through the observations of Winter, Mosler, and Vogel, it has been established that the rise and fall in the hourly amount of phosphoric acid is a regular one during each twenty-four hours, the rise invariably taking place soon after the principal meal of the day, which was taken at noon. The maximum secretion was observed during the hours of the evening; the quantity fell during the night, and was at the lowest ebb during the morning. These fluctuations are well illustrated by the following table given by Vogel.

Table showing the amount of Phosphoric Acid secreted by four individuals during one hour of the night, afternoon, and forenoon.

Individuals.	Afternoon.	Night.	Forenoon.
A.	0·18	0·20	0·13
B.	0·28	0·21	0·11
C.	0·18	0·16	0·10
D.	0·11	0·14	0·11

This table shows that different persons discharge the phosphorus taken with their food at different periods after the ingestion, some more quickly, others more slowly; in some the process is spread over a longer period of time than in others. Thus B. discharged the greater part of the phosphorus taken with his dinner soon after it; the secretion of phosphoric acid reached its climax in the afternoon, and fell during the night and following morning until the next principal meal. The difference between the hours before the meal and after it is here greatest. In C. the climax of the secretion falls more towards the evening, and there is less difference between afternoon and night. In D. the maximum hourly average is in the night; and probably his digestion was much slower than that of the other three persons, though all four took their dinners at one and the same time, namely, 1 p.m.

Physiology of Phosphoric Acid in the Urine.

The evidence regarding this point, which may be obtained by analysis of the urine, is very similar to that given con-

cerning sulphuric acid. The introduction into the body of phosphorus, either in the form of the acid, or of phosphates, or in combination with albuminous substances, gives rise to an increase of the acid in the urine.

Total abstinence from food, or from food containing phosphorus, on the other hand, diminishes the amount of phosphoric acid in the urine. Total abstinence will, however, not cause the entire disappearance from the urine of phosphates, as has been observed with regard to chloride of sodium. This is, perhaps, partly due to the continued oxidation of albuminous substances. Of these positions proof is afforded in the following facts. Aubert observed the urine of a person to contain 2·8 grammes per day under ordinary circumstances. This person took 31 grammes of phosphate of soda, whereupon the amount of phosphoric acid in the urine rose to 4·1 grammes for twenty-four hours. When abstaining from food, Mosler found phosphoric acid to sink to half the ordinary quantity; when he took large meals of albuminous substances, the amount of the acid became doubled in consequence.

But the excretion of phosphoric acid is not exclusively dependent upon the quantities introduced. A series of observations demonstrate that the same influences which govern the excretion of chlorine and sulphuric acid, are active in the excretion of phosphoric acid. Different degrees or morbid changes of the secretory activity of the kidneys, actual disease of the kidneys, changes in the mode of disintegration of matter in the organism, must be looked to as causes of the variation of the amount of phosphoric acid. The varying influence of individual structure or individual disposition has been illustrated by Vogel's table. This observer states, moreover, that the drinking of large quantities of water causes an increase in the amount of phosphoric acid beyond the quantity introduced with the water, which can only be explained by an increased production in the body of phosphoric acid, by changes which make an increased amount of phosphates available for excretion, and by a stimulated activity of the kidneys. The organism may at one time contain an excess of phosphoric acid, at other times the acid may be deficient. It will, however, be difficult fully to establish these points, until the normal amount of phosphoric acid contained in all parts of the body and its changes and variations within the range of perfect health be known. And then the examinations will have to comprise a complete analysis of all food, and of all excretions.

We cannot do better than draw the reader's attention to the chapter on the inorganic constituents of the juices of flesh, p. 75 of Professor Liebig's 'Researches on Flesh' (respective meat). The remarkable facts there revealed throw much light on the physiology of phosphoric acid and its salts, on its relation to other component parts of the body, to other salts, to food, digestion, assimilation, to the formation of blood, its function, and depuration. These experiments, to use the words of the author, "however incomplete they may be, may serve as starting-points for future researches."

Quantity of Phosphoric Acid in the Urine of disease.

The results regarding this point obtained by Professor Vogel from more than a thousand examinations are, in the following sentences, given without any comment.

In acute but not very severe diseases, the amount of phosphoric acid in the urine decreases at first most probably in consequence of the low diet, and afterwards rises again with a more liberal allowance of food. During convalescence the normal amount is sometimes exceeded, in consequence of an increased quantity of food.

If the illness, though combined with violent fever, only lasts a short time, the decrease of the amount of phosphoric acid is sometimes very slight and scarcely perceptible.

Examples. *Males.*—1. A young man, affected by severe febrile angina tonsillaris, discharged 2·8 grammes of phosphoric acid on the day of his reception into the hospital. He had an emetic given to him, which caused violent vomiting. This was followed by low diet. On the second day the amount of phosphoric acid had fallen to 1·7 grammes. He now improved, and had quarter diet. The two following days showed 2·6 and 2·5 grammes of phosphoric acid respectively. He now was placed upon half diet; and on the following day, the PO_5 rose to 3·2 grammes. He recovered and was discharged.

2. Pneumonia, not very severe. The patient was discharged after eight days. The daily amounts of PO_5 were 2·4, 2·5, 2·9, 2·4, and 2·3 grammes.

3. Pneumonia, more severe. During the acme of the

disease the daily amounts of phosphoric acid were 1·7, 0·8, 2·1, 1·2, 0·9, 2·1, 1·9, 1·1 grammes.

4. Pneumonia, similarly severe, 1·6, 1·4, 2·2, 2·3, 1·6 grammes.

5. Febrile bronchial catarrh, 1·4, 1·5, 1·7, 1·5, 2·8 grammes.

6. Convalescence from severe pneumonia, 3·8, 2·7, 3·2, 3·5 grammes; 3·9, 1·8, 2·5, &c.

7. Similar case, 1·9, 5·6, 2·8, 1·5, 3·2, 2·8 grammes.

8. Convalescence from severe bronchial catarrh, 4·8 grammes.

9. Catarrh of the organs of digestion, with eczema and violent fever. The case took a rapid course, so that the patient was dismissed cured after eight days. The amount of PO_5 was 2·3, 2·6, 2·7, 2·6, 3·4 grammes.

Females.—1. Rheumatic fever, 2·1, 2·3, 2·2 grammes.

2. Catarrh of the stomach, 1·1; 1·2 grammes.

3. Catarrhal fever, acme of the disease, 1·6 grammes.

4. Convalescence from typhus, 5·2 grammes.

When the diseases are of a more severe nature, so as to cause a long abstinence from food, or to take a fatal turn, the decrease of phosphoric acid in the urine becomes much more considerable.

Thus a girl with severe febrile catarrh of the lungs discharged, during the acme of the disease, 0·7, 0·5 grammes of phosphoric acid; during convalescence it rose to 1·3 and 2·5 grammes.

Fatal end of acute tuberculosis of lungs, 0·4, 0·4, 0·3, 0·3, 0·2, 0·1, 0·08 grammes (day of decease).

Gangrene of the lungs, fatal issue, 3·0, 2·5, 2·20, 0·7 grammes.

In some exceptional cases the amount of phosphoric acid discharged during the height of acute diseases, may considerably exceed the amount discharged during health.

A man of middle age suffered of pneumonia, and was treated with large doses of digitalis, cured and discharged, 4·3, 5·1, 4·1, 8·4, 7·9, 4·5, 2·9, 5·0 grammes.

In chronic diseases the excretion of phosphoric acid takes a very irregular course, and though remaining mostly below

the normal average, may sometimes considerably exceed it. This is shown by the following cases :

Disease.	Number of days observed.	Minimum.	Medium.	Maximum.
MALES.				
Emphysema of lungs		0·6	1·3	2·3
Chronic bronchorrhœa	8	1·3	2·7	4·7
Cancer of the liver	11	1·6	2·2	2·6
Subacute rheumatism of joints	18	1·7	2·4	3·1
Hemiplegia, consequent on apoplexy	35	1·0	2·7	5·2
Hydruria	3	4·4	5·0	5·8
Dropsy, under influence of diuretics chlorides very much increased	2	—	1·8	—
FEMALES.				
Diabetes insipidus	14	3·2	4·8	7·8
Ascites	15	1·7	3·0	4·7
Chronic rheumatism	7	2·7	3·3	4·2
Spinal irritation	—	2·1	2·4	2·8
Amenorrhœa	—	2·1	2·2	2·3
Scrophulosis	—	2·6	3·5	5·2
Tuberculosis of lungs	10	1·5	—	3·9
Chronic erysipelas of face	11	1·5	—	3·6

CHAPTER XI.

FREE ACID OF THE URINE.

The nature of the acid which imparts an acid reaction to urine is not exactly known, though it is commonly admitted to be most probably phosphoric acid in the form of an acid phosphate. Now, as it is desirable to know exactly the amount of free acid discharged in a given time, several observers have deemed it useful and convenient to analyse the amount of free acid by finding the equivalent of oxalic acid, and to express it as such.

Mode of determining the amount of Free Acid in the Urine.

The analysis is simply performed by a standard solution of caustic soda, graduated so that a given volume corresponds to a certain amount of oxalic acid. With this a known bulk of urine is exactly neutralized, and from the amount of standard solution used we find, by calculation, the amount of oxalic acid which would be equivalent to the amount of unknown acid actually contained in the urine.

Preparation of the standard solution of Caustic Soda according to Neubauer.

This solution is to be graduated so that every cubic centimètre indicates exactly 10 milligrammes of oxalic acid. For this purpose we require a solution *of oxalic acid of known strength,* which is shortly prepared by dissolving one gramme of dry oxalic acid in so much water that the solution exactly amounts to 100 c.c. Every 10·0 c.c. of this solution contain 1·0 gramme of oxalic acid. This quantity is now measured off, put into a small beaker, and coloured red with several drops of tincture of litmus. After being placed upon a piece of white paper, the dilute solution of caustic soda is cautiously

added until the red colour has been changed into the original litmus blue. Suppose we have used for effecting this 6 c.c. of the solution of caustic soda, then they would correspond to 1 decigramme of oxalic acid. We now add to every 600·0 c.c. of the solution of soda 400·0 c.c. of water, and thus obtain 1000·0 c.c. of standard solution, of which 1·0 c.c. exactly neutralizes 10 milligrammes of oxalic acid. If, after the addition of 10·0 c.c. of this solution to 10·0 c.c. of the solution of oxalic acid reddened by litmus, the blue colour appears, the solution is correct and ready for use.

The fluid applied to the urine.—To 50 or 100 c.c. of quite fresh urine the standard solution of soda is added in small portions, say ½ c.c. at a time, and after every new addition the fluid is tested by the aid of litmus paper, as the yellow colour of the fluid would not allow the tincture of litmus to show the transition from red to blue, and therefore excludes its use in the manner described for the preparation of the test-fluid. The testing with litmus paper is best effected by placing a drop of the mixture upon neutral blue litmus paper. If, after a time, the spot covered by the drop does not become red any longer, the analysis is completed. To make sure, we may now test for an excess of alkali, and if the latter be found, a fresh analysis, guided by the experience of the first one, will lead to the exact point of neutrality.

Quantity of Free Acid discharged in a given time by healthy individuals.

As the result of numerous analyses Vogel designates 2 to 4 grammes of oxalic acid as the equivalent of the amount of free acid discharged by a healthy man during twenty-four hours. This amounts to 0·10 to 0·20 grammes per hour. The hourly quantities, however, were subject to considerable variations, dependent upon the time of the day, and these variations were quite parallel in four different individuals examined at one and the same time. The maximum amount of acid per hour was discharged during the night, the minimum during the forenoon, and a quantity intermediate between those of night and morning was secreted in the hours of the afternoon. Thus the frequent examination of the urine of one individual yielded 0·19 for the night, 0·13 for the forenoon, and 0·15 grammes of (oxalic) acid for the afternoon.

The amount of free acid in the urine is diminished by the ingestion into the system of caustic alkali, or of carbonates or substances capable of being transformed into carbonates.

All these substances have already been enumerated in the chapter on the chemical reaction of the urine.

The ingestion into the system of mineral acids increases the amount of free acid in the urine. As some organic acids, when taken in large doses, pass through the organism unchanged, as has been ascertained by Wöhler, and confirmed by Buchheim, they must also increase the amount of free acid in the urine.

A young man, labouring under hæmoptoe, was treated by Vogel with large doses of the sulphuric and hydrochloric acids. The daily amount of free acid in the urine was (the average of six days) 4·4 grammes, and on one day the quantity rose to 7·5 grammes.

All the causes which we have seen to determine the amount of phosphoric and sulphuric acid in the urine are, of course, active in determining the quantity of free acid.

Quantity of Free Acid in diseases.

In chronic and acute diseases Vogel found the amount of free acid mostly diminished, increased only in exceptional cases. The following are his results:

In males· In a case of pneumonia the free acid rose steadily from 0 to 1·50. Average of eight days, 0·5 grammes.

Another case of pneumonia, terminating fatally, showed fluctuations between 0·9 and 3·0. Average of four days, 1·9 grammes.

In a patient labouring under gastric fever, the amount of free acid fluctuated between 0·6 and 1·6. Average of four days, 1·1 grammes.

A case of acute rheumatism gave 0·7 and 1·0 grammes for several days.

In a case of chronic bronchial catarrh, the amount of free acid fluctuated during eleven days between 0 and 0·8. Average, 0·5 grammes.

In females: Girl with strumous glands, 1·6 to 2·4. Average of four days, 2·0 grammes.

A woman, 30 years of age, suffering from spinal irritation, 0 to 0·8. Average of five days, 0·4 grammes.

A woman, 70 years of age, with ascites, the consequence of disease of the liver, 0 to 3·1. Average of eighteen days, 1·41 grammes.

CHAPTER XII.

POTASH AND SODA.

Symbols: KO, NaO.

Equivalents:	K	39·115	Na	22·973
	O	8·000	O	8·000
	KO =	47·115	NaO =	30·973

There is only a very small quantity of potash present in the urine, by far the greater part of the acids being in combination with soda and the alkaline earths. The value which an accurate knowledge of the quantities of potash and soda would have, is evident from their relations to different parts of the animal economy; the salts of potash almost exclusively predominating in the muscles, and occurring in the blood only in very small quantities, while the salts with soda as their base prevail in the blood, and, it may be well assumed, form no part of the solids of the juices of the flesh.[1]

Mode of determining the quantity of Potash and Soda in the Urine.

The rationale of this analysis[2] is to remove sulphuric and phosphoric acid and organic matters, to transform the alkalies entirely into chlorides, and then to separate them by making one of them insoluble.

Of a solution of one part of acetate of baryta in 20 parts of water made strongly alkaline by means of ammonia, one volume, say 20 c.c., is mixed with two volumes, 40 c.c., of urine. After the precipitate has begun to settle, it is sepa-

[1] Liebig, 'Unters. über das Fleisch.,' p. 85.

[2] Rose, Analyt. Chemie. ii, 11. For some particulars see Neubauer, loc. cit. p. 138.

rated from the fluid by filtration. Of the alkaline filtrate, which contains an excess of baryta, 45 c.c., corresponding to 30 c.c. of urine, are evaporated on the water-bath in a platinum dish, dried, and exposed to red heat until the carbon is entirely burned. Water is now added to the ashes until the soluble part is entirely dissolved. After the addition of some ammonia, carbonate of ammonia is added, to precipitate all baryta in the form of carbonate. The fluid is now separated from the insoluble parts and precipitate by filtration, and the filter is washed carefully. The filtered fluids are then acidulated by means of hydrochloric acid, evaporated in a platinum capsule of known weight, exposed to a gentle red heat, and weighed. The alkalies, the weight of which in the form of chlorides has thus been ascertained, are dissolved in a little water; chloride of platinum is then added in great excess, the mixture is evaporated nearly to dryness on the water-bath, and digested for several hours with spirits of wine of 80 per cent. When the supernatant strata of the mixture indicate by a deep-yellow colour that a sufficient amount of chloride of platinum is present, and when after frequent stirring of the mixture all chloride of sodium and platinum is probably dissolved, the solution is filtered from the chloride of potassium and platinum, and the precipitate and filter are well washed with spirits of wine, dried and weighed. The weight, less the weight of the filter, is chloride of potassium and platinum; 100 parts of the latter correspond to 30·51 parts of chloride of potassium. By subtracting the amount of the latter from the amount of the united chlorides, the rest gives the amount of chloride of sodium. The amount of chloride of potassium found, gives, by multiplication with 0·6317, the corresponding amount of potash; and the amount of chloride of sodium found, multiplied by 0·5302, gives the corresponding amount of soda.

Physiological relations of Potash and Soda.

The facts adduced by Professor Liebig are of so remarkable a nature, that to follow them out promises to be a source of progress in practical medicine. The analysis of the urine will always be the principal means for ascertaining the proportions of these alkalies to each other, and to the other ingredients of the juices of the body. The problem is therefore a physiological one; and the analysis above detailed should not be considered as a mere exercise in the laboratory.

Many animals take with their food no phosphate of soda, a

salt indispensable to the integrity of the blood and body. But they take phosphate of potash, and a salt of soda, chloride of sodium. In these animals, however, we find in the blood phosphate of soda, and in the muscles chloride of potassium; neither of which salts they have taken with their food. From this fact, and from other experiments in the laboratory, the conclusion is inevitable, that phosphate of potash, when mixed with chloride of sodium, gives a part of its potassium off to some chlorine, which in its turn parts with some sodium. The latter combining with the oxygen liberated from the potassium, joins the phosphoric acid, phosphate of soda being formed.

The relations of the salts of potash to the muscles are not as yet understood. But the same physiological law which confines phosphate of soda to the blood, and makes it indispensable there, is, no doubt, active in confining the salts of potash to the muscles. To bring about an understanding of these relations is a problem of experimental physiology.

CHAPTER XIII.

LIME AND MAGNESIA.

Symbols: CaO and MgO.

Lime and magnesia occur in the urine in combination with phosphoric acid, as acid phosphates in solution. They are met with as deposits in alkaline urine, and as concretions in urinary calculi, of which they most frequently constitute the crust.

Formulæ: $\left.\begin{matrix} PO_5+2CaO+HO \\ PO_5+2MgO+HO \end{matrix}\right\}$ in solution.

Equivalent of phosphate of lime:	PO_5	= 71·436
	$2CaO$	= 56·000
	HO	= 9·000
		136·436
Equivalent of phosphate of magnesia:	PO_5	= 71·436
	$2MgO$	= 41·302
	HO	= 9·000
		121·738

Some authors calculate the formula for phosphate of lime and magnesia so that the three equivalents of water of phosphoric acid are replaced by three equivalents of the earths, PO_5+3CaO, and PO_5+3MgO. These formulæ are transferred from the formulæ of bone-earth, obtained by incineration of the bones. But as incineration of phosphates in the presence of carbon always causes a loss of phosphoric acid, these analyses cannot be depended upon as regards the composition of the phosphates. Moreover, the composition of the triple phosphate (of magnesia) militates against the basic formula. The precipitates, however, obtained from urine by the addition of caustic fixed alkalies, both show the composition of three of oxyde to one of acid, the magnesia salt retaining five equivalents of water after drying at the heat of boiling water.

Aggregation.—As generally met with, both phosphates of lime and magnesia are amorphous. But they are obtained crystalline, the one from certain solutions, the other in combination with a third equivalent of base and water of crystallization.

When a solution of phosphate of lime in acetic acid is allowed to stand some time, the phosphate has a great inclination to fall down from this solution in a crystalline state, particularly when the mixture is warmed a little, and when the phosphate is prevalent.

Separation of Phosphate of Lime and Magnesia from Urine, and determination of their collective amount.

This is simply effected by adding to urine some ammonia, until a strong alkaline reaction is observed. The earthy phosphates thus precipitated may be collected on a filter, washed, exposed to red heat, and weighed. Or, after collection on the filter, they may be redissolved in acetic acid, and in this solution the amount of phosphoric acid, found by the analysis described above, may, by the equivalents known, indicate the amount of earths in combination. Or, if the phosphates of the alkalies are to be determined also, the analysis described at p. 185 may be used, by which, in the first instance, the entire amount of phosphoric acid contained in the urine, and then of phosphoric acid in combination with the alkalies, is determined, the difference corresponding to the amount of phosphoric acid in combination with the earths.

Modes of ascertaining the separate quantities of Lime and Magnesia in Urine.

All the following methods are preceded by the separation from urine of both earths by means of ammonia, and by the solution of the washed precipitate in acetic acid. From the latter solution the lime is always obtained as the oxalate. From this point the analyses begin to vary.

Determination of the Lime as Sulphate.

The oxalate of lime obtained by addition of oxalate of ammonia to the solution in acetic acid of the precipitate, which a measured quantity of urine yielded after addition of ammonia, is exposed to a strong red heat in a platinum cap-

sule. To the lime thus transformed into carbonate, partly into caustic lime, some sulphuric acid is added, with great care, in small portions, by means of an elastic pipette, until an acid reaction is observed. After drying, and a second exposure to red heat, the lime is obtained in the form of sulphate, which, by multiplication with 0·4118, gives the amount of lime contained in the sulphate.

Determination of the Magnesia as Pyrophosphate.

The filtered fluid obtained from the oxalate of lime in the course of the foregoing analysis, is treated with ammonia until alkaline, whereby the magnesia is precipitated in the form of $PO_5+2MgO+NH_4O+12Aq$, triple phosphate, or ammonio-phosphate of magnesia. As the crystals settle easily to the bottom of the vessel, this salt may be washed by decantation of repeated quantities of water, containing some ammonia, added to it. It is then collected in the platinum capsule, and exposed to red heat. If collected on a filter, the latter, after removal of the greater bulk of the crystals into the platinum capsule, has to be burned separately by Bunsen's process, described in the introduction. Precipitate and filter, when united, are then exposed to red and white heat. The triple phosphate, by losing all its water and ammonia, is thus transformed into pyrophosphate of magnesia, of the composition PO_5+2MgO. The amount of the latter, multiplied by $\frac{40{\cdot}000}{111{\cdot}360} = 0{\cdot}3592$ (111·360 equivalent of pyrophosphate of magnesia, containing 40·000 of magnesia)—more accurately $\frac{41{\cdot}302}{112{\cdot}738} = 0{\cdot}3687$, gives the amount of magnesia.

Hempel's method of determining the Lime as Oxalate, by means of Permanganate of Potash.

From the solution of the mixed earths in acetic acid the lime is precipitated by oxalate of ammonia, collected on a filter, and, after washing, is dissolved in a few drops of hydrochloric acid. To this solution, after warming it a little, a graduated solution of permanganate of potash is added, so long as discoloration continues to take place. From the amount of solution of permanganate of potash used, the amount of oxalic acid is found, and from this the amount of lime originally combined with phosphoric acid.

Preparation of the solution of permanganate of potash.— As the solution of permanganate of potash cannot be kept as such for any length of time without undergoing changes, its graduation has to be checked before each analysis. For this purpose, and for the original graduation, a solution of oxalic acid in water is used, which in every cubic centimètre contains 10 milligrammes of oxalic acid. The solution of permanganate of potash is then graduated so that 1·0 c.c. will exactly suffice to oxydize 10 milligrammes of oxalic acid, and to make the signal of the completed oxydation by the appearance of the red colour.

The solution of oxalic acid is simply made by dissolving one gramme of the acid, dried at 212° F., in 100 c.c. of water. Of this solution 10 c.c. are taken by means of a pipette, and transferred to a beaker. We now add, from a burette, of the solution of permanganate of potash which is to be graduated, as much as necessary to produce the lasting red test. Supposing that 8·3 c.c. have been used for that purpose, we then add to every 830 c.c. of the solution, 170 c.c. of water, whereby we obtain 1000 c.c. of solution, of which 10 c.c. will exactly suffice for oxydizing 10 c.c. of the solution of oxalic acid, containing 100 milligrammes of the acid.

It is, however, less troublesome to merely determine the quantity of solution of permanganate of potash required for oxydizing a known amount of oxalic acid, without adjusting its bulk to that of the solution of the acid.

If, therefore, the above solution be taken as it is, without adding the 170 c.c. of water, then its value would be expressed by 8·3 c.c. = 100 milligrammes of oxalic acid. The calculation after the use for real experiment would therefore be 8·3 c.c. of standard solution : 100 milligrammes of oxalic acid $= n$ c.c. standard solution : x milligrammes of oxalic acid.

This analysis has been combined by Professor Vogel with the volumetrical analysis of phosphoric acid, so that by two analyses the quantities of phosphoric acid and both earths are determined. He for that purpose takes the precipitates from two equal quantities of urine, and determines in the one the entire amount of phosphoric acid, in the other the amount of lime as just described. From the total amount of phosphoric acid the equivalent for lime is now deducted ; the rest of the acid indicates the amount of magnesia with which it was combined.

The operator must take care to use a Gay-Lussac's burette for the solution of permanganate of potash, as this fluid is decomposed by the India rubber of Mohr's burette.

Determination of the Lime by a graduated solution of Hydrochloric Acid.

We give this method after Neubauer, who obtained accurate results by it. The oxalate of lime obtained as above is transformed into carbonate by the aid of heat, and dissolved in hydrochloric acid of known strength. The amount of acid not neutralized is then ascertained by a graduated solution of soda.

Preparation of the standard solution of hydrochloric acid.—One cubic centimètre of this acid is exactly to neutralize 10 milligrammes of lime, or CaO. One litre of the acid would therefore have to correspond to 10 grammes of CaO or 18·93 grammes of carbonate of soda. A small quantity, say about one gramme, of carbonate of soda, after having been made red hot and allowed to cool again, is weighed and dissolved in water. Some tincture of litmus is now added to colour the solution fairly blue. It is then made boiling hot, and the dilute hydrochloric acid is added from a burette, until the blue colour of the solution has given way to a light-red colour, resembling the red of onion-peel. It is well to keep the fluid at the boiling point during the addition of the acid, in order to remove all carbonic acid as quickly as possible, which latter, by giving the fluid a colour of red wine, would not permit of the transition of the blue colour into red being accurately perceived. Suppose we have found that one litre of the dilute hydrochloric acid employed corresponds to 41·6 grammes of carbonate of soda, then 18·9 grammes of the latter will exactly require 457·0 c.c. of the acid for saturation.

We take therefore . 457·0 c.c. of the acid,
and mix them with . 543·0 c.c. of water,

whereby we obtain . 1000·0 c.c. of standard solution,

of which 1·0 c.c. corresponds to 0·0189 grammes of carbonate of soda (NaO, CO_2), or 0·010 grammes of CaO. The correctness of the solution is to be checked by several experiments.

Preparation of the solution of soda to correspond to the former solution.—Of this solution 10 c.c. must exactly neutralize 10 c.c. of the solution of hydrochloric acid, so that after the addition of the last drop of the 10 c.c. of the solution of soda to the acid, the red colour of the latter (by litmus) is changing to blue. To observe the colour accurately, it is well to take care that the solution of soda be free

from carbonic acid. To 10 c.c. of the standard solution of hydrochloric acid, coloured red by means of tincture of litmus, we add the dilute solution of soda, which is to be graduated, from a burette, until the red colour has changed to blue. Suppose we have used, for 10·0 c.c. of the standard solution of hydrochloric acid, 8·0 c.c. of the solution of soda, then we add to

800·0 c.c. of solution of soda,
200·0 c.c. of water,

and thus we obtain 1000·0 c.c. of solution of soda,

of which 10·0 c.c. must exactly neutralize 10·0 c.c. of the standard solution of hydrochloric acid.

The fluids applied.—The oxalate of lime, obtained from a known quantity of urine, say 100 c.c., in the manner described, is exposed to red heat, and transformed into carbonate of lime and quicklime. It is then transferred into a balloon with the aid of some water; 10 c.c. of the standard acid solution are then added, and the solution thus obtained is heated until all carbonic acid has been driven away. The solution is then coloured red by means of litmus. The standard solution of soda is now added until the red colour has changed to blue. The number of cubic centimètres of the solution of soda subtracted from the 10·0 c.c. of standard acid leaves the number of cubic centimètres neutralized by the lime, each cubic centimètre corresponding to 10 milligrammes of lime. By multiplying by 10 the number of cubic centimètres of standard acid neutralized by lime, we obtain the per centage of lime contained in the urine when 100 c.c. of it have been taken for analysis.

Determination of Magnesia by means of volumetrical analysis of its Phosphoric Acid.

For this purpose the magnesia is isolated in the form of triple phosphate, and dissolved in acetic acid. In this solution the phosphoric acid is now determined by means of the graduated solution of chloride of iron. This method does not give very accurate results.

Deposits of Earthy Phosphates.

As a rule, deposits of earthy phosphates can exist only in urine exerting an alkaline reaction upon test-paper. The

presentation of an acid reaction by urine, therefore, excludes the possibility of the occurrence of these deposits. There is only one (questionable) case in which a deposit of an earthy phosphate is compatible with an acid reaction of the urine; namely, when urine containing little or no free acid exerts an acid reaction from the presence of chloride of ammonium. In this case a deposit of phosphate of magnesia may perhaps exist; for this salt is little or not soluble in chloride of ammonium. But phosphate of lime is so soluble in the latter salt, that it could not exist as a deposit so long as any acidity of the chloride of ammonium is not neutralized.

The observations which are said to have been made of urine having an acid reaction, and yet containing a permanent deposit of phosphates,[1] if they cannot be explained in the way just detailed, must be considered as fallacious. They are contrary to the commonest law of chemistry. I have made some observations, which may serve to explain the manner in which such statements have come to be called observations. Clear acid urine was allowed to stand for three hours, when a pellicle of phosphates was observed on the surface. Blue test-paper, immersed an inch deep into the fluid, on being withdrawn had become red. Another piece of the blue test-paper was now laid flat upon the surface of the fluid, when no reaction took place. The upper stratum of the urine had evidently become alkaline under the influence of the air, while the lower strata had retained their acidity.

Urine may be acid for a short time and yet contain a deposit of phosphates; or it may contain a deposit of phosphates for a short time, and yet remain acid, under the following circumstances. If to acid urine in the bladder a secretion of alkaline urine be superadded, and the person remain very quiet, the lower strata of the urine in the bladder may be alkaline and contain a deposit, while the upper remain acid. Of course this may vary according to the different densities of the two secretions. My explanation is based upon a case in which urine was discharged acid, and yet thick from the presence of phosphates. But the upper strata of the urine soon became quite clear, and a little cloud at the bottom of the vessel dissolved on agitation.

We have already seen that an alkaline reaction of the urine may be due to various causes, and have distinguished between alkaline reaction from fixed alkalies, derived from the blood, and that which is due to the presence of ammonia from decomposition of urea. The deposits of earths taking place

[1] Dr. G. Bird, 'Urin. Dep.,' p. 260, § 261.

under the neutralizing influence of both alkalies are identical as regards phosphate of lime, different as regards phosphate of magnesia. For the latter is deposited by fixed alkali, as $PO_5 + 3MgO + 5HO$, while in the presence of ammonia it takes up one equivalent of this base and water of crystallization, and appears as $PO_5 + 2MgO + NH_4O + 12Aq$. A deposit containing this latter salt is therefore due to the presence of ammonia from decomposed urea. If the acid, by means of which phosphate of lime is kept in solution in the urine, be a volatile one, namely, carbonic acid, as was observed in one case, which will be quoted in another page, the spontaneous or intentional evaporation of the acid may cause a deposit of lime to appear.

Deposits of Phosphate of Lime.

Physical characters.—Deposits of phosphate of lime, as usually occurring in the urine and mixed with magnesia, are always white, amorphous, under the microscope appearing in granules, sometimes of a greenish tinge, which exert a refracting action upon light. Crystallized deposits of this substance have not been observed; but it is more than doubtful whether it does not enter into the chemical composition, or is an admixture of some crystalline sediments.

Crystallization.—Phosphate of lime may be obtained in a crystalline state from its solution in acetic acid. When this solution is allowed to stand some time, the phosphate has a great inclination to fall down from this solution in a crystalline state, particularly when the mixture is warmed a little, and when the phosphate is prevalent. By precipitation of phosphate of soda with chloride of calcium, an amorphous gelatinous deposit of phosphate of lime is obtained. This after standing some days becomes transparent, like solution of gum. When a sunbeam is now allowed to fall on the precipitate, myriads of glistening crystalline points may be observed disseminated through the amorphous part of the deposit. Under the microscope these crystals appear as delicate, thin, clino-rhombic plates, very much like the crystals of oxalate of urea.[1]

Chemical diagnosis of deposits of phosphate of lime.—The occurrence in neutral or alkaline urine only is the first point to be observed. The deposit is insoluble in water,

[1] For a perfect crystallographical description, see Schmidt, C., 'Krystallonomische Untersuchungen,' 1846, p. 58.

soluble in weak acids, such as acetic acid, and is again precipitated from the acid solution in its original form by ammonia. From the acetic acid solution oxalate of ammonia throws down oxalate of lime. This latter test distinguishes it from the phosphate of magnesia, with which it is always mixed. Phosphate of lime alone does not easily fuse before the flame of the blowpipe.

When diffused in urine, the deposit appears like a dense cloud of mucus, from which it is not easily distinguished, because it is mostly mixed with it, and resembles it in colour. When it appears in urine on the application of heat, its resolution on cooling, or by the addition of an acid, distinguishes it from albumen.

Deposits of Ammonio-phosphate of Magnesia.

Physical characters.—Deposits of this substance always occur in well defined crystals in ammoniacal urine. No substance commonly occurring in the urine, and being insoluble in water, presents the same glistening glass-like appearance.

Form of crystallization.—The triple phosphate crystallizes in the rhombic system. The form most commonly met with is the vertical prism, combined with terminal planes derived from macro- and brachy-diagonal horizontal prisms. Some of these forms[1] resemble hippuric acid very much. But there is this crystallographical distinction between them, that on crystals of hippuric acid we frequently observe planes derived from the rhombic octahedron, which in triple phosphate are scarcely ever met with. See plate III, fig. 2.

Not rarely these crystals have a tendency to cross each other at regular angles. This is best seen in crystals obtained from blood. The latter serve to explain other forms observed in the urine, namely, the stellæ,[2] which are not merely acicular prisms cohering at one end, but prisms crossed at regular and symmetrical intervals. They very much resemble crystals of snow. These latter, however, being prisms of the hexagonal or rhombohedral system, cross at equal angles (of one sixth of the circle each), since the triple phosphate crystals cross at angles of which only four are equal, the other two being equal to each other.

[1] *Vide* Schmidt, loc. cit., p. 48.
[2] *Vide* Dr. G. Bird, p. 275, fig. 46.

The stellar and foliaceous crystals are not all formed by crossing only, some being appositions of groups of crystals in the prolongations of the axes of a central crystal. In this way the most fanciful forms are obtained.

The crystals of triple phosphate polarize light, and then appear tinted with prismatic colours. When seen in a sunbeam reflected through the polarizing microscope, they appear the finest objects for studying the phenomena of polarization.

Chemical properties.—When kept in water the triple phosphate disintegrates, the surface of the crystals becomes corroded, and at last there is nothing left but amorphous phosphate of magnesia. This corrosion is prevented by the presence of free ammonia, which makes them quite insoluble in water, and is therefore eligible as a preserving fluid for microscopical specimens. When the transparent crystals are exposed to a boiling heat, they lose water of crystallization and become opaque. They are easily soluble in acetic acid, and from this solution may be obtained again by excess of ammonia.

When heated with a solution of potash, the triple phosphate is decomposed, the potash combining with the phosphoric acid and setting free the ammonia and the magnesia. The former volatilizes, and may be detected by the smell, while the magnesia is precipitated.[1] $(PO_5 + 2MgO + NH_4O + 12HO) + 2KO = (PO_5 + 2KO + HO) + NH_3 + 2MgO + 12HO$.

Earthy Phosphates in Calculi.

Not quite 10 per cent. of all calculi[2] have a nucleus of mixed phosphates. But these substances enter into the composition of about 34 per cent. of all calculi, forming either their body, one or more layers, or the crust. This shows that the presence of deposits of mixed phosphates in the urine scarcely ever gives rise to the formation of calculus, but that the presence in the bladder of other calculi frequently causes a deposit of phosphates to be formed around them, in which respect every calculus is nothing else than a foreign body.

[1] Bowman, 'Med. Chem.,' § 300.

[2] Twenty-two out of 233 in Guy's Hospital Museum. Dr. Golding Bird gives the number of calculi preserved there as 374, which is inclusive of 142 calculi taken from one individual. For calculating the comparative frequency of calculi, such a mode of reckoning is unavailable. We therefore take the 142 as 1, and then we have $374 - 141 = 233$.

Prout found the proportion of phosphate of lime calculi to the whole number contained in various museums as 1 to 117. The proportion of calculi composed of pure triple phosphate was 1 to $126\frac{2}{3}$. The relative proportion of the mixed phosphates he put as 1 to $12\frac{1}{4}$. The general proportion of all the calculi, arranged under the heads of the phosphates in different museums, he found as 1 to 10. In alternating calculi, the phosphates succeeded to uric acid in the proportion of 1 to $9\frac{1}{6}$. The ratio in which the phosphates succeeded to urate of ammonia (and soda) was as 1 to $12\frac{1}{2}$; and in which the phosphates succeeded to the oxalate of lime was as 1 to $7\frac{1}{2}$. On the contrary, three instances only occurred in which the uric acid, or urate of ammonia, succeeded to a phosphate; and the proportion in which the oxalate of lime succeeded to the phosphates was as 1 to $253\frac{1}{3}$ only. The general proportion in which the phosphates succeeded to the other ingredients, was as 1 to $4\frac{1}{15}$.

From these facts, Prout deduced the general law that, in urinary calculi, a decided deposition of the mixed phosphates is not followed by other depositions.

Calculi of phosphate of lime have mostly a smooth surface, and are composed of concentric layers, which, when the calculus is broken, separate from each other with great facility, forming detached crusts. These are almost infusible before the blowpipe, requiring for fusion so intense and prolonged a heat, that few can succeed in fusing it (Bowman). The chemical characters of these calculi are those of phosphate of lime, as described above.

Calculi composed entirely of triple phosphate are generally crystalline, or consisting of aggregated prismatic crystals; they often contain cavities filled with the largest and most perfect crystals of triple phosphate, or have their surface covered with a smaller variety of them. Specimens of this kind are contained in the Museum of the College of Surgeons.

Before the blowpipe, the triple phosphate gives off the smell of ammonia, swells up, gradually becomes gray, and ultimately fuses.

Calculi composed of phosphate of lime and triple phosphate are commonly called fusible calculi, from the readiness with which they fuse before the blowpipe, giving off ammonia and water, and leaving a mixture of phosphate of lime and pyrophosphate of magnesia.

Physiological quantities of Earthy Phosphates in the Urine.

The proportion in which the phosphate of lime in the urine stands to the phosphate of magnesia has been determined by Kletzinsky[1] to be about two to one; namely, 67 parts of phosphate of lime and 33 parts of phosphate of magnesia in 100 parts of mixed earthy phosphates precipitated from healthy urine.

The average amount of phosphates of the alkaline earths discharged by a healthy man in twenty-four hours, has been determined by Beneke[2] to be 1·2 grammes. Under ordinary diet, Lehmann discharged 1·09 grammes; Boecker,[3] 1·48 grammes. These observations give, as the average of mixed phosphates during twenty-four hours, 1·28 grammes.

Mosler and Hegar determined the quantity of earthy phosphates by calculation from their phosphoric acid. The former made two series of observations upon himself, the first series comprising six days in April, the second four days in October. His results were as follows:

Observations of the quantity of Phosphoric Acid combined with Earths in the Urine.

	First Series. Amount of PO_5.		Second Series. Amount of PO_5.	
	During one hour.	During one day.	During one hour.	During one day.
	Grammes.	Grammes.	Grammes.	Grammes.
Minimum . . .	0·015	0·370	0·007	0·170
Medium . . .	0·048	1·152	0·015	0·390
Maximum . . .	0·075	1·800	0·027	0·660

In other healthy individuals, Mosler found the average per hour of PO_5 to fluctuate between 0·015 and 0·019 grammes. Hegar found from observations, extending over eight days, that he discharged 1·31 grammes of phosphoric acid in combination with earths. Six months afterwards, the average of four days was only 0·902 grammes of PO_5. Neubauer determined directly the amount of lime and mag-

[1] Heller's 'Archiv,' 1852, p. 270, et seq.

[2] 'Zur Physiol. und Pathol. des Phosphors. und Oxals. Kalkes,' Göttingen, 1850.

[3] 'Beiträge zur Heilkunde,' Crefeld, 1849.

nesia discharged by two healthy persons. His results are arranged in the following table:

Observations of the quantity of Lime and Magnesia discharged during twenty-four hours.

	First Individual. Average of seventeen days.		Second Individual. Average of twenty-one days.	
	Lime.	Magnesia.	Lime.	Magnesia.
	Grammes.	Grammes.	Grammes.	Grammes.
Minimum . . .	0·057	0·096	0·118	0·084
Medium . . .	0·096	0·173	0·250	0·219
Maximum . . .	0·169	0·271	0·356	0·262

From all the observations taken together, it follows, that the amount of earthy phosphates in the urine varies in different individuals, and in the same individuals at different times. A general average for any given weight of individual can therefore not be drawn at present. It can only be obtained by extended observations on the urine, taking into consideration the quantities of earths ingested with the food, and those discharged by way of the bowels.

The influence which different qualities of food have upon the quantity of earthy phosphates discharged by the urine is well illustrated in the experiment of Lehmann. As we have already stated, when eating mixed food, his average amount of earthy phosphates was 1·09 grammes. But when he restricted himself to animal diet, the amount rose to 3·56 grammes, being more than three times his ordinary average.

Pathological indications.

1. *The presence of earthy phosphates in the urine is indicative of the alkaline condition of that fluid.*

2. *If the precipitate of earthy phosphates is entirely amorphous, we may conclude that the alkali which caused it was not ammonia.*

3. *If, however, the precipitate contains crystals of triple phosphate, it indicates the presence of ammonia, arising most probably from decomposition of urea.*

An excess or deficiency of earthy phosphates in the urine can only be ascertained by quantitative chemical analysis. The

mere presence in the urine of a deposit of this kind, or its appearance in the urine on heating, is by no means indicative of an excess, as is yet too commonly believed. The originators of the term phosphatic diathesis and phosphuria, and their followers, linked a series of the most varied disorders together under this term, which had nothing in common but one symptom, namely, alkaline urine. The following facts and considerations may perhaps serve to explain some opinions, which, by the weight of authority, are rather widely circulated, but nevertheless require a thorough reformation.

Animal diet has a tendency to increase the acidity of the urine; vegetable diet easily makes it alkaline. The dyspeptic, therefore, eating little or no meat, will easily cause his urine to be alkaline by eating a little fruit, for which he not unfrequently has a longing. But even if no fruit has been partaken of, and but little meat, the secretion may be alkaline; in the former case from the presence of carbonates, in the latter from that of alkaline phosphates from the blood, which the free acid has not been sufficient to transform into acid salts.

What want of appetite for animal food causes in the dyspeptic patient, want of animal food causes in poor, old people. The alkaline urine of the octogenarian dependent upon parochial relief, is the consequence of his not being able to afford meat once a week. Hence, in these cases, the acidity of the urine is restored by a proper allowance of meat.

The anæmic girl and the diabetic patient are instances of the same character. In the former, the phosphates may be altogether absent for a day or two, so that the urine, being alkaline, will form no deposit. Meat diet will soon restore acidity and phosphates. In diabetic patients, phosphate of lime is sometimes altogether absent, and the alkaline urine deposits the triple phosphate only. Lehmann observed such a case. The glittering crystalline deposit of triple phosphate contained no trace of lime. We may here observe, that the microscopical analysis is not sufficient to prove the absence of phosphate of lime. For Vogel (p. 203) observes that deposits of the latter salt are often so transparent, and their outlines are so little defined, that when mixed with the triple phosphate they are easily overlooked, unless the observer takes particular care in illuminating his object. It is for this reason, that we cannot take any notice of statements regarding the occurrence of deposits of the triple phosphate, unmixed with phosphate of lime, which are not sustained by exact chemical tests.

Urine becomes alkaline when retained in the bladder for

any unusual length of time. This will not so much occur when absolute retention takes place, as when from any cause the bladder is never emptied entirely of its contents. This causes irritation of the mucous membrane, and an increased discharge of mucus, which, being retained also, is present in unusual quantity. Whether by means of the mucus, or on its own account, we do not pause to discuss—but urea is decomposed, making the urine ammoniacal. A small part of this ammoniacal urine is always retained, and induces quickly an analogous decomposition in the fresh arrivals from the ureters. The urine is then discharged alkaline, thick, and fetid. But when the bladder is thoroughly emptied and washed out by injection, an acid urine will immediately collect in it.

This is the physiological explanation of these cases, as proved by experience, reason, and experiment. Let the retention be due to paralysis of the bladder, from whatever cause,—affection of any part of the spine, from hemiplegia or paraplegia, or from difficult childbirth; let it be due to the presence of diverticles of the bladder, to calculi or foreign bodies, to enlarged prostate, to stricture of the urethra; or let the retention be caused by the perverse will of insanity, in which excretions are frequently held back, entirely or in part; or let partial retention occur in the coma of fever—it will always have the same effect, decomposition of urea and ammoniacal urine.

There are some rare and extraordinary cases, in which phosphate of lime is said to continue to be discharged in the urine for a long time without apparently doing much mischief. Such a case is recorded by Dr. G. Bird (p. 294). The patient was an old man, an habitual dyspeptic, and had laboured under pyrosis from boyhood. He had during many years been in the habit of passing almost milky urine, which on repose deposited such an extraordinary quantity of phosphate of lime, that he brought to Dr. G. Bird, at one time, more than an ounce of the salt. He had during the last fifty years been under the treatment of half the hospital physicians and surgeons in London. At the same time this man's general health was so good, that there was scarcely an excuse for submitting him to any course of treatment, beyond the apprehension of the possible formation of a calculus. This man was most probably an impostor. No pretence could lead him to the hospital, from which during a fifty years' experience he had derived no benefit regarding a symptom, which, if really present, left his health intact. To collect an ounce of the earthy phosphates must have engaged him for sixteen days, supposing it all to be derived from his own

excretions. And no man will take that trouble knowingly for no purpose; his object must be to make himself interesting in the eyes of the physician, and, if possible, to derive the benefit of being kept in the charity some time.

If the reader should not share our doubts, he may adopt the explanation by Dr. G. Bird, for which, however, there is no basis in fact; or he may explain it upon the ground of the following observation recorded by Dr. Prout (p. 323, note). This physician examined the body of a gentleman who, during the greater part of his life, had suffered from renal disease, remarkable for being attended by the secretion of large quantities of the earthy phosphates. Both kidneys were not only extensively disorganized, but most of the natural cavities, as well as many cysts, were found distended with numerous earthy concretions, of various sizes and composition. The concretions found in those cavities *to which the urine had access*, consisted of the phosphate and carbonate of lime, and more or less of the triple phosphate of ammonia and magnesia, while those cavities or cysts distinct from the renal structure, and to which, therefore, *the urine had no access*, consisted of the calcareous phosphate and carbonate only, without any admixture of the triple phosphate.

From a consideration of many cases of earthy calculi, it is apparent that the mere presence in the bladder of deposits of the earthy phosphates never gives rise to calculi. For such a concretion to form, it requires the presence of some binding material, such as ropy mucus, or a clot of blood, or fibrine. It is for this reason that urine, which deposits the earths in the bladder under the influence of fixed alkali, has never been known to form a calculus. It is only with the aid of hæmaturia, or chronic disease of the mucous membrane, that calculi are formed. In accordance with this, calculi are rare in the bladder of herbivora, which discharge alkaline urine, and therefore always mixed with a large proportion of a deposit of earthy phosphates.

Carbonate of lime is met with in some urinary concretions, but very rarely. The above observation of Dr. Prout illustrates the circumstances under which it may occur. It is a regular ingredient of the urine of herbivora. I have examined prostatic concretions consisting nearly entirely of this substance. But it is always questionable whether the lime or carbonic acid were in any case derived from the urine.

CHAPTER XIV.

IRON.

Symbol: Fe. Equiv.: 28·0.

I am obliged to treat of iron in this place, though it would perhaps have been more properly arranged under Uræmatine, of which substance Dr. Harley has shown that it always forms an integral part, thus indicating its derivation from hæmatine proper. In the course of time we may perhaps succeed in finding the proportion in which iron is contained in uræmatine; and in that case this metal would be valuable for determining the quantities of this colouring principle in the urine.

Besides the iron normally combined with uræmatine, an accidental quantity may be present in the urine, after the ingestion into the system of preparations of iron. These latter combinations yield the ordinary tests for iron with the usual reagents, and therefore differ considerably from the iron combined with uræmatine, which is not influenced by the addition to the urine of the usual test-solution for iron. For the iron of uræmatine to exhibit its ordinary properties, it requires the total destruction, by heat, of the organic substance with which it is combined, and, after solution in a mineral acid, it becomes accessible to the tests.

Chemical properties.

When to the solution in hydrochloric acid of the ashes of urine a drop of nitric acid is added, and afterwards sulphocyanide of potassium, a reddish colour is produced by the presence of the smallest traces of iron, and a deep red by the presence of larger quantities.

Another portion of the solution of the ashes, after boiling with a little nitric acid and dilution with water, may be treated with ferrocyanide of potassium, when immediately a

precipitate of Prussian blue will ensue, if the quantity of iron present be large. If, however, traces only are present, it will require several hours' standing for the blue flakes or light clouds of Prussian blue to become visible by deposition.

Marguerite's method of determining the quantity of Iron in Urine.

When a solution of suboxyde of iron in an excess of hydrochloric acid, is mixed with a solution of permanganate of potash, the suboxyde is transformed into oxyde, and the permanganate reduced to manganate. One equivalent of permanganate of the composition $Mn_2O_7 + KO$ yields 5 equivalents of oxygen, and thereby transforms 10 equivalents of suboxyde of iron into oxyde. A solution of permanganate of potash of known strength, therefore, may serve to determine the quantity of iron contained in any solution in the form of suboxyde, if added in a quantity just sufficient to effect the oxydation. This quantity may be accurately determined by the loss of colour which the permanganate undergoes as long as it is continued to be reduced; but a single drop of this fluid which is added, over the quantity necessary for effecting the transformation into oxyde of the whole of the suboxyde present, imparts to the mixture a light-red colour, which indicates the completion of the analysis.

Preparation of the standard solution of permanganate of potash.—We dissolve crystallized permanganate of potash in an *ad libitum* quantity of water, and determine the strength of a given volume of this solution by the following *standard solution of ferrocyanide of potassium*, given by Neubauer:—7·543 grammes of pure, crystallized, dry ferrocyanide of potassium, containing 1·0 gramme of iron, are dissolved in so much water, that the solution exactly amounts to one litre. 10 c.c. of this solution contain exactly 10 milligrammes of iron. 10 equivalents of ferrocyanide of potassium require 1 equivalent of permanganic acid to be transformed into 5 equivalents of ferricyanide of potassium.

Of this solution we now take 10·0 c.c., containing 10 milligrammes of iron, dilute it with about 50 c.c. of water, acidulate with hydrochloric acid, and after having placed the beaker upon a piece of white paper, we add the solution of permanganate of potash to the solution of iron, which latter is kept in a rotating motion. The appearance of a yellowish-red colour indicates the completion of the test. Supposing the 10 milligrammes of iron contained in the 10 c.c. of solution of the ferrocyanide required 20 c.c. of the solution of per-

manganate of potash for complete oxydation, 1 c.c. of the latter fluid would correspond to $\frac{0{\cdot}010}{20} = 0{\cdot}5$ milligramme of iron. The strength of the solution of the permanganate of potash may also be determined by the solution of chloride of iron of known strength described under phosphoric acid, or by the solution of oxalic acid of known strength, described under the analysis for phosphate of lime. By calculation of the equivalent, it may easily be adapted to the equivalent of iron.

Application to the urine.—The ashes of a given bulk of urine, say 100 c.c., burned perfectly white, if necessary, by the aid of nitrate of ammonia, are dissolved in hydrochloric acid. The chloride of iron has now to be reduced to the state of subchloride. This is best done by dissolving pure zinc, which has been expressly ascertained to be free of iron, in the acid solution, until the latter has lost all its colour (method of Schwarz[1]). It is now freed from the excess of zinc and other matters by filtration, and diluted to the bulk of about 50 c.c. The solution of permanganate of potash of known strength, as determined before use, is now added to the solution of iron, and mixed with it by agitation until the red test appears. Supposing 1 c.c. of the solution of permanganate of potash to be graduated for 0·0005 grammes of iron, and supposing that we have used for the oxydation of the suboxyde of iron obtained from 100 c.c. of urine, 3 c.c. of the standard solution of the permanganate, they would indicate $3 \times 0{\cdot}0005$ grammes $= 0{\cdot}0015$ grammes of iron. Supposing that of this urine 1500·0 c.c. were discharged during twenty-four hours, the amount of iron thus secreted would be 0·0225 grammes.

The disappearance of the red colour test after standing a little while, is due to further changes not in connection with the analysis, and need not, therefore, be regarded by the experimenter.

Physiology and Pathological indications of Iron.

We know that iron is a component part of the red colouring matter of the blood or hæmatine, and that a deficiency of iron in this substance, or in the blood and organism generally, constitutes a feature of certain diseases, which generally pass under the name of chlorosis and anæmia. The similarity to hæmatine which uræmatine exhibits, by its con-

[1] 'Maassanalysen,' p. 120.

taining iron in chemical combination, is one of the strongest reasons for considering it a derivate of the former. We are the more struck by the analogy which the uræmatine, as regards its quantity, bears to the hæmatine in the diseases above mentioned. But so much remains here to be ascertained by fact, that I think it dangerous to do more than give a glimpse in this direction at present.

The analysis of the urine may prove useful for determining the amount of iron which enters the blood and circulation, when it is taken as a medicine.

CHAPTER XV.

AMMONIA.

According to Professor Liebig,[1] fresh healthy urine contains only very small or very doubtful traces of ammonia, and gives no precipitate with chloride of platinum. The crystals which form overnight in urine mixed with chloride of platinum exhibit all the properties of the chloride of platinum and potassium. And if any chloride of platinum and ammonium should be mixed with them, it is uncertain whether these are not due to the decomposing influence of the chloride of platinum upon the organic constituents of the urine. By the application of heat to the urine, ammonia will be evolved. When subjected to distillation in a retort, the fluid which goes over will contain ammonia to the last—a phenomenon which has been explained by the decomposing influence of the acid phosphate of soda upon urea and colouring matter. The phosphate of ammonia and soda thus formed has the property of giving off its ammonia at a temperature of 212° F., and the acid phosphate thus left is again and again a generator of ammonia, as long as any organic substances are left capable of yielding that base. The influence of the alkaline earths, as lime and baryta, upon the urea in the urine is so great, particularly in higher temperatures, that it will require strong proof to show that any of them can with safety be used, even at the common temperature of the air, for liberating from the urine any ammonia that may be present as such in combination with an acid. It has been stated in a former chapter, that ammonia occurs in combination with uric acid, and that urate of ammonia might be an ingredient of all healthy urine. It is here the place to state, that the difficulty of affording a direct proof for this assumption cannot be disguised. For, that urate of

[1] 'Ueber d. Constitution des Harns, &c.,' p. 195.

ammonia may occur in a deposit, is in itself no proof that it may occur under ordinary circumstances; for a deposit is a morbid feature, however slight the symptoms may be which the individual experiences at the time of its occurrence. And if, on the other hand, urate of ammonia forms on the surface of evaporating urine, this cannot be assumed as a proof simply of over-saturation of the fluid with this salt, for the reason already stated, namely, that in higher temperatures ammonia is produced from urea by the decomposing influence of the acid phosphate.

To prove the presence of ammonia in a deposit of the ordinary urates is by no means an easy task. It is easy enough to filter off the deposit, to wash and dry it, and by solution in caustic potash to prove an evolution of ammonia. But to get the deposit pure and free from all matters which, with caustic potash, are capable of giving off ammonia, is at present almost impossible. In fact, the proof that the ammonia obtained by the process just mentioned was combined with uric acid, is altogether wanting. Under these circumstances we cannot be astonished to find that accurate observers, as Lehmann and Scherer, share the doubts of Liebig regarding the presence of ammonia as a normal ingredient in urine. The analyses of Heintz[1] are by no means calculated to set the question at rest, as some authors have rather precipitately assumed. For if the chloride of platinum were a reliable test for the decision of this question, such a man as Liebig would never have set it aside in the manner indicated. The researches of Boecker, Boussingault, and De Vry have had no decisive result; though the analyses of Boussingault seem to support the presence of ammonia in the urine. The best proof as yet advanced of the regular presence in the urine of certain quantities of ammonia seems to be afforded by the analyses of Neubauer,[2] who adapted the method of Schlösing for the volumetrical analysis of ammonia in the urine. There is only one objection to this method, which I have already advanced; the ammonia is set free by the addition to the urine of milk of lime. Now, if it can be proved that milk of lime at the ordinary temperature of the air does not within a reasonable limit of time create ammonia from urea and the other organic substances, we are bound to say that an essential progress would be effected by these researches of Neubauer. The subject of ammonia in connection with the animal economy would be of immense import-

[1] Poggendorff's 'Annalen,' 1845, p. 118.
[2] 'Journal für Practische Chemie,' Bd. 64, p. 177, and 'Anleitung,' § 56.

ance, if it should be proved beyond the shadow of a doubt, what Dr. Richardson[1] has endeavoured to show, namely, that ammonia is a regular constituent of the blood, and the solvent of fibrine in the living body.

Symbol: NH_3.

Equivalent = 17·0.

H_3	= 3·0	— 17·65
N	= 14·0	— 82·35
NH_3 = 17·0		100·00

The chemical properties of ammonia, as far as it is necessary to give them here for our special purpose, are easily defined. It is the only volatile alkali with which chemistry is acquainted; and of this property we avail ourselves for its analysis.

It is driven out of its combinations and salts by caustic lime, and evaporates spontaneously from watery solutions when exposed to the air.

In a mixture of perfectly neutral solutions of sulphate of silver and arsenious acid, the slightest trace of ammonia causes immediately a delicate but dense yellowish-white precipitate of arsenite of silver, which is easily soluble in the slightest excess of acid. This is the most delicate test for ammonia. Upon this I have based the following proceeding:

Demonstration of the presence of Ammonia in Urine.

The ammonia, which has been liberated from urine by means of milk of lime, is made to pass in the form of gas into a solution of sulphate of silver and arsenious acid; the precipitate ensuing is evidence of its presence.

Determination of the quantity of Ammonia in Urine by volumetrical analysis.

The method just described may, with slight modifications, be used for determining the quantity of ammonia thus evolved. Into a potash bulb is put a known amount of sulphuric acid of known strength, and the ammonia evolved from the urine by lime is made to pass through it by means of an aspirator. All ammonia of the urine will be combined with the sulphuric acid in the apparatus. The acid, thus combined with the ammonia, is now put into a beaker,

[1] Astley Cooper Prize Essay for 1856, 'On the Cause of the Coagulation of the Blood.'

and saturated with a solution of caustic soda of known strength. The point of neutrality is indicated by the appearance of a white precipitate of arsenite of silver, when the solution of sulphate of silver and arsenious acid has previously been added to the sulphuric acid, and by the reappearance of the blue colour when tincture of litmus has been used as the indicator. The former test is particularly useful, when we have to work with artificial light, which does not permit the distinctions between red and blue litmus to be accurately perceived. From the amount of solution of soda used less than would have been required for saturating the same bulk of sulphuric acid of known strength, if no ammonia had been combined with it, the amount of ammonia is found by calculation.

The following method by Neubauer is preferable in some respects. It is based upon the fact that ammonia evaporates from its watery solution, and, if confined with free sulphuric acid in a closed space, is entirely absorbed by the acid. The rest is done by volumetrical analysis as above.

Preparation of standard solution of sulphuric acid.—Fourteen grammes of hydrated sulphuric acid are diluted with 200 grammes of water; and, after the mixture has cooled down to the ordinary temperature of the air, the amount of sulphuric acid contained in every 10·0 c.c. is determined in two such portions by means of chloride of barium, in the usual way. When both analyses agree pretty nearly, the average of them may be taken as correct. For instance, if we have found that 10 c.c. of the dilute acid contain 0·505 grammes of sulphuric acid, they will be exactly neutralized by 0·2146 grammes of ammonia, NH_3; 1 c.c. of the dilute acid therefore corresponds to 0·02146 grammes of NH_3.

Preparation of standard solution of caustic soda.—A dilute solution of freshly prepared soda in alcohol is made, and its strength is determined by finding the quantity required to neutralize 10·0 c.c. of the sulphuric acid just described. To 10·0 c.c. of the sulphuric acid, therefore, reddened by tincture of litmus, or mixed with the solution of sulphate of silver and arsenious acid, the solution of soda is added from a burette until the point of neutrality is indicated by the restoration of the blue colour of litmus, or the appearance of the precipitate of arsenite of silver. Suppose we have used to this point 30·0 c.c. of the solution of soda, then we know that every cubic centimètre of it exactly corresponds to 0·00715 grammes of ammonia; as the 10·0 c.c. of sulphuric acid, which were neutralized by 30·0 c.c. of soda, correspond to 0·2146 grammes of NH_3.

Application of the fluids.—20·0 c.c. of fresh filtered urine are put into a glass or china dish of four inches in diameter, and one inch in height. A triangle, made of a glass rod, is now put across the top of this dish, to support a smaller flat dish containing 10·0 c.c. of the standard sulphuric acid. This is now placed under a receiver on a ground-glass plate, closed hermetically by the aid of tallow. A dinner-plate and some mercury may also be used for the purpose. When the entire apparatus is thus completed, 10·0 c.c. of milk of lime are added to the urine in the lower dish, and the apparatus is quickly closed and put aside. After the lapse of forty-eight hours the whole of the ammonia formerly contained in the urine will be found to have been driven out, and to have been absorbed by the sulphuric acid in the upper dish. If the sulphuric acid is now neutralized by the standard solution of soda, so much less of this solution is required as is equivalent to the amount of ammonia contained in the acid. Thus, if the 10 c.c. of sulphuric acid (containing 0·505 grammes of SO_3, corresponding to 0·2146 grammes of NH_3), after exposure to the vapour of ammonia evolved from the urine under the glass shade, require only 26 c.c. of the solution of soda instead of the 30 c.c. for which they are graduated, they have absorbed an amount of ammonia equivalent to 4 c.c. of the solution of soda, of which it has been seen that every cubic centimètre corresponded to $\frac{0{\cdot}2146}{30} = 0{\cdot}00715$ grammes of NH_3. The 20 c.c. of urine, therefore, evolved or contained $4 \times 0{\cdot}00715 = 0{\cdot}0286$ grammes of NH_3. 1000 grammes of urine would therefore contain 1·43 grammes of NH_3; and every other quantity in proportion.

Neubauer found that healthy fresh urine, free from mucus, does not undergo alkaline decomposition during the first forty-eight hours after being passed. But it is not so with the urine from patients, which very frequently begins to decompose a few hours after emission. Such urine, therefore, requires some precautions; and of these, the first to be noticed is the advice of Vogel, to empty the bladder by means of the catheter, and then to collect the freshly secreted urine through the catheter, which is left in the urinary passages. The urine is thus protected from the decomposing influences, both of the secretions of the bladder and of the higher temperature of the body. If this precaution be not feasible, the colouring and other easily decomposing matters may be removed by means of a mixture of equal volumes of solutions of basic and of neutral acetate of lead. Of this mixture 30 c.c.

are mixed with an equal volume of urine, and of the liquid filtered from the precipitate 40 c.c., corresponding to 20 c.c. of urine, are taken for the analysis of ammonia. If the operator will take a little more trouble, he may control the analysis performed *with* milk of lime, by putting urine into a second apparatus *without* it. If the latter evolve no ammonia, spontaneous decomposition of the urine has probably not taken place.

The method of finding the amount of ammonia in urine by means of chloride of platinum, given by Heintz, requires so much time for its execution that it becomes simply impracticable. In that respect it shares the fate of the analysis of urea by the same indefatigable observer; but there is that difference, that the analysis for urea gives an accurate result for the trouble, of which we are not sure regarding ammonia, for reasons already advanced. It is therefore not to be wondered at, that the amount of ammonia found by Heintz in the urine of twenty-four hours should be more than double the quantity of that found by the above analysis of Neubauer, a fact which adds to the probability that chloride of platinum produces ammonia in urine by decomposition of some of its constituents, not being simple salts of ammonia.

Quantity of Ammonia discharged in the Urine during twenty-four hours by healthy individuals.

Neubauer examined the urine of two male individuals of twenty and thirty-six years of age respectively. The average of twelve analyses of the urine of the man of twenty years gave 0·6137 grammes of ammonia for twenty-four hours. The average of the second subject, as found by the same number of analyses, was much higher than that of the first, namely, 0·8351 grammes of ammonia for twenty-four hours. The minimum was 0·3125; the maximum 1·2096 grammes of ammonia each day. Expressing these facts in round figures, we may say that the average amount of ammonia excreted by a healthy man is, minimum, 0·3; average, 0·7; maximum, 1·0 gramme.

Physiological origin of Ammonia.

The only reliable knowledge on this point consists in the following facts: *The ammonia of the salts of ammonia, when the latter are taken into the stomach, passes unchanged through the system and is discharged in the urine.* This has been proved beyond doubt by the analyses of Neubauer.[1] The

[1] 'Journal für Practische Chemie,' Bd. 64, p. 281.

subject of his experiments was the young man of twenty years of age, whose average discharge of ammonia during one of twelve days had been ascertained to be 0·6137 grammes. He took now 2 grammes of hydrochlorate of ammonia in a glass of water for five successive nights; and, in the urine collected for five successive periods of twenty-four hours, analysis showed an excess of 9·957 grammes of hydrochlorate of ammonia over the amount of ammonia previously ascertained to be the normal average.

It remains to be seen whether caustic ammonia and carbonate of ammonia are eliminated in a similar manner. It remains, also, to be ascertained whether the organism produces any ammonia under ordinary circumstances, or whether the ammonia in the urine is simply introduced by our food and drink, or by the air which we breathe. Some articles of food are rich in ammonia, *e.g.*, radishes. The smoke of tobacco contains a large share of ammonia; and any person remaining for any length of time in a room filled with this ambrosial offering to Apollo, must inhale such quantities of ammonia as must materially increase the ordinary amount in his urine. If ammonia be really essential to the blood, the anti-tobacco leaguers may yet hear the argument advanced, that tobacco-smoking is really essential to keep our fibrine in solution, and that smoking has of late become so much more common, because the ordinary sources of this "food," the cesspools, dunghills, and other like accompaniments of human and animal habitations, have been done away with. A still greater amount of ammonia is of necessity inhaled where both the sources just mentioned flow without restraint.

Pathological indications.

If what some have ventured to bring forward as a defined feature of certain forms of disease of the kidney can really be maintained, namely, that the urea retained in the blood may there undergo decomposition into carbonate of ammonia, and give rise to the symptoms described as uræmia, the pathological indications of ammonia in the urine would be all important in those diseases. And though quantities of ammonia might be excreted by the lungs, skin, and bowels, yet the urine would be that excretion in which the ammonia would be most accessible to our analysis. However probable such a process, under given circumstances may be, actual and direct proof would be required to make it a fact; and this we cannot say to have been afforded by the originators of the theory. We know,

on the contrary, that the test said to be diagnostic of the presence of ammonia in the breath, the formation of white vapours on contact of the breath with a glass rod dipped in hydrochloric acid, frequently fails in cases with the most marked symptoms of uræmia. We must, therefore, expect further proofs, analyses of the blood and the excretions, before we can give that extension to toxæmia as a cause of various severe affections, which by various authors has been attributed to it. It is the same with putrid or septic fevers, under those conditions in which the blood is said to be in a state of dissolution. For all we know, ammonia may be a product of these pathological processes; and then we might expect to find it, in part at least, in the urine.

If urine is ammoniacal, and we should wish to determine the amount of ammonia thus formed from urea, we may precipitate the ammonia by the addition to a measured quantity of a salt of magnesia. If the mixture is well stirred for a little while, the triple phosphate thus formed will subside, and by its weight, when in the form of pyrophosphate, the amount of free ammonia contained in the urine may be calculated.[1] But this analysis should not be depended upon for any very accurate conclusions, as the sources of error surrounding it are numerous.

[1] Schmidt, 'Krystallonomische Untersuchungen,' p. 55.

CHAPTER XVI.

CARBONIC ACID.

Symbol : $C\ O_2$

Equivalent = 22			
. C =	6	—	27·27
O_2 =	16	—	72·73
	22		100·00

THERE is a little carbonic acid in the urine, as in most animal fluids; and a method has been devised by Marchand[1] for determining its quantity. From a measured quantity of urine the carbonic acid is evolved by warmth and diminished air pressure, and caught in baryta water. This is the principle of the analysis; the following are the particulars: 100 c.c. of urine are put into a balloon, closed by a cork, which is pierced by two glass tubes. One tube dips into the urine, and above the cork is drawn out into a long point, and closed by the blow-pipe. The second tube begins with the cork, has a double bend, and is connected with a second, but empty bottle, out of which a second doubly bent tube leads to a third balloon, half full of clear baryta water. Several bottles with baryta water may yet be attached. To the last one the air-pump is fixed. The whole apparatus being made air-tight, the balloon containing the urine is placed in the water-bath, and its temperature raised to 112° or 140° F., after which the air is gently pumped out of the apparatus. The urine soon begins to boil, and distils partly into the empty bottle, and the solution of baryta in the several bottles becomes turbid from carbonate of baryta. After the lapse of about half an hour or more, the thin point of the first tube is broken off, and air is gently drawn through the apparatus. The carbonate of baryta is afterwards separated by filtration, washed, and dissolved in hydrochloric acid; the solution is precipitated by sulphuric acid; and from the weight of sulphate of baryta thus obtained the amount of carbonic acid is calculated.

[1] 'Journal für Practische Chemie,' Bd. 44, p. 253.

CHAPTER XVII.

BLOOD AND ITS ANATOMICAL ELEMENTS.

Blood is a wandering tissue; and as such is composed of an element possessing form, the corpuscles, and a liquor in which these are suspended; a second element, which may be termed anatomical, because it admits of mechanical demonstration, and separates from the liquor when withdrawn from the circulation, and becomes solid, is fibrine; a third anatomical element is the serum, which may be defined as an alkaline solution of albumen in water.

The presence of any of these elements of blood in urine indicates serious lesion in some part of the urinary organs. When blood is mixed with the urine, it indicates a breach of surface: in the kidneys, produced by stasis in the capillaries; in their pelves and the ureters, by the mechanical violence of a concretion; in the bladder, by rupture of enlarged veins, ulceration, irritation of a calculus, or malignant disease. The presence of blood-corpuscles amounts to a demonstration of the presence of the three elements of blood, for obvious reasons. It is best ascertained by the microscope. The presence of fibrine in any form also admits of anatomical demonstration. But albumen requires chemical tests, which, though of a simple nature, yet must be used with certain precautions, in order not to mislead our conclusions. The presence of fibrine or of albumen may be due to exudation without breach of surface.

Blood, Blood-corpuscles, and Coagula.

When very small quantities of blood are present, it is diffused through the whole mass of urine without damaging its colour. In that case it is necessary to let the urine repose in a white china vessel, or in a glass vessel placed on a white sheet of paper, when the blood-corpuscles will collect at the

bottom in form of a a rusty-brownish sediment, not easily to be mistaken for anything else, so that it may serve for the diagnosis, by the naked eye, of even very minute quantities of blood.

If a little more blood is present in the urine, it gives it a dirty, dingy, or smoky hue, when diffused, forming a larger rust-brown deposit on repose. If the urine is of a low specific gravity at the same time, the corpuscles yield part of their red colouring matter, and the urine assumes the pink colour of flesh-washings, or the cold extract of flesh. This pink colour passes through all gradations, until the colour of the urine is almost like blood itself. When blood is effused in any considerable quantity at a time from larger blood-vessels, such as veins of the bladder, or small arteries opened by a concretion, it then coagulates in irregular, mostly lumpy masses, of a black or reddish-black colour. Though these coagula cannot easily be mistaken for anything else by the naked eye, they may yet present certain variations, according to whether they have been formed in the urinary passages, or after the excretion of the urine. When formed in the urinary passages, as is mostly the case when they are formed at all, they may be retained in the bladder or in the narrow canals leading to and from that organ, thus causing irritation of the bladder, dysuria, stranguria, or retention of urine. When retained in the bladder, they may give rise to concretions. When retained in the bladder for a short period only, and there exposed to the influence of a dilute urine, secreted in consequence partly of the stimulus transferred to the kidneys from the irritated bladder, coagula of blood may give up all their colour and be discharged as colourless lumps of fibrine. Such coagula, modified by a sojourn in the bladder, I have known to be declared fibrinous casts of the urethra. The diagnosis of the presence of blood in all these cases, when at all doubtful, is ensured by the—

Microscopical appearances and reactions of Blood-corpuscles.

Under a power of 400 diameters, these bodies appear as circular discs, with the edges rounded off. The centre of the discs may be light, and the circumference dark; or on changing the focus the reverse may be the case. Their colour is a light-brown or reddish-brown hue. On setting the fluid in which they are contained in motion, their true shape becomes at once apparent: for we see the disc excavated on either side. On adding water to the corpuscles, we perceive them to expand; the concavities begin to rise, and

disappear, and the biconcave disc gradually is transformed into a globule somewhat analogous in shape to the globe of the earth—compressed between the two poles. The equator of the blood-disc becomes a little smaller by this expansion in the direction of the formerly shortest axis. The central marking, shadow or light, according to the focus, now disappears, and the corpuscle assumes the illumination of a globular body. Under a continued influence of the water, they gradually yield their colour to the surrounding fluid, becoming themselves pale, and ever more imperceptible, until at last they seem entirely to disappear. But they do not disappear in fact, for, if a concentrated solution of any neutral salt be now added to the fluid in which the corpuscles are invisible, they gradually again become visible, but now are without any colour, and mostly of a corrugated outline, their regular shape being scarcely ever restored. This phenomenon of their becoming invisible in water is explained by the nature of the endosmotic and exosmotic changes which occur: the fluid contained in the corpuscle and that surrounding it, together with the membrane, have all the same coefficient for refraction of light, and hence neither by itself makes any impression upon sight.

When the normal corpuscles are treated with concentrated solution of any neutral salt, or with syrup, or with a solution of any neutral organic substance, they immediately become flatter, and the excavations deeper, which is indicated by the central shadow approaching nearer to the circumference. At last they begin to crumple, and turn up their edges, which become indented and irregular. The corpuscles now assume the most irregular shapes and outlines; and though they have lost part of their colouring matter, yet they are by far more distinct than at first. If to the solution water is now added in sufficient quantity, they assume their former shape, and under the continued influence of the water undergo the changes before described.

In the caustic alkalies, ammonia included, the corpuscles are entirely soluble; and from this solution they cannot by any means be again obtained. In acetic acid the corpuscles become clearer, expand, and after a time are almost invisible, but do not dissolve. In nitric acid the outline of the corpuscles becomes darker and thicker, whilst the globules become smaller in circumference. Similar effects are produced by hydrochloric acid and the gastric juice. Acid urine only requires a longer time, otherwise its effects are similar to those of the reagents last named, combined with those of solutions of salt. The irregularities of the margin are fre-

quently of such a nature as to represent granules arranged round a central nucleus. When, however, blood is present in the urine in any quantity sufficient to nearly or altogether neutralise any acidity of the urine, these changes do not take place to that extent, the corpuscles remaining either unchanged, or, when the urine is very watery, only giving up part of their colouring matter, or adhering to each other in rouleaux like rolls of coins, in the same way as the corpuscles in blood which is not mixed with any urine. The several modifications of blood corpuscles are represented in fig. 5, of pl. III.

Chemical diagnosis of Blood in Urine.

In most cases the microscope affords conclusive evidence of the presence of blood. In very rare cases, however, the blood is to be looked for in ammoniacal urine; and then the corpuscles are not easily to be found, as they are too soluble in that fluid, which then merely has a red colour, and coagulates under certain circumstances. In this case, the presence of blood may be ascertained by the following tests for hæmatine and albumen. The urine is cautiously neutralised, with a trace of acetic acid in excess. It is then heated in a water-bath to 151° F., when all albumen will be found insoluble in the form of a white coagulum, surrounded by a reddish fluid. The latter is separated by filtration from the precipitate, and again heated in the water-bath; when near the boiling point, a second coagulation of globuline and hæmatine, in reddish-brown flakes, will demonstrate the presence of these bodies. Both tests, when presented conjointly by urine, are conclusive evidence of the presence of blood, or of an equivalent of its several constituents.

Pathological indications.

After having, in the introduction to this chapter, noticed the general indications of the presence of blood in urine, it here remains to state the particular conclusions which may be drawn from this morbid ingredient of urine under various circumstances.

Most frequently the presence of blood in urine is a symptom of the first or acute stage of those diseases of the kidney which are caused by the entrance into the blood of a specific poison; such as acute desquamative nephritis. The blood then proceeds from the congested and ruptured Malpighian corpuscles, as evidenced by the following facts, which stand in perfect accordance with physiological reasoning.

The *tubuli contorti* of the kidneys are frequently found full

of blood, in cases where the urine contained blood during life.

The capsules are also filled with blood, and the Malpighian bodies collapsed. This fact was first ascertained by Bowman,[1] and established, with further proofs, by Dr. G. Johnson.[2]

When the blood thus effused into the tubuli is quickly discharged, either by a continuance of the hæmorrhage or because it is mixed with urine or much serum, it will appear in the urine after emission as diffused blood, and cause the appearances described. But when the blood is effused in masses, so as to fill the entire lumen of the tubule, and is not actively pushed on, it may coagulate in the tubule, and make it impervious, or at a later period may be discharged with the urine in the form of blood-cylinders, which, by an admixture of epithelium of the tubuli, and by their form—being that of casts of the tubuli—show their origin in a most unequivocal manner. Together with these cylinders, there are mostly other casts present in the urine, characteristic of the affection of the kidney which produced the hæmorrhage. In some cases the poison producing hæmorrhage from the kidneys is a very tangible one; in the case from which the blood-casts of fig. 6, on plate III, were taken (case xxxi of Dr. Johnson), it was a dose of half an ounce of turpentine. In other cases it is a poison of a more obscure nature, like that of scarlatina; Dr. Johnson represents a Malpighian body and cortorted tubule from the kidney of a typhus patient, who discharged large quantities of blood during life; after his death nearly all the tubuli of his kidneys were found injected with blood in a similar manner.

In some cases of scurvy and purpura a similar hæmorrhage occurs from the kidneys. When the blood-casts remain in the tubuli for any length of time, they become much altered, but may always be distinguished from epithelium by their peculiar yellowish-brown tint, which the epithelial casts have not.

The presence of blood in the urine may indicate ulcerated cancer of the kidney. In this case the quantity of blood may be large or small, and may coagulate in the ureters or in the bladder. In advanced stages of the disease, pus and encephaloid matter is mostly present in the urine, thus characterising the hæmorrhage.

The presence of blood in the urine may be due to the mechanical effects of renal concretions, or to ulceration set up in the pelves and calyces of the kidneys by these bodies. The most

[1] 'Philos. Transact.,' 1842.
[2] 'Diseases of the Kidneys,' 1852.

general symptom of gravel in the kidneys is hæmaturia, increased by every kind of exertion. The nature of the hæmorrhage is sometimes ascertained by the presence of deposits in the urine on its being passed—by the passage of gravel. If the symptoms of renal concretion and hæmaturia are combined with the appearance of pus in the urine, it is probable that ulceration exists in the pelvis of the kidney. In these cases the diagnosis is ensured by the local symptoms.

The presence of blood in urine is indicative of certain diseases of the bladder. In these cases the local symptoms appear to be so well marked that there is not much difficulty in fixing upon the source of the hæmorrhage. Thus hæmorrhoids of the bladder are of a very chronic nature, and appear in periodical fits, like hæmorrhoids *per anum*. I observed such a case for several years. The subject of the observation was a lady. The irritability of the bladder was extreme; it was caused first by the venous congestion; this having lasted a day or two, blood escaped by the urine; clots of different forms and sizes remained in the bladder, or blocked up the urethra, requiring the use of the catheter; sometimes they required manual aid, when they had partly passed the urethra. Thus, even after the hæmorrhage had ceased for a time, the clots would continue to be passed, and they were the paler the longer after the cessation of the hæmorrhage they escaped from the bladder. This condition would last for weeks, with frequent intervals, during which no hæmorrhage ensued. Gallic acid in large doses always removed the complaint after a time. The patient would be well for months, until a new attack made its appearance. The last attack occurred during a severe illness from scarlet fever, of which the aged patient eventually died.

Stone in the bladder not rarely causes hæmorrhage from that organ; so does chronic cystitis, accompanied by erosion or superficial ulceration. I observed the case of a farmer, who consulted me for severe disease of the bladder. He discharged an alkaline, fœtid urine, with rags of pseudo-membranes, appearing under the microscope to be made up of fibrine with pus-cells closely imbedded; on some occasions he, after severe straining and retention of urine, passed a membranous bag, which, when suspended in water, showed itself to be a hollow membranous sac, a perfect cast of a very small bladder. With these membranes of inflammatory origin, he passed clots of blood, and fluid blood mixed with the urine, but altered considerably.

Another form of hæmorrhage from the bladder is due to softening cancerous growths of that organ. This disease is

by far more frequent than vesical hæmorrhoids, and its presence is supposed to be indicated by every hæmorrhage from the bladder, in the opinion of some authors, who doubt the occurrence of hæmorrhoids of the bladder.

The differential diagnosis of these cases is established by the collateral and local symptoms of each case, which mostly are so marked that there is not much difficulty experienced in establishing distinctions. Happily, where it is difficult to distinguish, it is of not much practical importance to do so, as the treatment is directed against the hæmorrhage. Whether, in a given case, this proceeds from cancerous growths or from hæmorrhoids, is indifferent, as gallic acid, or any other astringent, will suit both cases equally well. The different course of the diseases would soon establish a diagnosis. But diagnosis is of far greater importance for the prognosis of a case of this kind; and as the latter is chiefly the service which it is possible to render to the patient, for the purpose of guiding his hygiene, an accurate diagnosis is essential.

The prognosis of all these cases, in the first instance, depends upon the nature of the disease, of which the effusion of blood is a symptom. As far, however, as the prognosis is dependent upon the hæmorrhage itself, we may say that it becomes bad in a direct ratio to the amount of blood discharged, to the time during which hæmaturia continues, and to the severity of the symptoms of irritation caused by the formation, retention, or passage of clots in and through the urinary passages. Of all the consequences of clots, the formation of a calculus round the clot as a nucleus is the most severe, and also the most rare.

CHAPTER XVIII.

HÆMATINE, OR HÆMATOGLOBULINE.

It is best to describe this substance as dissolved blood-corpuscles; for it is in fact a mixture of the albuminous fluid filling the corpuscles—globuline, and of the colouring matter, which may be obtained in crystals under certain conditions—hæmatocrystalline. The membranes of the corpuscles are either dissolved or invisible in urine where hæmatoglobuline occurs; and no corpuscles can be detected by the most careful searching under the microscope.

The per-centage of the elements of globuline is as follows:

Carbon . . .	54·5
Hydrogen . .	6·9
Nitrogen . .	16·5
Sulphur . . .	1·2
Oxygen . . .	20·9
	100·0

It is best distinguished from albumen by its point of coagulation being at 199·4° or 204·4° F., while that of albumen is 54° F. lower. It is not entirely coagulated by heat alone, but the presence of any neutral salt of the alkalies will effect complete coagulation. It is so intimately mixed with the red colouring matter proper, or hæmatine, that it includes the entire amount of this substance in its coagula. On boiling the latter with alcohol containing some sulphuric acid, hæmatine is dissolved, and forms a reddish-brown solution with the alcohol.

From this it follows that the distinction between the presence of dissolved blood, and that of hæmatoglobuline in urine, is very marked. For, though urine may contain albu-

men and hæmatoglobuline at the same time, yet they must be present in the same proportions as in the blood, before we can say that they are due to hæmorrhage, and consequent solution of the blood. No attention has hitherto been paid to this distinction, and in cases where the urine has been bloodcoloured, and gave a coagulum on boiling, the presence of hæmatoglobuline has been assumed, without a question as to the probable amount of albumen. These cases are therefore not quite satisfactory as regards the distinction between dissolved blood and hæmatoglobuline; a distinction the more important, as blood may be effused into the tubuli of the kidneys, there coagulate, and form blood-casts. These blood-casts may give up their hæmatoglobuline; and thus what really was a hæmorrhage may appear to be the secretion of fluid hæmatoglobuline. The blood-casts, in their altered state, are then frequently only expelled from the kidneys when all traces of hæmatoglobuline have long disappeared from the urine. Having drawn attention to this point, I will here quote the opinion of Vogel,[1] regarding the presence of hæmatoglobuline in urine. He says that in the body there is a constant disintegration of blood-corpuscles taking place, whereby hæmatoglobuline is set free, and subjected to further changes. Globuline probably serves for the nutrition of the muscles, and other albuminous tissues, and is at last removed from the economy in the form of urea and uric acid. Hæmatine is also further oxydised, and leaves the body in the form of biliary and urinary pigment, as cholo- and urohæmatine. In health, therefore, hæmatoglobuline never passes through the kidneys with the urine. But when there are pathological processes going on in the blood, the result of which is a wholesale destruction of blood-corpuscles, then the quantity of pure hæmatoglobuline in the blood becomes so large, that it cannot all be subjected to the normal changes, and it seems that a part may be secreted unchanged by the ordinary channels of the urine, just as other substances, such as sugar, bile, and perhaps albumen, when contained in the blood in excess, may pass over into the urine.

This explanation Vogel supports by the following observation. A professor of physics having performed an experiment with a balloon full of hydrogen, breathed some of this gas, when emptying the balloon of its contents by pressure. He became suddenly very ill, but soon recovered, and after the lapse of some time passed a urine, which was black like ink, coagulated on boiling, but contained no blood-corpuscles,

[1] 'Semiotik,' p. 186.

when examined under the microscope. This condition of the urine lasted for about twenty-four hours. It was found that the hydrogen used for the experiment contained arseniuretted hydrogen.[1]

Without in the least doubting the correctness of Professor Vogel's observation, as far as it goes, I cannot help expressing my opinion that the disintegration of blood-corpuscles *in* the circulation is by no means established by it. On the contrary, other observations of similar cases tend to make it probable that the complaint caused by the breathing of arseniuretted hydrogen, as it exhibits itself in the urine, is really hæmorrhage from the capillaries of the kidneys. Thus, in the case which has been related[2] by Dr. Schlinder of Greifensberg, deep reddish-brown urine, *mixed with clots of blood*, was discharged. In the case reported by Dr. O'Reilly,[3] however, there was first bloody urine, succeeded by suppression of urine, after which the face became copper-coloured, and the rest of the body greenish; symptoms probably indicating the presence of free hæmatoglobuline in the blood. As matters stand at present, there may be both hæmorrhage from the Malpighian bodies, and subsequent disintegration of the effused corpuscles, and also disintegration of the corpuscles in the blood, and subsequent discharge of the solution. The explanation by way of hæmorrhage is only more probable, and supported by collateral observations, and by the observations on the behaviour of blood-casts, which do not appear to have been mentioned by Professor Vogel.

This author also observed that a dog, after having breathed a quantity of arseniuretted hydrogen, discharged a blackish-brown urine, which contained a large amount of hæmatoglobuline.

In typhus, blood is not rarely discharged by the kidneys. Vogel, however, observed a case, in which there was only hæmatoglobuline present, no trace of blood-corpuscles being discoverable by the microscope. This happened during the acme of the disease, and disappeared after a few days; from which time the patient gradually rallied, and made a perfect recovery. I hope not to be found too sceptical, if I extend to this case the doubts mentioned above. The observations of Meckel, Heschl, and Planer,[4] quoted by Vogel in support

[1] Idem, in 'Archiv des Vereins für gemeinschaftliche Arbeiten,' Bd. i, Heft 2, p. 209.

[2] Buchner's 'Repertorium für die Pharmacie,' lxix, 271, *vide* Christison, 'On Poisons,' 4th edit., p. 326.

[3] 'Dublin Journ. of the Med. Sc.,' xx, 422.

[4] Ueber das Vorkommen von Pigment im Blute, 'Zeitschrift der Wiener Aerzte,' 1854, pp. 127 and 280.

of his opinion, undoubtedly prove that an excess of a granular pigment may accumulate in the blood in consequence of a copious destruction of blood-corpuscles; but the very fact of this (altered and insoluble) pigment accumulating in the blood, and causing dangerous symptoms, particularly in the brain, by blocking up the capillary vessels, shows that the formation of an excess of free hæmatoglobuline in the blood stands in no necessary connection with its discharge by the kidneys. For how could hæmatoglobuline accumulate in the blood, if it were secreted at the rate observed in Vogel's cases?

Pathological indications.

Leaving the question undecided for the present, whether the destruction of blood-corpuscles in the cases under consideration takes place in the blood or elsewhere, the destruction itself is certainly indicated by the appearance of hæmatoglobuline in the urine. Under all circumstances this is a sign of severe lesion; but it admits of a favorable prognosis, if it is limited to a certain short time, after which it does not reappear, as in the above cases. But when it is a symptom of severe scorbutic or septic disorders, it is a sign of great danger to the life of the patient. Suppression of the urine, and discoloration of the skin, when following the discharge of urine rich in hæmatoglobuline, are also very unfavorable, and are forerunners of a fatal termination of the case.

CHAPTER XIX.

FIBRINE. CHYLOUS URINE. FIBRINOUS CASTS.

Fibrine is anatomically well characterised by its spontaneous coagulation. Of its chemical properties little is known, if we except the per-centic elementary composition, which is almost identical with that of albumen and caseine. Bechamp has produced urea from fibrine by oxydizing agents, so that the ultimate fate of fibrine appears to be determined.

When fibrine occurs in urine, it always coagulates at some time or other after having left the circulation. It may become insoluble already in the urinary tubules, and then constitute the various descriptions of casts of those tubules—the common products of certain diseases of the kidneys. In other cases, not absolutely connected with disease of the kidneys, the fibrine may be kept in solution in the urine until its arrival in the bladder, and then coagulating may give occasion to difficulty in passing the urine. It may also keep in solution until the urine has stood for a time after its emission, and then coagulating, may assume the shape of the vessel in which it happened to be at the time.

When such coagulating urine contains fat in appreciable quantities, and is thereby made turbid and opaque, like milk, it is termed chylous urine. This coagulating or chylous urine establishes a very different prognosis from urine containing fibrine in casts, or in large coagula assuming the shape of the vessel formed after emission, and denoting acute disease of the kidneys.

Chylous Urine.

This description of urine is of very rare occurrence in Europe, about half the number of cases on record having been observed in natives of hot climates (East and West Indies, Mauritius, Barbadoes, Brazil), or in individuals who had

resided for many years in hot climates. The most accurate, and at the same time the most extensive, observations on this description of urine, have been made by Dr. Bence Jones,[1] on whose results I have mainly based the following description.

The properties of so-called chylous urine are due to the admixture of certain constituents of the blood, which is itself the effect of some peculiar disease of the kidneys. The urine which is secreted under the influence of that disease is characterised by the presence of either, or several, or all of the following abnormal ingredients.

Red blood-corpuscles, frequently mixed with some white ones. They may be entangled in fibrinous coagula, or form a deposit on standing. In either case they are easily diagnosed by the microscope.

Fibrine occurs in shreds and films, inclosing blood-globules, which rise to the top of the fluid on standing, and remain on the filter, through which the urine may be passed. Blood-globules frequently pass through the filter. When the fibrine occurs as a single coagulum, it may be small and partial, and occupy the centre of the vessel as a contracted mass, like the coagulum of the blood in its serum. On other occasions the whole of the urine, already in the bladder, or in the vessel into which it has just been passed, coagulates into a tremulous mass, which, when fatty, is like blanc mange, and assumes the shape of the vessel.

The coagulum, in both instances, particularly if it be broken up by agitation, gradually separates into two portions —a fluid or serous portion, more or less opalescent or milky, like the urine itself, and which, when left at rest for a few hours, frequently throws up a sort of creamy matter on its surface; and a very delicate fibrinous mass, small in comparison with the original bulk of the coagulated mass, of a flesh-like appearance, and generally tinged more or less of a red colour, from the presence of blood-corpuscles.

Albumen may be present in very small or very large quantities. It is then demonstrated by the usual tests—boiling and nitric acid.

Albuminoid matter—imperfect albumen of Prout—I have met with in apparently normal urine of the patient whose case has been so fully described by Dr. B. Jones. The urine gave no reaction for albumen, but yielded an abundant pre-

[1] 'Medico-Chirurgical Transact.,' vol. xxxiii, 1850. 'Philosophical Transact.,' 1850, part ii, p. 651. For earlier observations see Prout, 'Stomach and Urinary Diseases,' 3d edit., p. 112, and Dr. T Elliotson, 'Med. Times and Gaz.,' Sept. 19, 1857, p. 288. The anatomy of a case has been recorded by Dr. Priestley.

cipitate with tannic acid. This acid does not produce any precipitate in healthy urine. The albuminoid matter was not gelatine, as it did not gelatinize when the urine, after evaporation on the water-bath, was allowed to cool.

Fatty matters.—Their presence is the cause of the milky turbidity which may exist in all degrees from a pale opalescent white or amber, permitting the transmission of some light through layers not exceeding an inch in thickness, to milk-white, and quite impervious to light.

In this description of urine there are seen floating under the microscope myriads of infinitely minute particles; globules of oil are only rarely met with. The minute particles are scarcely resolvable under a power of 420.

This milky urine, when digested with its bulk of ether, on repose yields three layers—an upper ethereal solution, beneath this a thin filmy layer of albumen precipitated by the ether, and lowest the now almost perfectly clear urine, containing some ether in solution. The upper ethereal solution, after the ether has been removed by distillation from a balloon in the water-bath, leaves the fatty matters adhering to the bottom of the balloon. These matters, when digested with water for some time at the ordinary temperature, separate into oily drops, which collect on the surface of the water, and mainly consist of *oleic acid;* and into a solid matter remaining at the bottom of the vessel, but when disturbed likewise floating in water, and having the properties of margaric acid. On being warmed with a solution of phosphate of soda ($2NaO, HO, PO_5 + 24Aq$) this latter acid easily forms a permanent emulsion, a property not possessed by neutral fats or oleic acid. The margaric acid is peculiarly dissolved (emulsed) without, on standing, collecting on the surface of the solution. On boiling the above drops of oleic acid with solution of phosphate of soda, a slight emulsion is obtained, due to some margaric acid dissolved in the oleic; but the oleic acid, on repose, collects again on the top of the solution in the same drops in which it had been added. For this diagnostic test I am indebted to Dr. Marcet.

Pathology of so-called Chylous Urine.

The urine is oftener fatty when the patient subject to this disease lives on an animal diet than when he eats a more vegetable one. It is most clear before breakfast, and most fatty after dinner. It is oftener free from fat before breakfast, when the diet is vegetable, than when it consists more of animal food. Fat passes off in the urine after food

Casts of considerable diameter. $\frac{1}{300}$th of an inch.

The diameter of these casts is nearly equal to that of the urinary tubules in which they have been formed. They are mostly perfectly transparent, hyaloid, of a glistening aspect, resembling in appearance the surface of wax as it cools after having been melted, which similarity caused Dr. Johnson to term them "waxy." They rarely include much granular matter in their substance, owing to the very cause of their large size being the total absence of epithelium from the basement membrane in which they are moulded. When granular, however, in one part, and hyaloid in the other, they are, perhaps, not always of the largest size. Sometimes they may contain a few epithelial cells. Dr. Beale has observed and figured casts of considerable diameter, which were composed of a material in the interior differing from that which formed the circumference of the casts. With these large casts the sediment mostly contains granular casts of medium diameter, and granular *débris* of degenerated epithelium of the tubules. (Fig. 6, Pl. IV.)

Pathological indications of Casts of Uriniferous Tubules.

The presence in the urine of intratubular hyaloid casts indicates a chronic disease of the kidneys, termed non-desquamative nephritis, which is caused by a vitiated condition of the blood. As the expulsion from the organism of poisons causing this and similar diseases of the kidneys is mostly effected by a process, in which desquamation of the epithelium of the urinary tubules plays an important part, the fact of the epithelium not being cast off is an unfavorable symptom, indicating the retention of the poison in the blood. These casts, therefore, where they form the entire bulk or greater part of a urinary deposit, must excite serious apprehension for the ultimate welfare of the patient.

The presence in the urine of epithelial casts is a symptom of a disease of the kidneys, caused by the entrance into the blood of a morbid substance—a poison—the elimination of which is effected by these organs. The poisons of cantharides, turpentine, scarlatina, and cholera are illustrations of this. In all the diseases caused by these poisons, their elimination through the kidneys is accompanied by a process, of which the desquamation of the epithelium of the urinary tubules is an essential part. The presence of epithelial casts in urine for a limited period of time is therefore a favorable symptom of

the affection of the kidneys, as exhibited by other symptoms, and indicates that the poison is being actively eliminated. But when the epithelial casts become mixed with much blood or pus, or when the desquamation has a tendency to become of a chronic nature, from the causes continuing to influence it, then it becomes an unfavorable symptom in proportion to its duration.

The granular casts are indicative of chronic desquamative nephritis, and of degenerated condition of the epithelium of the urinary tubules. These casts and the casts containing fatty matter are frequently found in gouty subjects, and then give rise to an unfavorable prognosis. The prognosis is better in cases where the chronic desquamative nephritis is the sequel of the acute process.

The casts containing fat or fatty epithelium are most frequently the sequel of non-desquamative disease of the kidneys, and indicate the presence of fatty degeneration of the kidneys in the so-called granular form.

The casts of considerable diameter may occur in all diseases of the kidneys, and may therefore accompany all different descriptions of casts described. The presence of these casts is under all circumstances evidence that there are Bellinian tubules totally deprived of their epithelium. Their importance as a pathological indication is therefore in a great measure dependent upon the nature of the affection, in the course of which they have been deposited.

CHAPTER XXI.

ALBUMEN.

The *composition* of albumen, as it occurs in the blood, is very similar to that of white of eggs.

	White of eggs.	Albumen from blood.
Carbon . .	53·4	53·0
Hydrogen .	7·0	7·1
Nitrogen .	15·6	15·6
Oxygen . .	22·4	23·1
Sulphur . .	1·6	1·2
	100·0	100·0

We possess no chemical formula or symbol for albumen, as its rational composition is unknown. According to the quantity of sulphur, white of eggs must contain more than 90, and albumen of blood more than 110 equivalents of carbon.[1] Notwithstanding this, the chemical characters of both descriptions of albumen are so much alike, that it is difficult to distinguish them by chemical tests.

Albumen is formed in plants, and introduced into the animal economy as food; it there undergoes certain modifications, serves the purposes of the economy, and becomes disintegrated, leaving the body mostly in the form of urea. But when albumen, as such, is discharged in the urine, this is a sign of severe disease of the blood or of the kidneys.

General characters of Albumen.

Albumen occurs in a soluble and an insoluble modification. The former is present in all the fluids of animal and vegetable bodies, and may be transformed into the latter by

[1] Strecker, Dr. A., 'Kurzes Lehrbuch der organischen Chemie,' 2te Aufl. Braunschweig, 1857, p. 485.

boiling with water, or by contact with absolute alcohol, acids, or alkalies. The soluble modification may be obtained in a solid state by evaporating the solution at a temperature not exceeding 50° C. (122° F.), or by drying *in vacuo* over sulphuric acid. It is a yellowish transparent mass, of 1·314 specific gravity, which swells up with water, and, after a time dissolves. It has an alkaline reaction, and contains about 5 per cent. of free alkali and salts, which may be partly removed by washing with water, as they dissolve quicker than the albumen itself. The albumen, thus freed from alkalies, is insoluble in pure water.

The insoluble modification of albumen is a flaky or lumpy mass, without taste or smell, insoluble in water, alcohol, and ether, soluble in dilute caustic alkali by the aid of a gentle heat, from which solution it may be precipitated by the addition of an acid. The precipitate is changed in some degree, having lost part of its sulphur, which is sometimes evolved in the form of sulphuretted hydrogen. The insoluble modification is also soluble in concentrated acetic acid and common phosphoric acid; and in these solutions a precipitate is produced by ferrocyanide and ferricyanide of potassium. It is soluble in *very dilute* mineral acids, or at least is transformed into a jelly-like mass; the addition of a larger amount of acid to these solutions produces a precipitate. Concentrated hydrochloric acid, or sulphuric acid somewhat dilute, or a mixture of concentrated hydrochloric acid and some sulphuric acid, dissolve the insoluble modification of albumen formed by the aid of heat, and decomposes it. When this solution is boiled, and the air has free access to it, it becomes indigo-blue, or of a violet colour, which soon changes into brown. Concentrated nitric acid imparts a deep-yellow colour to solid albumen, when the mixture is gently warmed. A solution of mercury in nitric acid (containing salts of the suboxyde and of the protoxyde, Strecker), which is made by dissolving one part of mercury in two parts of nitric acid, containing 4½ equivalents of water, and having a specific gravity of 1·41 (Neubauer), imparts a saturated red colour to albumen in the solid or dissolved state, when the mixture is warmed to 140° or 212° F. The colour is not removed by the influence of the air, or by protracted boiling. This is said to be the most delicate test for albumen (Neubauer). On this I must remark that it is not applicable to the urine, as three different precipitates are formed in it by this mercurial solution; one of the suboxyde with chlorine (calomel), one of the protoxyde with urea, and one of the albumen with the free nitric acid of the mercurial solution.

These precipitates obscure the red colour so much, that frequently only a fawn or pale-red colour remains, and that only when the coagulated albumen is transferred into a second quantity of mercurial solution.

A solution of iodine in ioduretted hydrogen, or in iodide of potassium, imparts a brownish-yellow colour to albumen. When mixed with strong sulphuric acid and a solution of sugar, albumen yields a solution which is red at first, and afterwards assumes a violet colour.

When heated, albumen begins to melt at higher temperatures, and is decomposed, the mass swelling up, charring, and evolving an odour of burnt horn. When subject to the processes of destructive distillation, or allowed to putrefy, albumen yields a variety of substances, among which formic, acetic, benzoic, and some fatty acids, may be mentioned. Two crystallized substances of pathological significance are also obtained—leucine and tyrosine. When albumen is digested with permanganate of potash, urea is obtained as one of the products of the oxydation.

When a solution of albumen is precipitated with basic acetate of lead, the precipitate washed, and suspended in water, and carbonic acid is now passed through the mixture, the albumen is redissolved together with a little lead, which may be removed by sulphuretted hydrogen. The filtered solution, on evaporation at a temperature not exceeding 50° C. (122° F.), leaves solid soluble albumen, which is free from mineral constituents, and has an acid reaction when dissolved, as it contains some acetic acid.

When the temperature of a solution of albumen in water is raised to 60° C. (140° F.), it begins to get turbid in the upper strata, and, on the temperature being raised to 75° C. (167° F.), the albumen coagulates in large flakes, which become the more compact the higher the temperature is raised, or the longer the boiling is protracted. The more dilute a solution of albumen is, the higher is the temperature which it requires for coagulation. The free alkali, which is in combination with the albumen, requires to be neutralized before boiling, by means of acetic acid, otherwise a part of the albumen will remain in solution, unaffected by any temperature. The addition of alkali to a solution of albumen may prevent its coagulation by heat.

During the coagulation of albumen from the egg, an evolution of sulphuretted hydrogen takes place. This is not the case when albumen from the blood is coagulated.

Solutions of albumen are precipitated by the addition of

alcohol; strong spirits of wine transform the albumen into the insoluble modification; dilute spirits of wine, however, precipitate it without change. Creosote, aniline, and other products of destructive distillation, coagulate albumen. Most mineral acids precipitate solutions of albumen. (The tribasic phosphoric acid is an exception to this rule.) The precipitate contains the acid employed in combination with coagulated albumen. This precipitate is soluble in a large excess of water, so that if we attempt to free it from the acid by washing with water, it is almost entirely dissolved. Most organic acids—for example, acetic acid—do not precipitate albumen. A solution of albumen, however, slightly acidulated with acetic acid, and then diluted with a large bulk of water, or mixed with a concentrated solution of chloride of sodium, yields a precipitate of albumen. When gently warmed with an alkali, the soluble modification is transformed into the insoluble one, but remains dissolved in the alkali, from which it may be precipitated by acetic acid. Most salts of the oxydes of the heavy metals yield precipitates with solutions of albumen. The precipitation by corrosive sublimate may be mentioned prominently as useful; when sublimate does not produce any precipitate in urine, in which we have to determine urea by means of the mercurial solution, we may be sure that no albumen is present, likely to interfere with the correctness of the analysis.

A solution of albumen causes a turning of the plane of polarization towards the left.

The albumen of the blood is not precipitated by dilute sulphuric acid, yields no sulphuretted hydrogen on coagulation by heat, and contains less sulphur than the albumen of eggs. In all other respects both descriptions of albumen are pretty nearly identical.

Diagnosis of Albumen in Urine.

Coagulation by heat.—Care being taken that the urine have a slightly acid reaction, naturally or by the aid of some acid, as acetic acid, the albumen will coagulate at a temperature of from 60° to 100° C. (140° to 212° F.)

A precipitate of earthy phosphates cannot be mistaken for one of albumen, because it is soluble in a drop of almost any acid (nitric, acetic, hydrochloric, or phosphoric); because it never forms into flakes, as the albumen does, on protracted heating or ebullition; and because it redissolves on cooling; when formed under the influence of heat.

There is this caution to be observed—that an excess of any acid beyond the amount necessary for neutralizing the free alkali of the albumen, will, on boiling, or without it in *very dilute solutions of albumen*, keep a certain proportion of it in solution, just as the precipitate of albumen and nitric acid dissolves in an excess of water. A slight turbidity from albumen, produced by boiling, may therefore disappear on the addition of a drop of acetic acid. This test seems to have been considered by Heller[1] as the reaction of a modified albumen, but it is probably only the reaction of a very dilute albumen.

If the urine is alkaline, and the amount of albumen contained in it is small, it will not be coagulated by boiling. If the amount of albumen be larger, a part corresponding to the amount of free alkali will be kept in solution.

Nitric acid test.—The addition of nitric acid to albuminous urine causes a white precipitate of a compound of nitric acid and albumen. This test, if used with certain precautions, is extremely delicate and handy. I can strongly recommend the proceeding advocated by Heller.[2] A small conical glass is filled to two thirds of its height with urine, and some nitric acid is then allowed to flow along the wall of the glass towards the bottom, where it collects. It mixes with some urine, and forms a clear reddish, mostly dark stratum of fluid. If albumen is present, there will be, lying immediately on the acid, a turbid layer of a precipitate, so strongly distinguished both from the acid and the supernatant urine, that it cannot easily be overlooked. When the amount of albumen is very small, the precipitate sometimes appears only after a few minutes, or becomes more distinct; but after standing longer, it diffuses in the fluid. But in most cases it appears readily and distinctly.

The addition of nitric acid to some descriptions of urine may cause a precipitate of uric acid. In the few cases in which I have met with this precipitate (cases of scarlet fever during the acme), it consisted of the hydrate of uric acid, as, on heating, the urine became speedily clear, and now was full of uric acid crystals. Under the microscope the precipitate was amorphous, transparent, in jelly-like masses, which when left to themselves quickly agglomerated into crystalline forms. This precipitate in every respect corresponds to that obtained by throwing a solution of urate of soda into hydrochloric acid of the ordinary temperature. When the hydrochloric acid is previously made hot, the uric acid obtained is

[1] 'Archiv für Chemie und Microsc.,' 1852, p. 167.
[2] Ibid., p. 167.

not jelly-like and hydrated, but crystallized, and with only two equivalents of water. In correspondence with these facts, the urine gave no precipitate of fawn-coloured hydrate of uric acid with nitric acid, when it was heated before the addition of the acid, and the crystals formed quickly in a clear fluid. It is very improbable that urates should be precipitated from their solution in urine by nitric acid. But whether this precipitate be made up of urates, as Heller believes, or of uric acid, as in the above-mentioned cases, not only the characters described by me, but also some described by Heller, readily distinguish it from albumen. For the precipitate resting on the clear layer of acid, when made up of uric acid or urates, diffuses in cloudy streaks through the entire stratum of supernatant urine, which the precipitate of albumen never does. And if in one and the same urine both albumen and uric acid are precipitated by nitric acid in the manner described, then the layers of the mixture are so arranged, that upon the lowest clear layer of acid the layer of albumen follows; upon this there is another layer of clear urine; and uppermost floats a stratum of urine which is turbid from clouds of uric acid (or urates).

Quantity of Albumen in Urine.

It is sometimes useful to know the quantities of albumen which a patient loses with his urine. The amount of lesion in the blood and kidneys may be approximately determined by this analysis, when all other symptoms are taken into consideration.

A measured quantity of filtered urine—50 c.c. when much, 100 c.c. when little albumen is present—are most carefully neutralized or slightly acidulated by means of dilute acetic acid. They are then put into a Florence flask; the flask is placed in a water-bath, and the water is kept boiling for some minutes, until the thermometer, when placed in the flask, indicates that the temperature of the urine has risen to above 194° F. When the urine has contained little albumen, the flask may be taken out of the water-bath, and placed over the free fire, and the urine heated to ebullition. The coagula are then collected on a filter of known weight, washed, and dried, first in the water-bath, afterwards in the air-bath, until no further loss of weight takes place. The amount of dry albumen thus found, when multiplied by the total amount of urine discharged in a given time, and compared with the known amount of albumen in the serum of the blood, gives

us the key to the pathological deductions as to the nature and amount of the lesion, of which the exudation of albumen is a symptom.

Pathological indications.

Leaving out of consideration all cases where the urine is albuminous from the presence of blood, pus, or, perhaps, though rarely, from an admixture of semen, *the presence of albumen in the urine indicates a pathological condition of the kidneys, of a temporary, chronic, or permanent nature.* The most elementary condition coming under this head is that of stasis of the blood in the capillary vessels, commonly called congestion. We know, from experiments on animals, that compression or ligature of the renal veins causes albumen to appear in the urine. We know that paralysis of the vascular and other nerves of the kidneys, which enter with the artery, by temporary constriction of the artery, or by complete division, a tube being inserted to keep up the circulation, has the same effect. We know, moreover, that a vitiated condition of the blood will make it unfit to pass the capillary vessels,[1] and thus produce stasis in the kidneys. It is very probable that this is the mode of action of most diuretics, such as cantharides, turpentine, digitalis, and others, by which indeed albumen and blood may be made to appear in the urine; and this is also the most probable explanation of the way in which the specific poisons of scarlatina and allied diseases, and of typhus, gout, and rheumatism affect the kidneys. In all these diseases, or in certain stages thereof, albumen in the urine is of more or less common occurrence. We are acquainted with some other morbid conditions of the blood, artificial or the consequences of disease, not being due to the introduction of a poison, which cause stasis in the kidneys and albumen in the urine. Thus the injection of large quantities of water into the blood, or a watery condition of the blood in the course of disease, with diminution of the albumen of the blood, known by the name of hydræmia and hypalbuminosis, will cause albumen to appear in the urine. The injection of dissolved albumen into the blood has also sometimes had the same effect. But whether in these cases, as after injection of water, and the ligature of the abdominal

[1] The arguments regarding these conditions of the blood, and their consequences, have been so fully put forth by Dr. Johnson in his treatise on 'Cholera,' that I am induced to call the attention of the reader to the deductions there arrived at. See also my paper on the Cause of the Emptiness of the Arteries after Death, in the 'Assoc. Med. Journal.'

aorta below the origin of the renal arteries, the appearance of albumen is due to increased pressure of the blood in the vascular system, or to the vitiated condition of the blood, or to both causes, remains to be decided.

Under all circumstances, however, the immediate cause of the exudation of albumen through the kidneys is increased pressure of the blood in the Malpighian bodies, whereby these bodies expand, and allow a certain amount of albumen to pass through their tissue. When the pressure becomes greater, rupture of the arteries is the necessary consequence.

The appearance of albumen in the urine is of very variable significance, according to the nature of the disease in the course of which it happens. It is most common in those diseases which find a local expression in the degenerations of the kidneys comprised under the name of Bright's disease, but which more lately have been appropriately classified according to their anatomical and symptomatic natures. The appearance of albumen, when due to any of these lesions, is always qualified by other symptoms, particularly the appearance of the fibrinous casts described in a former chapter.

In the course of some diseases albumen may appear in the urine for a single day, or for several, or for many days; and may disappear without leading to anatomical lesions of the kidneys. Thus in typhus albumen is not unfrequently found, particularly during the acme. I have observed albumen in the urine from acute cases of rheumatism. A girl, aged 15 years, was affected by violent rheumatic fever. On the worst day of the illness, when most joints of the limbs began to swell, she only discharged 60 c.c. of urine in twenty-four hours, which was dark red and highly albuminous, without blood or casts. I have found albumen in several cases of acute and chronic rheumatism; in the latter particularly when an acute attack was threatening. In a case of hypertrophy of the heart I found albumen in scanty urine; and there being no evidence of organic lesion of the kidneys, the case was most successfully treated by diuretics. A similar experience in cases of typhus, pneumonia, and rheumatism, makes it probable that these remedies, though increasing the stasis for a day, and, perhaps, acting in another way by increasing the secretory activity of the kidneys without causing mere stasis, are the very remedies to remove the cause of the original stasis, namely, the poison in the blood. And though I perfectly agree with the opinions condemnatory of the *indiscriminate treatment* of renal dropsies by diuretics,

yet I cannot join in the general outcry against these remedies, and their exhibition in certain stages of these diseases. For I have known patients saved who were in a soporose condition, and nearly moribund, by a strong diuretic, which was administered with a full consciousness of the effect it would have upon the patient's kidneys. And though the kidneys were made worse for a day, yet the patient was got over the critical period, and time was gained to bring other remedies into operation, under which the aggravated condition of the kidneys abated, and the patient was saved.

Albumen in the urine of patients labouring under an acute attack of gout is also common. Albumen in the urine of gouty and rheumatic patients seems to me to indicate that the disease, should it become of a chronic nature, has a tendency to produce those morbid conditions of the kidneys known as chronic desquamative disease, chronic purulent disease, wasting and fatty kidney, in the course of which the epithelium of the tubuli disappears, or degenerates fatty, or granular, as evidenced by the appearance of hyaloid, fatty or granular fibrinous casts.

Many researches will yet be required to bring the symptoms of diseased action into connection with the anatomical lesion of the kidneys, and the latter in connection with the causes, local or general, giving rise to them. But we are on a progressive route in this direction, and many appearances augur success to pathological forays in these regions.

CHAPTER XXII.

PUS.

The diagnosis of pus in urine rests upon the presence of pus-corpuscles, to be ascertained by the microscope, and upon the tests for albumen, as the presence of pus invariably makes the urine albuminous.

When pus is present in ordinary acid urine, even in small quantities, it always forms a deposit, the corpuscles subsiding towards the bottom of the vessel, while the albuminous liquor remains dissolved in the fluid. The deposit is easily diffused by agitation, but soon settles, first like a cloud in the lower strata of the urine, afterwards again to the bottom of the vessel. When pus is present in larger quantities, it forms clouds in the lower strata of the urine.

Pus-corpuscles.

These bodies are nucleated cells, and do not differ in structure and reaction from the white cells of the blood or lymph-corpuscles. In shape they are more or less globular, and hence are called pus-globules. Their diameter varies between $\frac{1}{1000}$th and $\frac{1}{1700}$th of an inch. The nucleus, single or compound, is always present, and if not visible at once, may be made so by chemical agents. The outlines of many corpuscles are only faintly visible, better in a dull light than when illuminated too strongly. Many corpuscles have a granulated appearance, from matter deposited in the interior of the cell. (Fig 3, Pl. V.)

When brought into contact with water, the corpuscles swell up and become pale; and their outline is rendered indistinct. The granular appearance mostly disappears, but the nuclei and nucleoli become visible or more distinct.

Acetic acid and dilute mineral acids cause the corpuscles to become pale and swell up, and the cell-membrane frequently bursts under their influence, or disappears altogether. The nuclei are then set free, and exhibit their variable size, shape, and composition.

When pus-globules are introduced into a concentrated solution of any neutral salt of the alkalies, such as sulphate of soda, the endo- and exosmotic changes cause the globules to collapse; to assume irregular, star-like, angular appearances; and to become granular, so as to appear as if covered with granules. The nucleus, under this treatment, mostly disappears in part or altogether. Similar changes are produced by these solutions on corpuscles which have been previously treated with acetic acid or water. When the nuclei have been made invisible by solutions of salt, the addition of acetic acid will not always afterwards make them visible again.

When treated with caustic alkalies, the pus-globules are disintegrated, almost entirely destroyed, and on the addition of water are dissolved almost entirely, merely leaving a small gelatinous residue, in which some light and dark points are to be distinguished. If a deposit of pus from urine is agitated with an equal quantity of liquor potassæ, it forms a dense translucent, gelatinous, or mucous mass, often so solid, according to Dr. G. Bird, that the tube can be inverted without any escaping. Similar changes are induced by the carbonate of ammonia formed from urea during the decomposition of urine. The deposit of pus then becomes viscid, and so very much resembles mucus that it is not rarely mistaken for it. The globules disappear, being transformed into a gelatinous mass. Dr. G. Bird affirms that the addition of acetic acid to this viscid urine will convert the mucous mass into a white granular deposit.

Urine containing pus is mostly slightly alkaline, and, as I have already stated, always albuminous. When the quantity of pus is very small, the albumen may escape detection, and the corpuscles being found as a sediment may induce the belief that pus might be present without albumen. But when the albumen is coagulated by boiling, it may, though not visible to the naked eye, yet be seen with the microscope. For if, to the urine thus boiled, some solution of iodine in iodide of potassium is added, and the mixture is allowed to rest for a while, we find shreds and flocculent membranes, coloured brownish-red, in the lower strata of the fluid, when they are brought under the microscope.

Pathological indications.

The presence of pus in the urine indicates suppuration in some part of the urinary organs or adjoining regions. But the diagnosis of the seat of that suppuration is in practice frequently surrounded with great difficulty. The principal pathological conditions which may give rise to the appearance of pus in the urine are the following.

Purulent disease of the kidneys. Suppurative nephritis.— This disease is sometimes the sequel of non-desquamative or desquamative nephritis, and then begins with the appearance of intra-epithelial, small, or large intra-membranous fibrinous casts, containing pus-corpuscles. But when the basement membrane of the tubuli becomes destroyed, the pus no longer assumes the shape of casts, but is simply mixed with the urine. In this manner one or both kidneys may be destroyed. When no history of the case is known, and no purulent casts are found, these cases sometimes remain obscure for a period. If the discharge of pus in albuminous urine continues regularly for a length of time, even without local or general symptoms, I think that purulent nephritis is pretty sure to exist. (Pl. IV, figs. 1 and 2.)

Inflammation of the mucous membrane of the pelvis of the kidney, or pyelitis, in consequence of retention of urine from various causes, as taught by surgery, may cause pus to appear in the urine. The presence of concretions in the pelves and calyces may have the same effect. The relative symptoms ensure the appearance of pus to be assigned to its proper cause.

When the pus comes from the *ureters,* its formation is mostly accompanied by pain along the course of these organs.

In the bladder, pus may form under various circumstances. Many diseases of the kidneys cause by the altered quality of the urine irritation of the bladder, and an increased discharge of mucus. There is no difference between mucus- and pus-corpuscles, if considered singly: it is therefore natural that the line where mucus ends and pus begins is not very distinct, at least to our present means of diagnosis. The distinction is of no great importance if the locality of the formation is known to be the bladder; which it is easy to know, as local symptoms are scarcely ever absent when the bladder is the seat of even superficial and secondary irritation. Catarrh of the bladder, in consequence of alkaline urine and its various causes as enumerated under that head, is one of the conditions to be mentioned. It always ac-

companies stone in the bladder, and is a frequent consequence of lithotrity.

The pus may have its origin *in the urethra,* as in gonorrhœa, and its frequent sequel, stricture. In these cases, particularly those of the former class, pus may always be obtained from the urethra without the admixture of urine.

In females the urine may have an admixture of pus from the *vagina* or the *uterus.*

Abscesses, which sometimes form in the pelvis, the sub-peritoneal cellular tissue, in consequence of puerperal fever, or other lesions, such as gun-shot wounds, may open into any part of the urinary passages. I have observed such a case in an unmarried woman, where a pelvic abscess discharged itself entirely by way of the bladder.

When an abscess has become encased, without opening, the pus-corpuscles undergo fatty degeneration. We then find the cells larger, transparent, and filled with numerous fat-granules. The membranes are soon destroyed, and we see the few granular cells left over imbedded into a mass of albumen and granular fat, from broken-up cells. When this description of pus, which has the colour, consistence, and odour of cream, is mixed with the urine, it gives it a perfectly milky appearance. This admixture of pus, which may occur in the course of certain forms of purulent nephritis (as in the case described by me in the 'Association Medical Journal' for April 26, 1856), must not be mistaken for chylous urine. Another mistake here to be referred to is that of Lehmann, who interprets all cases of chylous urine as purulent urine metamorphosed by alkalinity.

Vogel has drawn attention to the importance of observing the particular shape of the pus-corpuscles. Quite normal pus-corpuscles of a perfectly circular outline, which, after treatment with acetic acid, exhibit the characteristic nucleus, composed mostly of two or three nucleoli, admit of the conclusion that the disease giving rise to their formation is of a mild form—a simple catarrh of the mucous membrane. But when the pus-corpuscles are irregular in form and outline, and on treatment with acetic acid show an irregular nucleus, or an indistinct granular mass in their interior, or when such corpuscles are mixed with irregular débris, not particularly defined, then purulent destruction is evident, and the integrity of the organ where this formation takes place is in great danger, or lost altogether. Such pus would be the product of ulceration and tuberçulosis.

CHAPTER XXIII.

MUCUS.

I HAVE already described the appearances of mucus as a normal ingredient of urine, and here only recur to the subject for the purpose of mentioning a few points in the diagnosis of mucus from pus, particularly when the mucus is present in excess.

Chemical characters of Mucus.

Sometimes it is possible to obtain pure mucus by filtration, free from epithelial elements; it is then a glass-like mass, almost invisible under the microscope. It does not coagulate by heat, but by the addition of alcohol. The precipitate is soluble in water. Acetic acid precipitates flaky masses, not soluble in an excess of acid. Mineral acids give precipitates, easily soluble in an excess of acid. I have frequently used hydrochloric acid for liquefying tough mucus, and making it fit to pass a filter. Gallic acid and basic acetate of lead precipitate the solutions of mucus; neutral acetate of lead, alum, and corrosive sublimate cause a turbidity.

The analysis of mucus yields the following result:

Carbon	52·1	
Hydrogen	7·0	
Nitrogen	12·5	
Oxygen	28·4	
	100·0	(Strecker.)

Physical characters of Mucus.

Mucus is tough and ropy; when urine in which it is contained is filtered, it remains on the filter, rarely passing

through it. After drying, it forms a glistening membrane, like its prototype, the mucus on the track of snails. Its diagnosis is always ensured by the number of epithelial cells imbedded in its substance. But should there be any doubt whether there be any mucus in a microscopic specimen or not, the addition of a little dilute tincture of iodine will, by its precipitating and colouring effect upon the mucus, readily decide the question. The admixture of spermatic filaments, oxalate of lime and triple phosphate crystals, phosphate of lime, urate of ammonia, and tubular casts, may be ascertained by the microscope and the respective tests.

Physiological quantity of Mucus.

This depends mainly upon the nature of the urine passing through the bladder. Concentrated urine causes the exudation of more mucus from the bladder; dilute urine, when not altered otherwise, has no such effect. The largest quantity of mucus seems to be secreted during the night, perhaps owing to the concentrated nature of the night urine, or to the irritating influence of its longer retention.

The normal amount of mucus cannot be expressed in figures. It is best to accustom the eye to an estimate by frequent inspection in transmitted light of urine in glass vessels. Any excess at all important will then easily be perceived by the increased bulk of the cloud.

Excess of Mucus.

This may be caused by pathological conditions of the urine, particularly alkalinity from decomposed urea. A large quantity of free acid may have a similar effect. Thus, the strongly acid urine, which is voided by a person on the morning after the night on which larger doses of benzoic acid were taken, exhibits a mucous cloud double the size of that voided under ordinary circumstances.

The Pathological indications

of an excess of mucus must depend upon the causes which produce it. As such, we may mention all conditions which are characterised by irritation of the urinary organs. Pathological conditions of the urine, the presence of foreign bodies and concretions in the bladder, idiopathic diseases of the bladder and its appendages—all these, and some others, may

be indicated in part by an increased amount of mucus in the urine.

When the characteristic symptoms of other defined diseases are absent, and the secretion of an excess of mucus from the bladder is the only characteristic symptom, then it is termed blennorrhœa of the bladder, or cystorrhœa. The pathological conditions of the mucous membrane giving rise to this excessive secretion are probably not always alike; but they are mostly those of catarrh or chronic inflammation, and of venous engorgement, from enlarged vesical veins.

CHAPTER XXIV.

FAT AND OIL.

Apart from any accidental admixture of these substances, which we caution the reader to guard against most scrupulously, they may occur in the urine as the products of diseased action in the body or urinary organs in *three different forms*.

a. As large and small oil-drops, floating on the surface of the urine. Such oil-drops, called oil because they remain fluid at the ordinary temperature of the air, and are salts of oleic acid, I found on the urine, taken from the bladder after death, of a woman who died of chronic purulent nephritis, with fatty degeneration of the left kidney. The oil-drops make a greasy spot appear on paper, and are easily soluble in ether.

b. As granular fat, most probably solid, or if not surrounded by an albuminous sphere, like the fat in an emulsion (Ascherson's cells), identical with the granular fat enclosed in pus-cells, or epithelial cells of the urinary tubuli, being a product of their degeneration, called fatty from the presence of the fat. These cells and the granular fat are frequently imbedded in fibrinous casts.

c. As fat in very minute particles, appearing as mere points under the highest powers of the microscope, but rising to the surface of the urine, and collecting as a cream, as in some forms of chylous urine.

Chemical characters.

These are very little known, but seem to be identical for the different descriptions enumerated. What we call fat and oil are most probably mixtures of different proportions of oleate and margarate of glycerine, or of the organic base,

which by taking up water forms glycerine, when the acid is separated from the fat by alkalies. The fat, which is fluid at the ordinary temperature of the air, is in all probability the oleate.

Fat and oil are soluble in ether, and are deposited unchanged when the ether is evaporated; but when they are surrounded by cell-membranes, or albuminous husks, ether may fail to take up the whole of the fat. It then becomes necessary, not only to shake the urine with some ether, but to evaporate it to dryness, to boil the residue with some alcohol and acetic acid, to evaporate again, and then to extract the residue with ether (Kletzinsky[1]). Even this extract may be impure from some hippuric acid, which is to be removed by alcohol or water.

Kletzinsky found in the urine of persons labouring under Bright's disease the following quantities of fat in 1000 parts of urine: 0·24, 0·28, 0·35, 0·37, 0·48, 1·27 parts. Beale[2] found 14 in 1000 of fat in urine on one occasion.

Pathological indications.

Fat in coagulating or albuminous urine, when causing a milky appearance, is a feature of chylous urine. When occurring in drops, granules, and cells, it is an indication of fatty degeneration of the kidneys, particularly when the cells or granules occur in fibrinous casts of the tubuli.

[1] Heller's 'Archiv,' 1852, p. 287.
[2] 'Microscopical Journal,' January, 1853, pp. 1, 2.

CHAPTER XXV.

CANCER-CELLS AND TUBERCULAR MATTER.

The mucous membrane of the urinary bladder is a favorite seat of a certain variety of medullary, and perhaps, in some instances, of epithelial cancer, called villous cancer by Rokitansky and subsequent anatomists, from its peculiar mode of growth in fine villous processes, which make it resemble the surface of a chorion. On the exterior of these villi, the elements of a medullary or melanotic cancer-juice adhere to it, consisting of nucleated cells of various shapes, which form a soft, or a more consistent deposit, and are often present in such quantity, that they make up the greater part of the morbid mass in the bladder, into which then the vegetations seem to grow.[1]

The cancerous matter, according to Vogel, appears in the urine in small lumps of cells. The latter may be large, enclosing secondary ones; or they may have thick walls, and become elongated into spindle-like bodies. The urine at the same time mostly contains blood and coagula. From these and the collateral symptoms, the diagnosis of this disease offers no difficulties.

When, however, the appearance of cancerous matter is due to cancer of the kidneys, it is frequently difficult to form a diagnosis.

Of tubercle, and consequent phthisis, of the kidneys, I saw a remarkable instance some years ago, when paying an occasional visit to the Brompton Hospital. It was there secondary to tuberculosis of the lungs, as it almost always is. In these cases, the deposit consists of tubercular matter, irregular pus-cells, fragments of cells and their nuclei, granular indefinable matter, and, more rarely, pieces of crystals of cholesterine.

[1] Paget 'Surgical Pathology,' vol. ii, p. 513.

The form of tuberculosis which most frequently gives rise to the appearance of tubercular matter in the urine is that which has its seat in the mucous membrane of the urinary organs generally, and hence proceeds to deeper structures. Tubercles of the kidneys, however, may primarily form in the cortical substance. The diagnosis between the two forms is not aided by the microscopic analysis of the urinary deposit.

CHAPTER XXVI.

ECHINOCOCCUS HOMINIS.

There are several cases on record, in which cystic entozoa have been passed by the urethra. They are formed mostly, it appears, in the kidneys; more rarely grown in other parts of or adjacent to the urinary organs.

The cysts vary in size, from a pin's head to an inch in diameter. Their external surface has a semiopaque granular, or smooth, enamel-like appearance. In shape, they are more or less globular; sometimes flattened, at other times very irregularly formed; sometimes, particularly the large ones, shrunken, as if they had lost a portion of their fluid contents. They contain a fluid and some granular matter, in which latter fragments of echinococci and their characteristic hooklets may be mostly detected. The walls of the cysts are made up of several layers of structureless membrane; the innermost covered with a layer of granular matter; in the larger cysts with numerous prismatic, feather-shaped, and crossed crystals of triple phosphate. (Pl. v, fig. 1.)

The echinococci are found imbedded in the granular matter of the inner surface, from which—the cœnurus—they are grown, and to which they sometimes are found to be attached. But as the cysts met with in the urine are usually very old, the echinococci are mostly detached from their basis, and partly or entirely disintegrated, so that in some cases neither echinococci nor hooklets can be detected by the most careful examination. Thus, in the case recorded by Dr. Sieveking,[1] the echinococci had become disintegrated. In the case related by Mr. Simon,[2] the cysts were passed entire, and contained swarms of perfect echinococci in different stages of growth, together with innumerable hooklets of

[1] 'Lancet,' Sept. 10th, 1853.
[2] Ibid., Sept. 24th, 1853.

parasites, dead and decomposed at some earlier period. In the case published by Dr. Barker,[1] the large cysts contained echinococci, the small cysts mostly contained none.

The echinococci are mostly retracted, more rarely stretched out at full length. (Pl. v, fig. 2.)

The symptoms incidental to the discharge of these cysts have been closely described by all observers. When the cysts proceeded from the kidneys, there was dull, aching pain, accompanied with sensation of fulness in the loins, obstruction in the ureter, with lancinating pain along its course, an immediate sense of relief incident upon the cyst finding its way into the vesical cavity; lastly, straining attempts to micturate, pain along the urethra, and particularly at its termination, with obstruction to the flow of urine, until the emission of the cyst made a sudden end to the distressing symptoms.

In the case communicated to Dr. Barker, by Mr. J. J. Evans, the urine was opaque, and contained flakes of membrane, fragments of cysts. Such membranes were also passed in Dr. Sieveking's case.

The number of cysts thus passed by one patient, at various periods, stretching over many years (eight in the case of Mr. Evans), may be extraordinary, exceeding hundreds at a time, and thousands in the aggregate of all discharges.

There can be no difficulty in the diagnosis of these parasites; for, even if the echinococci themselves should not be found in the cyst, yet the peculiarity of the latter, in being composed of structureless layers of a hyaline or opaque substance, the produce of the parasite, will distinguish it from all membranous matters that may by any chance pass by the urethra.

[1] 'Glasgow Med. Journal,' 1856, and separate pamphlet. See also a report in the 'Med. Times and Gazette' for Feb. 17th, 1855, where about ten cases of this description are related.

CHAPTER XXVII.

SPERMATIC FILAMENTS, OR SPERMATOZOA.

The occasional admixture of semen with the urine causes the characteristic filaments to appear in the deposits that may be examined for the purpose, or for some other object. The admixture with urine of semen in any quantity, so as to form a deposit for itself and to make the urine albuminous,[1] is not frequently, if ever, met with in disease. In health, this may occur under a variety of circumstances.

In the urine of males, the presence of spermatic filaments in any quantity is necessarily the consequence of an emission of semen, which leaves some residue in the urethra, to be removed by the first urine passing the canal after the act. The emission itself, however, may be due to coition, or to spontaneous sexual excitement during sleep. Onanism may lead to the same result, and hence may sometimes be discovered thereby.

The following I give upon the authority of Dr. G. Bird: A certainly not unfrequent cause of the escape of semen is extreme constipation; for after the passage of hard and scybalous fæces, an oozing of fluid from the urethra, full of spermatozoa, is not uncommon.

Excluding the habitual emissions during sleep of persons affected with spinal disease, an ailment called spermatorrhœa has no existence. The few honest practitioners who believe in the existence of such a disease, are the credulous victims of onanists, who find it a strange satisfaction to seek relief and undergo all sorts of treatment for a supposed ailment, the continued cause of which they themselves knowingly are. I will exempt some cases, in which the victims of this vice

[1] 'Verhandl. d. Phys. Med. Ges. in Würzburg,' Bd. vi, 1855. 'Microscop. Journ.,' No. 12, July, 1855, where several German Papers on Spermatic Filaments are given in extract.

think that medical treatment might heal them of their bodily passion, as they erroneously believe it to be. I make this statement in consequence of the confession of a young man, which he made to me and the clergyman in the hour of his death. This confession opened my eyes regarding these cases; and I have since that painful experience seen several cases, in which the complaints of spermatorrhœa and nightly involuntary emissions, on close examination, resolved itself into a continuance of guilty acts of the individual.

When found in the urine of women, where there is no possibility or probability of a fraudulent admixture, the spermatic filaments are evidence that coition has taken place. In medico-legal inquiries, the discovery of spermatozoa may sometimes lead to the disclosure of crime or vice.

Dr. Lionel Beale states, that the urine should be examined for spermatozoa as soon as possible after it has been passed, as they very rapidly become destroyed (l. c., p. 205). According to Dr. G. Bird, however, urine, beyond making the filaments quiescent, exerts no further action upon them, as they may be detected, scarcely changed, even after it has become ammoniacal (p. 359). Neubauer (p. 77) makes a similar assertion. The truth seems to be that the spermatic filaments are differently affected by different fluids; thus, in faintly alkaline or neutral urine they retain their motility much longer, but in acid or strongly ammoniacal urine they quickly become quiescent. (Kölliker.) In urine containing pus, they retain their motility much longer, most probably because it is alkaline, as alkaline fluids, particularly caustic alkalies, are special excitants of the spermatic filaments, and may revive their peculiar motions almost under all circumstances, which may be more particularly seen in the papers quoted on p. 269. From the experiments there detailed, it appears that the spermatozoa are very tough, and by no means easily destroyed.

When few spermatozoa are to be detected, the urine must be allowed to repose in a conical glass vessel; the deposit is then removed from the bottom by means of an India-rubber pipette, brought into a cell, and examined under a power of from 300 to 400 diam.

CHAPTER XXVIII.

BILE AND BILIARY MATTERS IN URINE.

Human bile,[1] as met with in the gall-bladder, is a yellow, greenish, or brown fluid, of a consistence imparted to it by the admixture of a gelatinous mucus, of faintly alkaline reaction, and of bitter taste. It consists of nine tenths of water; the amount of solids being only one tenth. The solids are made up of fatty matters (glycerides), containing oleic, margaric, and stearic acids; an indifferent crystallizable matter (probably an alcohol), cholesterine, and one or several colouring matters, biliverdine and bilifulvine; the main constituents, however, are the salts, with alkalies, of two nitrogenized organic acids—cholic and cholinic.

When bile is evaporated to dryness and treated with absolute alcohol, the latter takes up the principal constituents, with the exception of mucus and the greater proportion of inorganic salts. The solution is then digested with animal charcoal, which removes the colouring matters. The addition of ether to the clear filtrate now produces a tough amorphous precipitate, which, on standing for a longer period in a still place, at a low temperature, which must be produced artificially in summer, is transformed into crystalline groups of needles. These crystals are a mixture of the salts of cholic and cholinic acids. They may be separated and freed from their bases by adding dilute sulphuric acid to their watery solution; cholic acid is precipitated in a crystalline state, cholinic acid remaining in solution.

[1] In the chemical description of bile, I have closely followed Dr. A. Strecker, 'Lehrb. d. organ. Chemie,' p. 369, a short and most original account of this secretion.

Cholic or Glycocholic Acid.

Elements : HO. $C_{52}H_{42}NO_{11}$.

Cholic acid forms colourless hair-fine needles, which are at first voluminous, and on drying shrink together, so as to form a paper-like mass, glistening like silk. It is very little soluble in cold water, more in boiling water ; easily soluble in alcohol ; little soluble in ether. It has a faintly acid reaction, and a sweet taste. It melts at a higher temperature and is decomposed, evolving at the same time a peculiar odour. When warmed with sulphuric acid and sugar, it yields a fluid of an intensely violet colour.

The salts of cholic acid with bases have a neutral reaction. The salts with alkalies and alkaline earths are easily soluble in water and alcohol, but insoluble in concentrated solutions of hydrated caustic alkalies or salts of alkalies. The salts with the oxydes of heavy metals are mostly insoluble in water. They do not crystallize from their solutions, if they are evaporated ; but the addition of ether will usually transform them into crystals.

Cholate of lead (PbO. $C_{52}H_{42}NO_{11}$) may be obtained when bile, previously discoloured by means of animal charcoal, is precipitated by acetate of lead. The colourless salt may be decomposed by hydrothion (sulphuretted hydrogen), and cholic acid obtained pure by evaporation.

Decompositions.—Cholic acid is soluble in concentrated sulphuric acid without discoloration ; and on raising the temperature of the solution an amorphous precipitate forms, which is insoluble in water, and easily soluble in alcohol. It is a product of the decomposition of cholic acid, and is termed *cholonic acid.* It forms a salt with baryta, which is insoluble in water. It contains two equivalents of water less than cholic acid, its composition being $C_{52}H_{41}NO_{10}$.

When cholic acid is boiled with dilute hydrochloric or sulphuric acid, it separates into glycocoll, $C_4H_5NO_4$, and an acid free from nitrogen—choloidinic acid, of the composition $C_{48}H_{39}O_9$.

$$\underbrace{C_{52}H_{43}NO_{12}}_{\text{Cholic acid.}} + HO = \underbrace{C_{48}H_{39}O_9}_{\text{Choloidinic acid.}} + \underbrace{C_4H_5NO_4}_{\text{Glycocoll.}}.$$

Choloidinic acid is an amorphous, colourless, resinous sub-

stance, which melts easily, is not soluble in water, easily soluble in alcohol, less soluble in ether. It has an acid reaction; and with all bases, except the alkalies, forms salts, which are insoluble in water.

When choloidinic acid is heated for some length of time with hydrochloric acid, it changes its properties. It melts less easily, becomes insoluble in alcohol and alkalies, but more easily soluble in ether. The substance thus modified is called dyslysine—$C_{48}H_{36}O_6$. It differs from choloidinic acid in containing three equivalents of water less than this acid. It can also be obtained by heating choloidinic acid to 200° C. (392° F.)

Cholic acid is also decomposed under the influence of caustic alkalies and alkaline earths. If a strong solution of hydrate of baryta is boiled with cholic acid, the latter becomes broken up into glycocoll and an acid free from nitrogen, called cholalic acid—$C_{48}H_{40}O_{10}$.

$$\underbrace{C_{52}H_{43}NO_{12}}_{\text{Cholic acid.}} + 2HO = \underbrace{C_{48}H_{40}O_{10}}_{\text{Cholalic acid.}} + \underbrace{C_4H_5NO_4}_{\text{Glycocoll.}}.$$

Cholalic acid, which differs from choloidinic acid in containing one more equivalent of water, crystallizes from alcohol in octahedra and tetrahedra belonging to the quadratic system. The crystals contain five equivalents of water of crystallization, are colourless, reflect the light like glass, and are very frangible. Under the influence of dry air they lose water and become opaque. They taste bitter and sweet at the same time; they are easily soluble in boiling alcohol, less soluble in cold alcohol; they are soluble in 27 parts of ether, insoluble in water.

The salts of cholalic acid with the alkalies are easily soluble and crystallizable; those with the earthy alkalies are little soluble; and those with the other oxydes mostly insoluble.

The composition of cholic acid corresponds with that of hippuric acid. It may be considered as a copulation of cholalic acid with glycocoll.

Cholinic or Taurocholic Acid. $C_{52}H_{45}NO_{14}S_2$.

When cholic acid is precipitated by dilute sulphuric acid from the solution of bile, cholinic acid remains in solution. It

is best isolated from bile in the following manner. Fresh bile is treated with neutral acetate of lead, which precipitates colouring matter, mucus, and cholate of lead. By the addition of a little basic acetate of lead, the cholic acid is more completely precipitated. Cholinic acid is now precipitated from the filtrate by basic acetate of lead and ammonia. The precipitate, after decomposition by hydrothion (sulphuretted hydrogen), yields uncombined cholinic acid. It has an acid reaction, a bitter and sweet taste; when the solution is evaporated, it decomposes, so that the residue becomes partially insoluble. It is less changeable when in combination with alkalies; and the solution of such salts may be evaporated at a boiling heat. The watery solutions of these salts froth like soap-water; no metallic salt forms a precipitate with them—the sole exception being basic acetate of lead, and even that does not precipitate the whole of the acid.

When treated with caustic alkalies, cholinic acid is decomposed; cholalic acid and taurine being the products.

$$\underbrace{C_{52}H_{45}NO_{14}S_2}_{\text{Cholinic acid.}} + 2HO = \underbrace{C_{48}H_{40}O_{10}}_{\text{Cholalic acid.}} + \underbrace{C_4H_7NO_6S_2}_{\text{Taurine.}}.$$

Cholinic acid, therefore, has a constitution analogous to that of cholic acid; the difference consisting in the replacement of glycocoll by taurine.

Taurine, $C_4H_7NO_6S_2$, may be easily obtained from bile by boiling it with hydrochloric acid for some length of time. The fluid is filtered from the precipitate of dyslysine, evaporated, and mixed with spirits of wine, whereby taurine is precipitated; chloride of sodium and hydrochlorate of glycocoll remaining in solution. Taurine crystallizes in large monoclinometric prisms; they are colourless, transparent, little soluble in cold, easily soluble in hot water, insoluble in alcohol and ether. No other combinations of this body are known; but a key to its composition has lately been obtained by Strecker, who succeeded in producing it artificially, simply by exposing isæthionate of ammonia to a temperature of 220° C. (428° F.) The loss of two equivalents of water transforms this salt into taurine.

$$\underbrace{C_4H_9S_2NO_8}_{\text{Isæthionate of Ammonia.}} - 2HO = \underbrace{C_4H_7S_2NO_6}_{\text{Taurine.}}.$$

If we compare with this result the experiment of the decomposition of taurine by fusion with hydrate of potash, where ammonia and hydrogen are evolved, sulphurous and acetic acids remaining in combination with potash, we have a most remarkable instance of the arrangement of elements round certain nuclei or radicals. The formula of the decomposition of taurine by potash is

$$\underbrace{C_4H_7NO_6S_2}_{\text{Taurine.}} + 3KO + HO =$$

$$KO.\underbrace{C_4H_3O_3}_{\text{Acetic acid.}} + 2(KO.\,SO_2) + NH_3 + 2H.$$

Isæthionate of ammonia is

$$NH_4O.\underbrace{C_4H_5O}_{\text{Oxyde of Æthyl.}}.\,2SO_3 = (C_4H_9NO_8S_2).$$

We find the oxyde of æthyl oxydized at the expense of the oxygen of water and sulphuric acid, the radical acetyl C_4H_3 being formed from the radical æthyl. Two equivalents of hydrogen are thereby displaced, and finding all the available oxygen taken up by the oxydation of acetyl (to the hydrate of its oxyde, or aldehyde, lastly to its acid), go away uncombined. Two equivalents of oxygen from the two equivalents of sulphuric acid unite with the oxyde of acetyl, C_4H_3O, forming acid of acetyl, or acetic acid, $C_4H_3O_3$, which remains in combination with the alkali.

Colouring matter of Bile.[1]

The nature of the colouring matter of bile is very little known. It may be removed from its solution by animal charcoal. The alkaline solution of ox-bile is precipitated by means of baryta-water, or chloride of barium, as long as the precipitate has a purely green colour; the precipitate is then decomposed by means of hydrochloric acid, the fatty acids are removed by means of a little ether. A substance remains, which has been termed *biliverdine*, and is somewhat analogous to chlorophyll. When heated with nitric acid,

[1] Strecker, loc. cit., p. 376.

it becomes successively blue, violet, and red. This test is to a certain degree characteristic. When the alcoholic solution of bile is exposed to the influence of atmospheric air, the green colouring matter is transformed into a red one, which has a great similarity to the red colouring matter of blood.

When the inspissated residue of ox-bile is extracted with alcohol, there remains, beside mucus, a brown colouring matter, which is soluble in warm dilute spirits of wine, and is precipitated from this solution by alcohol. When dried, this body becomes of a bright, burning yellow colour, and hence has been termed *bilifulvine*. It is easily soluble in water, on combustion leaves carbonate of soda and lime, and for this reason appears to be the salt of an organic acid.

Diagnosis of Biliary matters in Urine.

It is not probable that biliary matters should occur in urine unaccompanied by colouring matter, though the latter frequently occurs unaccompanied by any of the acids or their salts. The brown, yellowish or reddish-brown colour of urine will therefore generally lead to a suspicion of the presence of biliary matters: the diagnosis may be positively established by the necessary tests.

The best and simplest test for biliverdine is the following. A thin layer of the urine to be tested is spread over a white china plate, and a drop of nitric acid, containing some nitrous acid, is placed in the centre of the circle. If biliverdine be present, the margin of the drop of nitric acid will cause a blue colour to appear in the next circle of urine; the blue circle enlarges towards the circumference of the plate, and the circle next to the drop of nitric acid assumes a violet colour. The blue and violet circles expand, and an inner red circle appears. The test is now completed. The discolorations to yellow and brown which follow are neither constant nor characteristic.

Most precipitates from bilious urine are strongly coloured. But to use the coloration of albumen, for example, as a test for biliverdine, possesses no advantage over the nitric acid colour-test; as, where the amount of colouring matter is so small as not to be indicated by the colour-test, it possesses no practical significance.

Both cholic and cholinic acids have been observed in the urine in a few instances. But they have been sought after so very seldom, that it cannot at present be said whether their occurrence is actually rare. Evidence of their presence is

obtained in the following manner.[1] The urine is evaporated almost to dryness, and the residue extracted with alcohol. The alcoholic solution is again evaporated; the residue is dissolved in a little water, and placed in a white Berlin china dish floating on cold water. A few drops of a solution of sugar are now intimately mixed with the solution in the china dish; and to this mixture concentrated sulphuric acid is added in drops. When biliary acids are present, the solution at first becomes a little turbid, then clears, becomes then of a pale cherry red, then pink, crimson, and at last of a saturated purple violet. Of course the intensity of these colours depends upon the quantity of biliary acids present, and upon the care which is bestowed upon keeping the temperature of the mixture as low as possible during and after the addition of sulphuric acid. This reaction bearing, from its discoverer, the name of Pettenkofer's test, is due to the presence of cholalic acid, as neither taurine nor glycocoll exhibit it when isolated.

Pathological indications.

The occurrence of the colouring matter of bile in the urine indicates that the flow of bile from the liver into the intestinal canal is impeded or entirely suspended. By absorption the colouring matter of bile enters the blood, and hence passes into all the secretions and tissues. Icterus, as this state of things has been termed, is as easily diagnosed by the coloured tissues and colourless fæces, as from the brown urine, and its reaction with nitric acid.

There is, however, a certain dissolution of the blood consequent upon or part of the pathological process of pyæmia, which produces the green or yellow icteric colour of the skin and tissues, without being accompanied by retention of bile; as the frequent fluid evacuations contain abundance of green colouring matter, and the dark-red or brown urine does not show the colour-test with nitric acid. The analysis of the urine distinguishes these cases from true icterus.

In yellow fever the urine is very rarely impregnated with biliary colouring matter.

The occurrence of cholic and cholinic acids in the urine indicates that these substances, after their secretion by the liver and resorption into the blood and chyle, have not undergone those changes, at present unknown, to which under ordinary circumstances they are subjected in the blood

[1] See also Lehmann, 'Physiol. Chemie,' vol. ii, p. 209.

or tissues. The appearance of these acids in the urine would therefore indicate either the existence of an abnormal process in the blood, preventing the normal consumption of biliary acids, the liver continuing materially sound and secreting the ordinary bile; or it would indicate an excessive activity of the liver, by which more biliary acids are secreted than the blood and tissues can disintegrate, in consequence of which a part passes into the urine. The experiments of Frerichs[1] seem to show that a very large excess of cholates and cholinates in the blood would be required to make them appear in the urine. For when large quantities of filtered bile were injected into the veins of dogs, the bile disappeared in the blood without leaving traces anywhere, and without causing symptoms. In one case only, where a large quantity of a concentrated solution of pure cholate and cholinate of soda had been injected, a part of it could be discovered in the urine.

[1] 'Wien. Med. Wochenschrift,' iv, No. 30.

CHAPTER XXIX.

LEUCINE AND TYROSINE.

LEUCINE.

The elementary composition of leucine is expressed in the formula $C_{12}H_{13}NO_4$. It is homologous with glycocine or glycocoll and alanine, and has the same relation to valerianic acid and its aldehyde, as they have to formic and acetic acids and their aldehydes. When leucine is heated with potash, or allowed to putrefy, it yields up valerianic acid and some other products.

Leucine appears to be so frequent a product of diseased action in the human body, that I have thought it necessary to enter fully into the description of all its properties.

It was first (1818) discovered in rotten cheese by Proust,[1] who named it oxyde of cheese. Braconnot,[2] in 1820, obtained leucine as the product of decomposition of animal matter by oil of vitriol. The identity of oxyde of cheese and leucine was recognised by Mulder,[3] in 1838.

It has since been ascertained by a series of observers to be an almost constant product of the treatment, by concentrated or dilute sulphuric acid, and by caustic alkalies, of albumen, fibrine, caseine, muscle, glue, gluten, legumen, wool, and horn; it is also produced by the putrefaction of these substances, mostly together with some glycocine.

Frerichs and Städeler[4] have proved the occurrence of leucine and tyrosine in certain pathological conditions of the organism, such as typhus, and exanthematic fevers, as variola.

[1] 'Ann. de Chim. et de Phys.,' x, p. 40.
[2] Ibid., xiii, p. 119.
[3] 'Journ. für Pract. Chem.,' xvi, p. 290; xvii, p. 57.
[4] 'Wien. Med. Wochenschr.,' iv, No. 30. Müller's 'Archiv,' 1854, p. 387. 'Pharm. Centralbl.,' 1854, p. 861.

These substances were found in the urine, blood, and bile of the patients. In the urine the leucine seemed to have been partly transformed into valerianate of ammonia. The liver seems to be the organ in which leucine is formed during life, and where it is found most abundantly after the death of such patients. In the liver of healthy human subjects and of animals Frerichs and Städeler could not find any leucine. In a case of acute atrophy of the liver, these observers found the finer branches of the hepatic veins filled with zeolithic efflorescences, and firm yellowish-gray strings of matter containing crystals in the shape of balls with a radiary arrangement, and bundles and sheaves of needles. The balls were proved to be leucine by an elementary analysis; and the needles were tyrosine, forming a combination with sulphuric acid, and this combination forming salts with bases.

Leucine has been detected in the liver of the calf.[1] Dr. A. Cloetta[2] found it in the tissue of the lungs of the ox, together with inosite, uric acid, and taurine.

I found leucine in the urine of a man whose liver yielded a large amount of it. Goessmann found leucine in the charcoal, which is left in the retort when the residue from the evaporation of urine is subjected to dry distillation.

There is at present no very characteristic test for leucine; its diagnosis in urine, therefore, mainly depends upon the exclusion of all known normal and abnormal ingredients of that fluid, and upon the coincidence of several or all of the tests of leucine.

Production of Leucine.

According to Braconnot, leucine is obtained in the following manner. A piece of beef is chopped, washed with water, and subjected to strong pressure; the dry residue is warmed gently with its equal weight of sulphuric acid, until complete solution has taken place. After cooling, the fat collected on the surface is removed, and the solution is mixed with a quantity of water, amounting to three and a half times the weight of the meat originally employed. The mixture is kept boiling during nine hours, the water which evaporates being replaced from time to time. The sulphuric acid is then removed by carbonate of lime, the filtrate is evaporated to the

[1] Gregory's 'Handbook of Organ. Chem.,' 1852, p. 422.

[2] 'Verhandl. d. Naturf. Gesellschaft zu Zürich,' Bd. iv. 'Journ. für Pract. Chem.,' lxvi, p. 211, 1855.

consistence of a syrup, and the latter is repeatedly extracted by boiling alcohol. From this alcoholic solution leucine in a crystalline form is obtained by evaporation; the product of impure leucine amounts to about one thirtieth part of the muscular fibre used. It yet contains some animal matter, which may be precipitated from the watery solution by tannic acid. According to Mulder, it also contains some glycocine.

Hinterberger[1] adopts the following proceeding. One part of horn turnings and filings is mixed with four parts of sulphuric acid and twelve parts of water, and boiled during thirty-six hours, the water being replaced from time to time. The sulphuric acid is next removed by an excess of milk of lime; the fluid with the precipitate is boiled for twenty-four hours longer, and strained. The filtrate is neutralized by means of sulphuric acid, and filtered again; acetate of lead is now added until all sulphuric acid is removed. The excess of lead is removed by means of sulphuretted hydrogen, and the fluid is boiled with the sulphuret of lead. On filtering (which should be done when the fluid is cold, and has again been saturated with sulphuretted hydrogen, Th.), a scarcely coloured fluid is obtained, from which, on concentration, tyrosine crystallizes. From the mother-liquor leucine is obtained (mixed with a great deal of acetate of lime, from which it must be separated by extraction with boiling alcohol. Th.) It may be further decolorized by treating it with hydrated oxyde of lead, sulphuretted hydrogen, and animal charcoal.

Zollikofer[2] found that the elastic tissue of the animal body yields leucine as the sole crystalline product of decomposition by sulphuric acid. The nuchal ligament of horses or of oxen is particularly suitable. It is first freed from fat and fibrous (cellular) tissue by mechanical means, and then (Goessmann's improved proceeding) dissolved in its equal weight of concentrated sulphuric acid at the ordinary temperature of the air. This solution is then mixed with its own bulk of water, and boiled from ten to twelve hours, during which time the loss of water by evaporation is being frequently made up. After cooling, and removal of the fat floating on the surface, the solution is diluted and neutralized by milk of lime. The excess of lime is precipitated by carbonic acid, and the filtrate is evaporated, when leucine crystallizes. It is taken up with

[1] (1849) 'Ann. d. Chem. und Pharm.,' lxxi, p. 70. 'Pharm. Centralbl.,' 1850, p. 213. Liebig and Kopp's 'Jahresber.,' 1849, p. 502.

[2] (1852) 'Ann. d. Chem. und Pharm.,' lxxxii, p. 162. Liebig and Kopp's 'Jahresber.,' 1852, p. 696.

boiling alcohol; its watery solution may be further decolorized by animal charcoal.

Method of Bopp.[1]—One part of dry powdered albumen, fibrine, or caseine, free from fat, is mixed with one part of caustic potash, while fusing on the fire in an iron pot, of about twenty-five times the capacity of space taken up by the quantities of albuminous matter and potash. The mixture froths up, by the evolution of hydrogen and ammonia; and after half an hour, when the brown colour of the mixture has passed into yellow, water is cautiously added, the alkali is neutralized with acetic acid, and the fluid filtered while hot. The filtrate on cooling deposits groups of needles of tyrosine. (In case the operation has well succeeded, these crystals fill the entire filtrate, but their amount is the smaller, the longer the melting process has been continued.) The fluid decanted from these crystals is then again evaporated, until a crystalline pellicle begins to form on its surface; it is then allowed to repose for twenty-four hours, and is then extracted with alcohol, which leaves a residue consisting of leucine and some tyrosine. A certain quantity of leucine remains in solution in the alcohol; to this solution sulphuric acid diluted with alcohol is now added as long as sulphate of potash is thereby precipitated. From the filtrate the alcohol is evaporated, the sulphuric acid removed by acetate of lead, and the excess of lead precipitated by sulphuretted hydrogen; the filtrate on evaporation now yields crystals of leucine, and an uncrystallizable syrup, the quantity of which is the smaller, the longer the melting process has been continued. In order to free the leucine from tyrosine and a peculiar colouring matter, it is dissolved in such a quantity of hot water, that on cooling only little leucine crystallizes, together with most of the tyrosine; the mother-liquor is digested with hydrated oxyde of lead, which removes the colouring matter and some leucine; the filtrate is treated with sulphuretted hydrogen, and, being now of a faint-yellowish hue, is evaporated in a balloon until a crystalline pellicle begins to form on the surface, when, on cooling, leucine crystallizes, which may be further purified by washing with cold water and spirits of wine, and by treating it with animal charcoal and recrystallizing it.

If it is intended to have leucine alone, the mixture of the albuminous substance with potash requires only to be heated until the strongest frothing up has passed; the same quantity of leucine is then formed, but no tyrosine.

1 'Ann. der Chem. und Pharm.,' lxix, p. 20.

As a product of putrefaction, leucine may be obtained by allowing one part of cheese, flesh, or albumen, with fifty parts of water, to decompose at a temperature somewhat above 20° C. (68° F.), for about six weeks. The dirty fluid is then boiled with milk of lime; the lime is precipitated by a slight excess of sulphuric acid; the filtrate is evaporated, and precipitated with acetate of lead; the filtrate from this is evaporated to a syrupy consistence; and the leucine which now crystallizes is freed mechanically and by the assistance of alcohol from the syrup; it is then dissolved in water, treated with sulphuretted hydrogen, and is obtained pure by crystallization from alcohol and water.

When the solution, at the stage where it contains gypsum and a slight excess of sulphuric acid, is evaporated slowly in an open china dish, the gypsum crystallizing acts as a very potent decolorizer. From the crystalline and black sediment of gypsum the fluid may be poured off while hot. The decanted fluid should then be evaporated to dryness and extracted with alcohol, whereby a solution is obtained which contains no lime, and may easily be freed from sulphuric acid by acetate of lead. Another mode of removing the lime and sulphuric acid is by treating the decanted solution with oxalic acid, until no more precipitate of oxalate of lime is produced. The excess of oxalic acid, together with the sulphuric acid, is removed by acetate of lead; the excess of lead from the filtrate by sulphuretted hydrogen; and the filtrate from this precipitation will be almost colourless, and on evaporation will yield leucine, which may be purified of the last traces of admixed foreign matter by alcohol and crystallization.

Chemical and Physical properties of Leucine.

The sublimate of pure, dry leucine appears under the microscope in strings of rhombic plates, as represented in fig. 5, pl. VI.

When crystallized from an alcoholic solution, leucine represents white scales, of the lustre of mother-of-pearl, much like cholesterine, floating on water, and imparting the sensation of an unctuous matter to the finger. Under the microscope, it has the appearance of minute larch-agarics, with which it was compared by Proust. In the liver, and the extract therefrom, it crystallizes in balls, with a radiary arrangement of particles.

It dissolves in 27 parts of water at the ordinary temperature of the air, and in 658 parts of alcohol of specific gravity 0·828 (Mulder), or in 1040 parts of alcohol, of 96 per cent., at the ordinary temperature; and in 800 parts of warm al-

cohol of 98 per cent. strength (Zollikofer). It is insoluble in ether, even when boiling. The presence of acetic acid and acetate of potash increases the solubility of leucine in alcohol and water. When heated cautiously in a glass tube, open at both ends, it is completely volatilized in the form of thick white fumes, appearing like oxyde of zinc, without previously melting. When heated suddenly it fuses, and leaves a mass of charcoal. It is easily soluble in dilute acids, and forms combinations, assuming readily a crystalline form. It is also easily soluble in ley of caustic potash, and in ammonia.

Decompositions.—When fused with caustic potash, it is decomposed into valerianate of potash, cyanide of potassium, and water, free hydrogen escaping.

$$\underbrace{C_{12}H_{13}NO_4}_{\text{Leucine.}} + 2KO, HO = \underbrace{C_{10}H_9KO_4}_{\substack{\text{Valerianate of} \\ \text{Potash.}}} + \underbrace{KC_2N}_{\substack{\text{Cyanide of} \\ \text{Potassium.}}} + H_2 + 3HO.$$

Under the influence of nitrous acid, leucine is transformed into leucic acid (Strecker),[1] nitrogen escaping.

$$2\underbrace{(C_{12}H_{13}NO_4)}_{\text{Leucine}} + 2NO_3 = \underbrace{C_{24}H_{24}O_{12}}_{\text{Leucic acid.}} + 4N + 2HO.$$

Zollikofer (1852) found that the watery solution of leucine is not precipitated by salts of metals, not even by the nitrates of the protoxyde and suboxyde of mercury, nor by corrosive sublimate; basic acetate of lead being the sole exception to this rule. This has been confirmed by Goessmann (1854). It is therefore a great oversight on the part of authors of systematic treatises on organic and medical chemistry, to continue to state in 1854 and 1857, what in 1852 had been proved to be incorrect.

Salts of Leucine.[2]—The combinations of leucine with acids may be produced in a direct manner.

Hydrochlorate of Leucine ($C_{12}H_{13}NO_4$, HCl) forms crystals easily soluble in water.

Nitrate of Leucine, or Leuconitric Acid ($C_{12}H_{13}NO_4$, NO_6H), appears in colourless concentric groups of needles. It forms a salt with lime, crystallizing in small warts, and containing water of crystallization; and another salt with magnesia, appearing in small granular crystals.

[1] 'Ann. d. Chem. und Pharm.,' lxxii, p. 89.

[2] Gerhardt, Laurent, and Cahours, 'Compt. Rend.,' xxvii, pp. 256, 265.

With nitrate of silver, leucine forms a crystallizable compound.

Leucine enters into combination with the oxydes of several metals.

Leucine and Oxyde of Copper. $C_{12}H_{13}NO_4$, CuO.—Hydrated oxyde of copper, when just precipitated, dissolves in a solution of leucine, easily, and in large quantities, forming a blue fluid. When this solution is evaporated on the water-bath, blue crystals of the above compound are obtained, which are very similar to the ammonio-sulphate of copper. If a solution of leucine is boiled with an excess of hydrate of oxyde of copper, the above soluble compound and an insoluble one are formed.

Leucine and Oxyde of Mercury. It may be prepared like the copper compound, or by neutralizing with potash a mixture of solution of nitrate of protoxyde mercury and solution of leucine. It contains one equivalent of protoxyde of mercury.

Leucine and Oxyde of Lead. $C_{12}H_{13}NO_4$, PbO.—When to a boiling mixture of solution of leucine and neutral acetate of lead ammonia is carefully and gradually added, little scales of the lustre of mother-of-pearl are deposited (Strecker).

If a solution of leucine is boiled with an excess of oxyde of lead, or if to a boiling mixture of solutions of leucine and acetate of lead ammonia is added in excess, an insoluble compound of the formula $C_{12}H_{13}NO_4$, $(PbO)_9$ is produced (Goessmann).

Mode of obtaining Leucine from Urine.

The above tests with lead may perhaps be made available for that purpose. I have obtained leucine as a deposit by concentration of the urine. The deposit may be washed with cold alcohol, and purified by lime, charcoal, and so on; or in one of the ways indicated above. All this will only serve to prove its presence: we have, as yet, no means for determining its quantity.

TYROSINE.

Elementary composition: $C_{18}H_{11}NO_6$.

The occurrence and mode of obtaining tyrosine have already been described. It was discovered by Liebig as a product of the decomposition of cheese by fused caustic potash.

Physical and Chemical properties.

It crystallizes in voluminous white needles, which on drying contract to a silky film of white colour and some lustre. As such I obtained it from the inspissated watery extract of the liver. It is without taste or odour.

In cold water it is scarcely soluble, easily in boiling water. It is insoluble in alcohol and ether. It dissolves rapidly in mineral acids and alkalies, yielding compounds which are even soluble in alcohol. From a solution in ammonia, it crystallizes unchanged, but in larger crystals on spontaneous evaporation of the fluid. From the alkaline solution it is precipitated by acids. Heated on the platinum foil, it burns without leaving any residue, emitting the odour of burnt horn.

When tyrosine is dissolved in strong nitric acid, the solution, after a short time, yields brownish-yellow crystals of nitrate of nitrotyrosine, $C_{18}H_{10}XNO_6$, HO, NO_5.

From its formula, tyrosine may be considered to be a copulated compound of glycocoll and saligenine.

$$\underbrace{C_{18}H_{11}NO_6}_{\text{Tyrosine.}} = \underbrace{C_4H_5NO_4}_{\text{Glycocoll.}} + \underbrace{C_{14}H_8O_4}_{\text{Saligenine.}} - 2HO.$$

Under the influence of boiling nitric acid, tyrosine is decomposed, oxalic acid being one of the principal products.

Nitrate of protoxyde of mercury causes a precipitate of red flakes in a solution of tyrosine while boiling. The precipitate subsiding to the bottom, leaves a clear fluid above it, which has an intensely pink or dark rose-red colour. This test is so nice, that it is obtained even when the watery solution of tyrosine, saturated at the ordinary temperature of the air, is diluted several times with its own volume of water (R. Hoffmann).

If some tyrosine and one or two drops of sulphuric acid are placed on a watch-glass, covered, and allowed to stand for about half an hour, and the mixture is then diluted with water, neutralized with carbonate of lime and filtered, and if to the filtrate a solution of chloride of iron is added, containing no free acid, a rich violet colour is immediately produced. Neutral chloride of iron will produce this test with all neutral salts of the tyrosino-sulphuric acid.

Tyrosine was discovered in the urine of typhus patients by Frerichs and Städeler. It is most probably formed in the liver, together with leucine.

CHAPTER XXX.

XANTHINE.

Elements: $C_{10}N_4H_4O_4$.		
	Carbon	39·48
	Nitrogen	36·84
	Hydrogen	2·63
	Oxygen	21·05
		100·00

Xanthine, or xanthic oxyde, was discovered by Dr. Marcet,[1] in 1819, and was first analysed by Wöhler and Liebig,[2] afterwards by Laugier.[3] It has as yet been found in three instances only, forming calculi from the urinary bladder of man. It contains one equivalent of oxygen more than hypoxanthine, from which, in its reactions, it is only distinguished by its insolubility in water.

Urinary calculi consisting of xanthine are light or dark yellowish-brown in colour, of even surface, hard in substance, of the hardness of the ordinary uric acid calculi, constructed of concentric layers without fibrous or crystalline texture. On friction the calculi assume the glistening appearance of wax.

Mode of obtaining Xanthine from Calculi.

The calculus is dissolved in caustic potash, and the filtrate precipitated by a current of carbonic acid. The precipitate, which is white and pulverulent, is washed, and on drying

[1] 'Essay on the Chemical History and Medical Treatment of Calculous Disorders,' London, 1819.

[2] 'Poggend. Annal.,' xli, 393. 'Ann. d. Pharm.,' xxvi, 340.

[3] 'Journ. de Chim. Med.,' v, 513. See Gmelin, 'Handb. d. Organ. Chem.,' 4to edit., 1852, vol. ii, p. 514, whence the article is transcribed.

forms into hard yellowish pieces, which become wax-like on friction, and are free from potash.

Chemical properties.

Subject to dry distillation, the xanthine calculus yields much prussic acid, and a sublimate of carbonate of ammonia, but no urea. Heated before the blowpipe, it breaks into pieces, blackens, emits a peculiar weak odour of burning animal matter, which is different from that of burning uric acid, and more like that of burnt horn, and then is burned, leaving only little ashes.

Its solution in nitric acid, on evaporation, leaves a lemon-yellow dry residue, which is partly soluble in water; this solution is yellow, becomes discoloured with acids, reddened by the addition of caustic potash, and then yields a carmine mass on evaporation, which is soluble in water with a yellow tinge. The solution in caustic potash gives a yellow precipitate with hydrochlorate of ammonia, and is decomposed by liquor sodæ chlorinatæ, the solution becoming dark at first, then colourless, under evolution of nitrogen gas.

Xanthine is slightly soluble in boiling water, from which solution it is precipitated on cooling in the form of a thin membranous layer.

It is soluble in oil of vitriol, and is not precipitated from this solution by the addition of acids. In dilute acids it is very little soluble. It is insoluble or scarcely soluble in hydrochloric acid.

It is more easily soluble in ammonia than uric acid, and the solution on evaporation leaves a yellowish lamellated mass, containing yet some ammonia.

It readily dissolves in caustic potash, and is precipitated from the solution by acids. The solution is dark greenish-brownish-yellow, like bile, and deposits xanthine immediately, when a current of carbonic acid gas is being transmitted through the fluid. The addition of hydrochlorate of ammonia to the solution also causes a precipitate, but only on evaporation, during which ammonia is being evolved.

Xanthine is soluble in a watery solution of carbonate of potash, insoluble in bicarbonate of ammonia, potash, or soda.

It is a little soluble in acetic acid.

It is insoluble, or scarcely soluble, in oxalic acid.

It is insoluble in spirits of wine and ether.

CHAPTER XXXI.

HYPOXANTHINE.

Elements: $C_{10}H_4N_4O_2$.	Carbon .	44·257
	Hydrogen .	3·219
	Nitrogen .	40·820
	Oxygen .	11·704
		100·000

This substance has been discovered by Scherer in the spleen and heart of man, and of cattle. In the heart it is frequently found in such quantities, as to form a precipitate when the extract by boiling water of this organ is allowed to cool. The blood of cattle also contains this substance, which has moreover been discovered in larger quantities in the blood and urine of patients labouring under leukæmia.

Mode of obtaining Hypoxanthine.

The organs are finely chopped and boiled in water. The solution, when strained from the fibres and coagula, is treated with baryta-water, which precipitates phosphoric acid with the baryta. The filtrate is evaporated, when the excess of baryta becomes insoluble, as carbonate. When the fluid is reduced to a small bulk, it is treated with sulphuric acid. The precipitate of sulphate of baryta now forming, throws down with it uric acid and hypoxanthine. The latter two substances are extracted by boiling solution of potash, and the solution is treated with chloride of ammonium, which precipitates uric acid, while hypoxanthine remains in solution, from which it may be precipitated by a current of carbonic acid gas.

Physical and Chemical properties.

Hypoxanthine appears as an indistinctly crystalline powder, which may be triturated without assuming the glistening surface of wax. It is soluble in 1090 parts of cold, and in 180 parts of boiling water. The watery solution is without influence on vegetable pigments. It is slightly soluble in boiling alcohol, falling down from the solution on cooling. In boiling nitric acid it is soluble with effervescence; and on cooling of the solution, white crystals appear, which most probably are a product of decomposition.

When the solution in nitric acid is gently evaporated, it leaves a residue of an intensely yellow colour, which by treatment with caustic potash becomes orange.

It is almost insoluble in cold hydrochloric acid, a little more soluble in the boiling acid, but forms no combination with it.

It is soluble in concentrated sulphuric acid, without the formation of charcoal or the evolution of gas.

It is soluble in caustic potash, and is precipitated from the solution by carbonic acid.

It readily dissolves in ammonia; and, when the latter evaporates, remains as a lamellated mass, with little adhesion to the walls of the vessel.

CHAPTER XXXII.

SARCINE (CARNINE).

Formula: $C_{10}H_4N_4O_2$.	Carbon . .	44·12
	Hydrogen .	2·94
	Nitrogen . .	41·18
	Oxygen . .	11·76
		100·00

History and Occurrence.

This substance has lately been discovered and described[1] by Professor A. Strecker, of Christiania, who provisionally gave it the name of sarcine. But as this name might lead to misunderstanding, by its being identical with the name of the alga, sarcina ventriculi, discovered by Goodsir in vomit, and which also occurs in the urine, I propose carnine as a temporary synonym, until the discoverer shall have definitely baptized this substance.

Carnine occurs in the juice of flesh, together with the several principles discovered and described by Liebig, and many others as yet undetermined. When to the mother-liquor of creatine a solution of either corrosive sublimate, nitrate of protoxyde of mercury, ammonio-chloride of zinc, or acetate of copper is added, a considerable precipitate is produced, which in every instance contains an organic base as an essential constituent. This organic base occurs in beef and horse-flesh in about equal quantities, and is also most probably an ingredient of human urine. The substance discovered by

[1] 'Quarterly Journ. of the Chem. Soc.,' vol. x, p. 121, July, 1857.

Strecker in human urine closely resembles carnine in its compounds; the only doubt as to whether it may not be guanine, Dr. Strecker is about to decide by further analyses.

Mode of obtaining it pure.

The most advantageous method of preparing this base is by precipitation with acetate of copper. The mother-liquor of the creatine crystals is diluted, and mixed with a dilute solution of copper. The copious precipitate thus produced is decomposed by sulphuretted hydrogen (hydrothion), when the base remains in solution. To remove colouring matter, the solution is boiled with hydrated oxyde of lead, which also takes up a small quantity of carnine. The filtrate from the lead is treated with hydrothion, and after filtration evaporated, when carnine is obtained in a crystalline form.

Physical and Chemical characters.

From its warm saturated solution, carnine, on cooling, is deposited as a white, indistinctly crystalline powder, frequently, however, adhering as a dense crust to the sides of the vessel. It is soluble in 300 parts of water of 15° C. (60° F.) temperature, and in 78 parts of boiling water; it requires 900 parts of boiling alcohol for solution. The solutions do not change the colour of litmus paper, and have not got any very characteristic taste. In hydrochloric acid, ammonia, and potash, carnine dissolves much more readily than in cold water; less readily in dilute nitric and sulphuric acid. It is largely soluble in concentrated nitric and sulphuric acid, without discoloration or evolution of gas.

In a boiling solution of carnine, basic acetate of lead produces a precipitate. From its watery solution, carnine is further precipitated by ammonio-chloride of zinc, by cadmium salts, the mercury salts already mentioned, and the salts of many other metals. Caustic alkalies, including baryta, dissolve carnine; from these solutions it is mostly precipitated by a current of carbonic acid gas. From these characters, and the nature of its combinations, it is evident that carnine is a base.

Compounds.

Carnine forms well defined combinations with acids, metallic oxydes, and salts.

Hydrochlorate of carnine. $C_{10}H_4N_4O_2$, HCl + 2Aq.—The

solution of sarcine in boiling concentrated hydrochloric acid, deposits, on cooling, colourless crystalline plates of the forementioned composition. When, however, the solution of hydrochlorate of sarcine in water is repeatedly evaporated to dryness on the water-bath, a residue is at length obtained, containing no hydrochloric acid. Water has therefore a decomposing influence upon this salt.

Hydrochlorate of carnine and bichloride of platinum. $C_{10}H_4N_4O_2$, HCl, $PtCl_2$.—On adding a solution of bichloride of platinum to a concentrated solution of crystals of hydrochlorate of carnine, this platinum salt is deposited in yellow crystalline masses, which are sparingly soluble in cold water, but readily dissolve in a higher temperature.

Nitrate of carnine.—The solution of carnine in concentrated nitric acid, deposits, on standing, transparent, colourless crystals (apparently rhombic octahedra) of nitrate of carnine, which, on exposure to air or water, become white and opaque, without any alteration of shape.

Sulphate of carnine.—The solution of carnine in concentrated sulphuric acid, deposits, on standing, or by addition of alcohol, colourless, needle-shaped crystals of sulphate of carnine, which, on coming in contact with water, crumble to a white powder.

Carnine, when treated with concentrated acids at a temperature of 240° F. (100° C.), does not undergo any decomposition. Its solution, when mixed with aqua regia and evaporated on the water-bath, leaves a residue, which consists mainly of unchanged carnine.

Carnine and baryta. $C_{10}H_2Ba_2N_4O_2 + 4Aq$.—A solution of carnine in baryta-water, on addition of a larger quantity of baryta-water, deposits transparent colourless crystals of carnine-baryta. From the solution of this salt the baryta may be precipitated by a current of carbonic acid gas.

Carnine and oxyde of silver. $C_{10}H_2Ag_2N_4O_2 + 2Aq$.—On adding a solution of sarcine to an ammoniacal solution of nitrate of silver, a flocculent precipitate, quite insoluble in water and ammonia, is obtained, which on drying becomes a hard mass, like alumina.

Carnine and nitrate of silver. $C_{10}H_4N_4O_2$, AgO, NO_5.—A solution of carnine in water, when mixed with a solution of nitrate of silver, forms a flocculent precipitate, which is insoluble in dilute nitric acid at the ordinary temperature. It is, however, completely soluble in boiling concentrated nitric acid, and from this solution is, on cooling, deposited in colourless scaly crystals, and so completely, that the filtrate scarcely yields any precipitate on addition of hydrochloric acid.

In its elementary composition it stands near to guanine, only containing one equivalent of nitrogen and hydrogen less than that base. It also presents great analogies to it in its compounds.

Its elementary composition is identical with that of hypoxanthine, the base discovered by Scherer in the spleen, and since found by him in various organs. The two substances likewise agree in certain other characters; hypoxanthine, however, is almost insoluble in water and hydrochloric acid—a difference from carnine, which cannot be accounted for by simple difference of purity of the preparations. Hypoxanthine dissolves in warm nitric acid with evolution of gas, and on cooling yields a product of decomposition. The solution in nitric acid, on evaporation to dryness, leaves a yellow residue, assuming a red colour on the addition of caustic potash. Carnine, on the other hand, dissolves in nitric acid without evolution of gas, and the solution by evaporation on the water-bath, leaves a colourless mass, which does not become yellow unless very strongly heated; on addition of potash this residue assumes a red colour. Xanthine and guanine have very similar reactions.

From its elementary composition, xanthine ($C_{10}H_4N_4O_4$) might be considered as a compound of uric acid with carnine,

$$\underbrace{2C_{10}H_4N_4O_4}_{\text{Xanthine.}} = \underbrace{C_{10}H_4N_4O_6}_{\text{Uric acid.}} + \underbrace{C_{10}H_4N_4O_2}_{\text{Carnine.}};$$

but its chemical affinities do not accord with this view. By mixing a solution of hydrochlorate of carnine with urate of soda, not xanthine, but an isomeric compound—urate of carnine—is obtained, which, under the influence of acids, separates into its original constituents.

CHAPTER XXXIII.

CYSTINE.

Elements: $C_6H_6NS_2O_4$.		
	Carbon	30·00
	Hydrogen	5·00
	Nitrogen	11·66
	Sulphur	26·67
	Oxygen	26·67
		100·00

Literature.

Wollaston, 'Philos. Transact.,' 1810, p. 223.—Cystine discovered, constituting a calculus, 1810.

Baudrimont and Malaguti, 'Journ. d. Pharm.,' vol. xxiv, p. 633.—Proved the presence of sulphur, which had been overlooked by Prout and Lassaigne.

Thaulow, 'Ann. d. Pharm.,' vol. xxvii, p. 197.—Best elementary analysis.

Marchand, 'Journ. d. Pract. Chem.,' vol. xvi, p. 255.

For the rest of the casuistic see Gmelin's 'Handb. d. Org. Chem.,' 4th edit., vol. ii, p. 133.

Occurrence.

Cystine is the principal constituent of a rare description of calculus; small calculi are sometimes made up of pure cystine, and then appear yellow, transparent, wax-like, of a crystalline texture. They cut like dry walnut, may be powdered, and are gritty between the teeth, tasteless, and neutral. When the calculi are not made up of pure cystine, they generally contain an admixture of earthy phosphates, and then are greenish-blue, dirty greenish-grey, or fawn-brown.

Cystine gravel has occasionally been obtained from dogs.[1] Latterly cystine has been discovered by Scherer[2] to be present in the liver of typhus patients. Another observer[3] has once obtained it from the kidneys of oxen, but could not meet with it again in the same substance. Two calculi of cystine were found in the calyces of the kidneys of an old woman by Professor Virchow.[4] Lastly, it is met with in the urine in solution and as a deposit. Where it occurs dissolved it is probably by means of some alkali, either the alkali by means of which it was excreted from the kidneys, or an alkali formed in the urinary passages, ammonia which has lost some carbonic acid, as is usual in decomposed urine.

But this is merely a supposition, supported, however, by the observation of Julius Müller,[5] who found cystine dissolved in the alkaline urine of a boy six and a half years old. Here the alkaline condition seemed to be due to the presence of a large cystine calculus in the bladder. After the operation of lithotomy, the urine became acid. Two months later, the urine became again alkaline, and gave a deposit which, when cleared of earthy phosphates by means of acetic acid, showed itself to be cystine again. The urine, on being filtered and treated with acetic acid, after the lapse of twenty-four hours yielded another precipitate of cystine. This case shows that the conditions under which cystine occurs in an insoluble or in a dissolved condition require further investigation.

Decompositions.

When subjected to dry distillation, cystine yields prussic acid, carbonate of ammonia, a fluid, thick and stinking oil, and leaves a spongy charcoal. Heated in the open air, it develops sulphurous acid, recognisable by the smell, but does not fuse, or melt, or blister. When fused with caustic potash, it gives off an inflammable gas, which burns with the flame of sulphocarbon and under production of sulphurous acid. (This gas is most probably sulphuretted hydrogen, as is made probable by the following reaction.) When cystine is boiled in caustic potash solution, in which some hydrated oxyde of lead has previously been dissolved, a large precipitate of sulphuret of lead is obtained (Liebig). The solution of cystine in excess of nitric acid, on evaporation by boiling,

[1] Heller, 'Heller's Archiv.' vol. vi. p. 458.
[2] Virchow's 'Archiv,' vol. x, Heft. 1 und 2, p. 228.
[3] A. Cloetta.
[4] 'Archiv,' loc. cit., p. 230.
[5] 'Archiv d. Pharmac.,' März, 1852, p. 228.

leaves at first a white, not transparent mass, which becomes brown and black, and contains sulphuric acid.

Cystine crystallizes in six-sided plates of the arrangements represented in fig. 1, plate VI. These crystals are very characteristic, and therefore a valuable means of diagnosis.

Cystine is insoluble in water, but soluble in dilute strong acids, from which solution it is precipitated by carbonate of ammonia. The solution on evaporation yields a salt, mostly crystallizing in groups of needles. The phosphate, sulphate, hydrochlorate, and nitrate are the compounds best known.

Cystine is easily soluble in a watery solution of ammonia, potash, soda, and lime; also in the bicarbonates of potash and soda, but not in bicarbonate of ammonia. The solution in ammonia on spontaneous evaporation leaves the cystine pure in crystals. The other solutions leave granular crystals, the composition of which is not ascertained. From the alkaline solutions, cystine is precipitated, after a few seconds, by acetic, tartaric, and citric acids, in the form of a fine white powder; these solutions are, however, not precipitated by either sulphuric, hydrochloric, or nitric acid.

Cystine is soluble in a watery solution of oxalic acid.

CHAPTER XXXIV.

ALLANTOINE.

Elements : $C_8H_6N_4O_6$.	Carbon	30·38
	Hydrogen	3·80
	Nitrogen	35·44
	Oxygen	30·38
		100·00

Literature.

Vauquelin and Buniva, 'Ann. Chim.,' vol. xxxiii, p. 269.—Discovered (1800) allantoine in the allantoic fluid of the cow, which was probably mixed with amniotic fluid.

C. G. Gmelin, 'Gilb. Ann.,' vol. lxiv, p. 350.

Lassaigne, 'Ann. d. Chim. et de Phys.,' vol. xvii, p. 301; also 'Journ. de Phys.,' vol. xcii, p. 406.—Showed that allantoine was peculiar to the allantoic fluid.

Liebig, 'Poggend. Ann.,' vol. xxi, p. 34.

Liebig and Wöhler, 'Ann. d. Pharm.,' vol. xxvi, p. 244; 'Pogg. Ann.,' vol. xli, p. 561.—Allantoine a product of decomposition of uric acid by oxydation.

Wöhler, 'Ann. d. Pharm.,' vol. lxx, p. 229.—Allantoine discovered to be a natural ingredient of the urine of sucking calves.

Städeler.—Allantoine in the urine of a dog, into whose veins oil had been injected.

Mode of obtaining Allantoine.

The allantoic fluid of the cow (which is mostly mixed with amniotic liquor) is evaporated to one quarter of its original bulk, and cooled down to make allantoine crystallise. Allantoine is also precipitated from the fluid, when it is allowed to stand for some length of time, and may then be separated, dissolved in hot water, and, after filtration, recrystallized.

The urine of calves is obtained (according to Wöhler) by tying the bladder before the animals are killed by the butcher. This proceeding can only be adopted in countries where the calves are killed very early, as in Germany and Switzerland. In this country, therefore, other proceedings must be had recourse to for obtaining the urine. Among those which are practicable, the catheterism of female animals appears to be most suitable. The urine thus obtained is evaporated on the water-bath to a syrupy consistence, and is put in a cold place for several days, then diluted with water. The gelatinous precipate of urate of magnesia is then removed by washing, when there remain only crystals of phosphate of magnesia and allantoine. They are now washed with a little cold water, boiled with water and a little good animal charcoal, and filtered, when most of the phosphate of magnesia remains on the filter. The addition of a few drops of hydrochloric acid to the filtrate keeps in solution the phosphate of magnesia, and, on cooling, colourless allantoine crystallizes from the solution (Wöhler).

Städeler obtained allantoine from the urine of a dog as follows: The urine, immediately after passing, was precipitated with basic acetate of lead, and the excess of lead was removed from the filtrate by sulphuric acid and hydrothion. The colourless fluid was evaporated on the water-bath. The residue was extracted with boiling spirits of wine of 82 per cent., and the yellowish solution put aside in a well-closed bottle. After the lapse of several days a large quantity of small white groups of crystals appeared deposited upon the sides of the bottle, which were almost insoluble in cold water, but dissolved in boiling water, and on cooling were deposited again in larger glistening crystals. This body was allantoine.

Mode of obtaining allantoine from uric acid.—Powdered uric acid is suspended in little water, and heated to near the boiling point. Peroxyde of lead in a finely powdered state is now added to the fluid, which is continued to be kept hot, until the last portions of the peroxyde are no longer transformed into a white mass. The mixture is

now filtered hot, and the filtrate, on cooling, and on further evaporation and cooling, yields allantoine in crystals; the mother-liquor contains urea, from the last traces of which the crystals of allantoine may be separated by recrystallization.

Physical and Chemical properties.

Allantoine crystallizes in glass-like needles; when obtained from uric acid it represents rhomboedric crystals, combined with the hexagonal prism or column. It is tasteless, colourless, and has no reaction on test-paper. Exposed to the air it undergoes no change; it contains no water of crystallization.

Subjected to dry distillation, it yields carbonate and hydrocyanate of ammonia, empyreumatic oil, and a spongy charcoal. Heated with oil of vitriol it is decomposed into sulphate of ammonia and a mixture of carbonic acid and oxyde of carbon.

When gently warmed with nitric acid of a specific gravity of 1·2 to 1·4, during which process no gas is evolved, the solution on cooling yields nitrate of urea in crystals. The solution, on being evaporated to dryness, leaves nitrate of urea and allanturic acid.

$$\underbrace{C_8H_6N_4O_6}_{\text{Allantoine.}} + 2HO = \underbrace{C_2H_4N_2O_2}_{\text{Urea.}} + \underbrace{C_6H_4N_2O_6}_{\text{Allanturic acid.}}$$

The same decomposition of allantoine can be brought about by boiling it with hydrochloric acid, by heating it enclosed with water in a strong tube to a temperature of from 110° to 140 C. (230° to 284° F.) (Here urea is further decomposed into ammonia and carbonic acid.)

Allantoine is soluble in 160 parts of cold water, in 30 of boiling water; it is soluble in hot alcohol, and crystallizes from both these hot solutions on cooling. It is soluble in cold solution of caustic potash, and is precipitated from this solution by the addition of acids. If, however, allowed to remain in this solution for any length of time, it is metamorphosed. It is soluble in solutions of the carbonates of the alkalies. When boiled with hydrate of potash or baryta, it is resolved into ammonia and oxalic acid. The same decomposition takes place under the influence of yeast, at a temperature of 30° C. (86° F.) Urea, oxalate and carbonate of ammonia, and a new acid, not investigated, are the products of the decomposition.

On adding to a boiling saturated solution of allantoine in water nitrate of silver, and then ammonia, so long as a precipitate is being formed, a combination of allantoine with oxyde of silver is obtained in the precipitate, which is a white glistening powder, and under the microscope appears in spherical balls. It is decomposed by all dilute acids, allantoine being set free.

A solution of allantoine is not precipitated by corrosive sublimate. It is, however, precipitated by a solution of nitrate of protoxyde of mercury, and, like urea, combines with mercury in various proportions, analogous to the compounds of urea. (Limpricht.)

It enters into combination with the oxydes of copper, cadmium, lead, and zinc, and the combinations crystallize.

Pathological indications.

In consequence of having found allantoine in the urine of a dog suffering from dyspnœa following the injection of oil into his veins, Frerichs and Städeler examined the urine of several persons suffering from dyspnœa, emphysema, and pneumonia, as also the urine of a woman who, to relieve the dangerous dyspnœa caused by an aneurism of the arch of the aorta, was obliged to have tracheotomy performed upon her. In neither of these cases were the observers able to find allantoine in the urine. It is therefore yet questionable how the appearance of allantoine in the urine of the dog has to be explained. It is also a question whether allantoine ever appears in the urine of man. But as there is a probability, I have thought it best not to omit the description of its properties, in order that there might be less chance of its being overlooked by future observers.

CHAPTER XXXV.

GRAPE-SUGAR.

Elements: $C_{12}H_{12}O_{12} + 2Aq.$	Carbon . . .	36·36
	Hydrogen . .	7·07
	Oxygen . . .	56·57
		100·00

Grape-sugar was found by Lowitz and Proust[1] to be distinct from cane-sugar. Thénard and Dupuytren[2] proved the sugar from the urine of diabetic patients to be identical with grape-sugar.

This substance forms a constituent of all sweet-tasting fruit, in which it is contained in various proportions. Raisins, figs, dates, and other dried fruit contain it crystalline, and in largest proportions. It is also contained in bees' honey, mixed with an uncrystallized sugar, termed glucose.

It is found in the human and animal organism after food containing sugar or starch; the contents of the upper part of the small intestines, the chyle, portal and venous blood, and the extract from the liver, give then unquestionable evidence of its presence. But it is more than doubtful whether the substance found in hens' eggs, in the urine of the fœtus of the cow and sheep, in the allantoic and amniotic fluid of cows, sheep, and swine, which reduces oxyde of copper in its alkaline solution, is really sugar; as allantoine, a substance found to be present in all the fluids

[1] Lowitz, Dr. Crell's 'Chem. Ann.,' 1792, i, pp. 218 and 345. Proust, 'Journ. d. Phys. et de Chim.,' lxiii, p. 257; lxix, p. 428. 'Ann. de Chim.,' lvii, pp. 131, 225.

[2] Thénard and Dupuytren, 'Ann. de Chim.,' xliv, p. 45.

just named, has been found to possess the same reaction as sugar.

In diabetes mellitus, sugar is found in all or most of the secretions, tissues, juices, and excretions of the body.

Grape-sugar may be made artificially from cane-sugar and starch, either through the influence of diastase, or by boiling with dilute acids (sulphuric acid), as was first discovered by Kirchhoff.[1] The transformation into sugar of cellulose, under the same conditions, was observed by Braconnot.[2] Many immediate principles of plants, such as amygdaline, salicine, phloridzine, rhodeoretinic acid, rhuberythric acid, arbutine, populine, quercitrine, esculine, caincic acid, chinovic acid, tannic acid, are, under the influence of synaptase, or of dilute acids or alkalies, transformed into grape-sugar and other compounds. These principles are comprised under the class of *glucosides*, or substances combined with sugar.

It has been ascertained by Pelouze, that the substance extracted from the liver by M. Cl. Bernard, and capable of transformation into sugar under the influence of unboiled liver ferment, is really dextrine, and not, as many at first believed, a modified albuminous substance.

Grape-sugar must not be confounded with *glucose*, the uncrystallizable sugar of acid fruits, and of honey. For though, in the course of time, glucose is transformed into grape-sugar by molecular changes, yet the different influence upon polarized light, the solubility in cold alcohol, and the amorphous condition, are essential differences, and must be regarded.

Mode of obtaining Grape-sugar.

Honey is treated with cold alcohol, which dissolves the uncrystallizable sugar or glucose, leaving the crystallized grape-sugar behind. The residue is washed with alcohol, pressed, dissolved in water, treated with animal charcoal and white of egg, evaporated, and allowed to crystallize. It may be recrystallized from boiling alcohol.

From raisins or dates (which latter, when good and large, I have found most advantageous) it may be obtained by ex-

[1] 'Journ. de Phys. et de Chim.,' lxxiv, p. 199. Schweigger's 'Journ.,' xiv, p. 389.

[2] 'Ann. de Chim. et de Phys.,' xii, p. 172. Schweigger's 'Journ.,' xxvii, p. 328.

traction with boiling water; the extract, when evaporated, is, after crystallization has taken place, treated in the same way as honey.

From diabetic urine grape-sugar may be obtained by evaporating the urine in the water-bath to dryness, extracting the crystalline dark-coloured residue on a filter or otherwise with cold spirits of wine, and purifying the residue by repeated recrystallization from water, after treatment with albumen and animal charcoal, and at last by recrystallization from boiling alcohol.

Physical and Chemical properties.

From not too concentrated solutions, grape-sugar crystallizes in semi-globular warts, or in masses like cauliflower. From the watery extract of dates, and from bulky solutions in alcohol, large, transparent crystals, with well formed planes, and double refraction of light, are sometimes obtained.

It is less soluble in water than cane-sugar, requiring $1\frac{1}{3}$ times its own weight of this solvent for solution at the ordinary temperature. In boiling water it is soluble in all proportions. It tastes less sweet than cane-sugar, and $2\frac{1}{2}$ parts of the former are required to equally sweeten the same bulk of fluid as one part of the latter. The solution of grape-sugar turns to the right a ray of polarized light.

The crystals contain two equivalents of water, which they lose at a temperature of 100° C. (212° F.), at which they fuse. At 140° C. (284° F.), another loss of three equivalents of water transforms grape-sugar into *caramel*—$C_{12}H_9O_9$.

Combinations.

Grape-sugar, like cane-sugar, unites with bases, but is easily coloured brown and decomposed while thus uniting. The baryta compound of the composition, $2(C_{12}H_{12}O_{12}) + 3BaO$ ($C_{12}H_{11}BaO_{12}$, Gerhardt), is obtained in the form of a flaky white precipitate by mixing together solutions in methylalcohol of grape-sugar and of baryta. A similar combination with lead ($C_{12}H_{12}O_{12} + 3PbO$) is obtained by precipitating a solution of sugar by acetate of lead under addition of ammonia ($C_{12}H_{11}PbO_{12} + 2PbO$, Gerhardt).

A compound of grape-sugar with chloride of sodium of the formula $2(C_{12}H_{12}O_{12})$, NaCl + 2HO (3Aq., Gerhardt), was

discovered by Calloud[1] in the inspissated diabetic urine. It may be easily obtained by mixing moderately concentrated solutions of one equivalent of chloride of sodium and two equivalents of grape-sugar, and by gently evaporating the mixture. The compound then crystallizes in hard, colourless, six-sided double pyramids; if an excess of chloride of sodium has been taken, this crystallizes first from the solution.

Grape-sugar is not influenced by dilute acids, and not blackened by concentrated sulphuric acid. If grape-sugar dried at a temperature of 100° C. (212° F.) is mixed with one and a half times its weight of concentrated sulphuric acid, it dissolves and forms with the acid a combination which is an acid itself, and has been called sulpho-saccharic acid. This may be dissolved in water, and freed from excess of uncombined sulphuric acid by carbonate of baryta. The addition of basic acetate of lead to the filtrate precipitates sulpho-saccharate of lead, which by decomposition with sulphuretted hydrogen yields sulpho-saccharic acid, a substance which easily undergoes decomposition.

Decompositions.

Grape-sugar combines with the oxydes of metals; the compounds are, however, very changeable. In the presence of bases it is easily oxydized, absorbs oxygen from the air, and assumes a brown colour. Thus when a solution of grape-sugar, diabetic urine for example, is heated with a solution of caustic potash, the mixture becomes brown at a temperature of from 60° to 70° C. (140° to 158° F.), and a smell of burned sugar is being evolved. Two new acids are produced by this process, *glucic* and *melassic* acid.

When the oxydes of several metals (copper, mercury, silver or gold, bismuth) in the form of salts are brought in contact with solutions of grape-sugar in a higher temperature, a reduction of the oxyde to a lower oxyde or to metal takes place.

Two reduction-tests in particular are of importance for the qualitative discovery and quantitative determination of diabetic sugar in urine: I allude to the tests with bismuth and with copper.

When diabetic urine, or any other solution of grape-sugar, is mixed with an equal volume of a solution of carbonate of

[1] 'Journ. d. Pharm.,' xi, p. 562. Erdmann and Marchand, 'Journ. für Pract. Chem.,' xiii, p. 111. Brunner, 'Ann. d. Chem. und Pharm.,' xxxi, p. 195.

soda (made of three parts of water and one part of crystallized carbonate of soda), and a pinch of basic nitrate of bismuth is added, and the mixture heated to ebullition, the bismuth becomes gray or blackish from the formation of suboxyde of, or metallic, bismuth. If the process be watched attentively, the yellow oxyde of bismuth is discovered as a transition stage. This test is very easy and delicate, and very true in its application to urine, as none of the ordinary normal or pathological constituents of that fluid have the same influence upon the bismuth salt.[1]

On adding to a solution of grape-sugar some caustic potash, and afterwards, by drops, a dilute solution of sulphate of copper, a dark fluid is formed; and, after a few seconds, a precipitate of hydrated suboxyde of copper ensues, even without raising the temperature of the mixture. On heating the mixture to ebullition, a discoloration of the fluid takes place, and all the copper is precipitated in the form of red suboxyde. A fluid containing one hundred thousandth part of its own weight of grape-sugar, when treated with caustic potash and a few drops of solution of sulphate of copper, yet yields a perceptible red precipitate on boiling. If a fluid contains one millionth part of its own weight of grape-sugar, the test is sufficiently delicate to give the fluid a reddish appearance, provided the fluid be in a thick layer (two or three inches in diameter) and properly illuminated.

The tests by Reich and Maumené are common to cane and grape-sugar; while the test with copper (Trommer's) excludes cane-sugar. The tests with caustic potash, bismuth, copper, and the analysis by optical means, furnish all evidence to be desired for analytical and practical purposes.

Grape-sugar, when brought into contact with ferments, undergoes a series of decompositions, of which the following are the most important and best known:

Vinous fermentation.—A faintly acid solution of grape-sugar, when brought into contact with yeast, or putrefying matter, yields alcohol and carbonic acid.

$$C_{12}H_{12}O_{12} = 2(C_4H_6O_2) + 4CO_2.$$

This test was formerly used for determining the quantity of sugar in solution, diabetic urine, &c. A known quantity of solution was mixed with yeast, and the carbonic acid, after passing through sulphuric acid for the purpose of retaining all the water, was allowed to escape. From the loss of weight in the apparatus, the amount of carbonic acid and its equivalent of sugar was determined by calcula-

[1] Henle and Pfeufer, 'Zeitschr. für Pract. Med.,' 1857.

tion. The experiment, however, requires too much time (three days) and too much attention, and the repeated use of the balance; and, if applied to urine, becomes unsafe, as other matters besides sugar are decomposed under the influence of ferment, so that it has been entirely abandoned.

Lactic acid fermentation.—In an alkaline solution and in contact with putrefying matters, grape-sugar is transformed into lactic acid, which possesses the same elementary composition as grape-sugar. Lactic acid may be further transformed into butyric acid, according to the following diagram:

$$C_{12}H_{12}O_{12} = C_8H_8O_4 + 4CO_2 + 4H.$$

It is possible that the discoveries of lactic and butyric acid in urine by some sporadic observers, were due to their production by ferments from sugar or other fermentable substances.

Viscous fermentation. — Under certain not well defined conditions, sugar is transformed into mannite and a viscous gum-like substance. This fermentation may be sometimes produced in diabetic urine by allowing it to stand in a stoppered bottle.

Quantitative determination of Grape-sugar by volumetrical analysis.[1]

This analysis is based upon Trommer's copper-test. An alkaline solution of oxyde of copper is decomposed by grape-sugar, as already described. The oxyde of copper is, however, only perfectly soluble in alkaline fluids containing a fixed organic acid, such as citric or tartaric acid. Such an acid is therefore a regular ingredient of the solution to be described.

Barreswill[2] was the first to use the copper-test for the quantitative determination of grape-sugar. His method was afterwards improved and extended by Fehling,[3] who determined the proportions between copper-salt and grape-sugar, and gave a prescription for a test-fluid, the composition of which seems to be the most suitable up to the present time, notwithstanding the many attempts at improvements which at different times have been made.

By adding a solution of grape-sugar of known strength to a solution of copper of known strength, until the latter was perfectly decomposed, Fehling found that one equivalent of grape-sugar decomposed 10 equivalents of sulphate of copper, or 180 parts of grape-sugar decomposed 1246·8 parts of sul-

[1] Mohr, 'Titrirmethode,' i, p. 205.
[2] 'Ann. d. Chem. und Pharm.,' Bd. lxxii, p. 106.
[3] 'Journ. d. Pharm.,' vi, p. 301.

phate of copper, or 5 parts of grape-sugar decomposed 34·64 parts of sulphate of copper. If, therefore, 34·64 grammes of sulphate of copper are dissolved in one litre of fluid, 100 c.c. of the latter correspond to 0·5 grammes of grape-sugar. The fluid is prepared in the following manner:

Preparation of test-fluid.—34·64 grammes of pure air-dry sulphate of copper are dissolved in 160 grammes of distilled water. In the one-litre mixing-bottle 150 grammes of neutral tartrate of potash are dissolved in from 600 to 700 c.c. of solution of caustic soda of 1·12 specific gravity: to this the solution of copper is added gradually, and then the bottle is filled up to the litre mark with distilled water.

Application of the fluid.—A known bulk (10 c.c.) of this fluid (of which 100 c.c., when completely reduced, indicate the oxydation of 0·5 grammes of grape-sugar) is put into a capacious china dish, diluted with a large quantity of water, say four times its bulk, and heated to nearly the boiling point. The urine, which has been diluted with ten or twenty times its volume of water, according to the quantity of sugar which in probability is contained in it, and which should not be less than 0·5, nor more than 1 per cent., and has been filled into the burette, is now allowed to flow into the boiling solution of copper. The suboxyde of copper is at once precipitated, and its red colour imparts to the blue fluid a greenish-brown colour, which gradually, under the cautious addition of more sugar-solution, is transformed into a burning red. At the same time the blue colour of the mixture is fast disappearing, and when it has become quite colourless the reaction is completed. Towards the end of the reaction great care is required not to add an excess of the diabetic urine, as the analysis would thereby become useless. The addition of urine in drops may be continued as long as it produces a light-yellow cloud on the surface of the fluid. This is newly formed hydrate of the suboxyde, which becomes at once transformed into the red variety, free of water. As soon as the urine on being dropped in ceases to produce a fresh cloud, it is necessary to remove the flame from underneath the dish, and to allow the precipitate to deposit. If the fluid appears quite colourless, the reaction is completed. If, however, the slightest blue tinge remains visible on the white china dish, then the addition of another drop of the urine, and another ebullition, is almost sure to remove it; and so on until the completion of the reaction is attained. The amount of urine which corresponds to the known amount of copper solution of known strength is now read off the scale on the burette, and from it the amount of sugar in the urine used, and that

secreted within a certain period of time, is now ascertained by calculation. If therefore 10 c.c. of the copper solution have been taken, the amount of urine used for the reduction contains 0·05 grammes of grape-sugar.

By this method it is possible to execute an analysis in about fifteen minutes, and more quickly if several analyses be made in succession.

The copper solution becomes decomposed by keeping, a part of the tartaric acid being transformed into racemic acid, which also reduces the oxyde of copper on boiling. If therefore the graduated test-fluid has been kept for some time, it is necessary to ascertain whether it has formed a precipitate in the bottle, and whether it is precipitated by boiling. In the former case it may be cleared by filtration, and afterwards regraduated upon a solution of sugar of known strength. If, however, it forms a precipitate on boiling, it is spoiled, and must be thrown away.

Kletzinsky[1] proposes to substitute, for tartaric acid, glycerine, which, according to him, makes the fluid keep longer. As a crystallization of sulphate of potash from the solution is unavoidable, according to his prescription, the test-fluid cannot at once be prepared for quantitative purposes, and offers therefore disadvantages which more than counterbalance the advantages.

Optical Saccharimetry.

A most accurate method of ascertaining the presence and quantity of sugar in solutions has been based by Biot[2] upon the optical properties of these solutions. Cane-sugar and grape-sugar divert towards the right the plane of polarization. If therefore a fluid contains either of these descriptions of sugar, and no other active substance, the quantity of sugar in solution may be accurately ascertained by measuring the degree of diversion which the fluid exerts upon the plane of polarization. For this experiment a very convenient apparatus has been constructed by the mechanical artist, M. Soleil,[3] in Paris, and a very similar one by Mitscherlich,[4] in Berlin. Both are very much used in the respective countries of their inventors, and will undoubtedly become more generally used for the saccharimetry of the urine, as soon as the price of

[1] 'Wien. Zeitschr.,' x, 2.

[2] 'Compt. rend.,' xv, pp. 619, 694; xvii, p. 755.

[3] The experiments for Soleil's apparatus were made by Clerget, who published several papers. *Vide* 'Compt. rend.,' xxiii, xxxii.

[4] 'Lehrb., d. Chem.,' 4th edit., Bd. i, p. 360.

the instrument shall have put it within the reach of everybody.

The use of the polarizing apparatus may be described here after Mitscherlich.

Before proceeding to determine the amount of sugar in a solution of grape-sugar (urine), it is necessary to make sure that the zero point of the apparatus be accurately determined. This is the case when, after the empty tube has been put in its place, and the light of a lamp has been placed an inch or two behind the posterior aperture of the apparatus, and in the axis of the tube, the posterior aperture appears perfectly dark—almost black—to the eye looking in at the anterior aperture. If the hand which moves upon the graduated circle surrounding the anterior aperture is now being moved from zero towards the right or left hand side, the posterior aperture becomes gradually lighted up, until at last it becomes quite a bright circle, the light being most intense when the hand shows 90° on the graduated disc, either on the right or left. On going back again from 90° to zero, the observer will find that the posterior aperture, even though the hand be exactly at zero, is faintly lighted up at two opposite margins, and that the diameter of the circle, which runs parallel with the faintly illuminated margins, is the darkest part of the circle or spectrum, and appears intensely black. This blackest part must exactly divide the spectrum into two equal halves, when the hand indicates zero: the apparatus is then ready for use.

If the tube is now filled with a colourless solution of sugar (diabetic urine is mostly quite colourless, and scarcely ever requires treatment with animal charcoal, but mostly filtration), and put into its former place, the spectrum, which was black before, will now appear illuminated in colours, which, when the hand is again turned from zero to 90°, appear in the following succession: yellow, green, blue, violet, red.

The formerly darkest line of the spectrum corresponds now to the line where the violet and blue colour change into each other, and this line is the zero point for quantitative determinations.

A little practice will soon accustom the eye to determine the point at which the spectrum is divided into two equal halves, of which the one is violet, the other blue, and each colour of about the same intensity.

In case it is necessary to turn the hand towards the right, in order to obtain the above succession of colours, then the fluid is said to divert towards the right the plane of polarization, or turn towards the right a pencil of polarized light; this effect is obtained by a solution of grape-sugar or saccha-

rine urine. In the contrary case, the plane of polarization is said to be diverted towards the left.

The angle in which the hand has to be turned is proportionate to the concentration of the fluid and the length of the column through which the polarized light has to pass, viz., to the length of the tube in the apparatus. In Mitscherlich's apparatus, the length of the tube is 200 millimètres ($7\frac{3}{4}$ English inches).

Supposing a fluid of a certain concentration to be put into the tube, the hand standing at zero, and that in order to see one half of the spectrum violet, the other red, a rotation of the hand of 40° be required, then the same fluid in a tube of half the length would turn the hand only to 20°.

On the other hand, if 15 grammes of sugar be dissolved in any certain quantity of water, and the solution be poured into the tube so as to fill it; and if then the hand be turned until the colours of the zero point appear—for which we will assume a rotation of 15° to be requisite—then a solution of 30 grammes of sugar in the same quantity of water as the 15 grammes were dissolved in, when filled into the tube, will require exactly double the rotation, namely 30°, for the test-colours to appear.

It has been found by accurate experiments that 15 grammes of pure and dry grape-sugar, when dissolved in so much water that the solution amounts to exactly 50 cubic centimètres, will make a fluid, a column of which, 200 millimètres in length, will turn the plane of polarization 40° towards the right.

Upon the basis of this experiment it is easy to determine the amount of sugar in any fluid. Supposing the above tube, full of bright, faintly yellow diabetic urine, requires a movement of the hand from 0 to 30, then

$$40 : 30 = 15 : x$$

$$x = \frac{30 \times 15}{40} = 11{\cdot}25$$

which, in other words, means that, with a rotation of 30°, there are 11·25 grammes of sugar contained in 50 cubic centimètres of this diabetic urine. Another equation shows the amount of sugar contained in the urine passed during a certain length of time.

It is not possible to approximatively determine the amount

of sugar from the specific gravity of urine, as has been shown by Dr. Bence Jones.[1]

Pathological indications of Sugar in Urine.

It has been stated that the urine of healthy persons occasionally contains sugar; it has also been stated that the urine of pregnant and suckling women is always impregnated with sugar, in the latter in a direct proportion to the amount of milk secreted by the breasts. These assertions theoretically, that is, viewing them from the aggregate of known facts, seem to be deserving of but little confidence. It is certainly incumbent upon the authors who made those assertions to prove that the substance which in their experiments gave the reaction of sugar, was really grape-sugar and nothing else.

In the course of some cases of acute disease, the temporary appearance of small quantities of sugar has occasionally been observed. In these cases, also, doubt has not been perfectly excluded, so that a pathological explanation cannot be attempted.

When the urine contains large quantities of sugar for a length of time, there is reason to believe that diabetes mellitus is present. The diagnosis is ensured by collateral symptoms of this disease, which as yet has eluded the most vigilant researches of physiologists. Some of these symptoms are, a large amount of urine of high specific gravity, great thirst, emaciation, dry skin, the appearance of boils, gangrene of parts most remote from the circulating centres, and tubercular consumption of the lungs.[2]

When grape-sugar in concentrated solution is injected into the veins of animals,[3] a part reappears in the urine after a short time. When, however, the solution is dilute, although the same quantity of sugar be injected in such solution as in the concentrated one, no sugar appears in the urine afterwards.

If the liver be freed from blood by washing the vessels with water, an extract made of a part of such liver will yield no sugar. If, then, the liver be allowed to remain exposed to the air for a variable length of time, sugar may be de-

[1] 'Med. Times and Gaz.,' February 4, 1854.

[2] For a review of the present state of the doctrine of diabetes mellitus, see Dr. Garrod's Gulstonian Lectures on Diabetes and Saccharine Conditions of the Urine, 'British Med. Journ.,' April, May, and June, 1857.

[3] C. F. Kersting, 'Saccharum sanguine receptum in urinam transire probatur experimentis,' Missenæ, 1845, viii, p. 12.

tected in the liver. It must have formed from substances in the liver, under the influence of oxygen, as in an atmosphere of hydrogen no sugar is formed. The substance found in the liver by M. Cl. Bernard, and capable of transformation into sugar, is a body nearly allied to dextrine, as has been confirmed by Pelouze.

The observation of M. Cl. Bernard, that the liver of carnivorous animals always contains sugar, does not prove that sugar is formed from albuminous substances. The meat and flesh eaten by carnivora contains *inosite*, which has the same elementary composition as grape-sugar, and tastes sweet, and is only different by its form of crystallization, greater amount of water of crystallization (4HO), and a few tests and reactions. This body might possibly be transformed into grape-sugar. It has long since been known that the milk of carnivora contains sugar proper to milk. This possibly may be derived from the inosite of flesh.

There is no foundation for the opinion of M. Mialhe, that grape-sugar, physiologically, is oxydized by the mediation of the bicarbonates of the alkalies, and that in diabetes it may be assimilated by means of these salts.

Some authors make a difference between diabetic sugar from animals and grape-sugar from plants, and assign to them different bearings in the economy. This idea, which seems to have emanated from some experiments with substances of a doubtful nature, is not supported by such evidence as can be considered sufficient by the present demands of chemistry.

The quantity of sugar in the urine of diabetic patients is diminished, or sugar is altogether absent for a short time, under the influence of the following circumstances:

Total abstinence from food.—Hence the urine in the morning is sometimes free from sugar.

Perfect rest in bed.—Sugar becomes less in quantity and disappears for a day or two. It reappears as before on the patient taking exercise.

Meat diet has the most important influence upon the quantity of sugar, which becomes very much smaller. It is the most important palliative in diabetes.

The remarkable experiment by M. Bernard, in which a wound inflicted upon the bottom of the third ventricle of the brain of dogs, causes sugar to appear in the blood and urine of the animal in a very short time, remains unexplained.

CHAPTER XXXVI.

ACETONE.

Elements: $C_6H_6O_2 = C_4H_3O_2 \atop C_2H_3$		
	Carbon . . .	62·1
	Hydrogen . .	10·3
	Oxygen . . .	27·6
		100·0

Mode of obtaining Acetone.

Acetone is produced by the dry distillation of acetates, particularly the salts of lime, baryta, magnesia or lead, or by exposing acetic acid to red heat. It is further one of the products of dry distillation of sugar, tartaric acid, and other bodies, and as such occurs in the common pyroligneous or pyroacetic spirits.

Physical and Chemical Properties.

Acetone is a colourless thin liquid of 0·814 sp. gr. at 0° C., and boils at 56° C. It is soluble in water, alcohol and ether, and may be mixed with them in any proportion. Like alcohol, it dissolves many substances which are insoluble in water, such as resins or pigments. In contact with the hydrate of an alkali and oxygen it becomes brown, and transforms into a resinous substance. On passing the vapours of acetone over heated potassa lime, hydrogen is evolved, acetate and formiate of potassa remaining.

Acetone in the Urine of diabetic patients.[1]

The urine of diabetic patients has a peculiar odour, which has been noticed by most authors on the subject of diabetes. Thus Hodges [2] describes the odour of diabetic urine as that of sour milk, Corneliani as that of violets. Th. Hodgkin [3] remarks that glasses which have during a longer time served for the purpose of determining the specific gravity of diabetic urine, evolve a distinct odour of musk. The same odoriferous substance occurs in other excretions of these patients.

[1] Petters, Untersuchungen über die Honigharnruhr, 'Vierteljahrschrift für die Pract. Heilkunde,' Prag, 1857, vol. iii, p. 81.

[2] 'London, Med. Gaz.,' 1843.

[3] 'Assoc. Med. Journ.,' 1854, No. 93.

It was noticed by Hodgkin in the fæces, containing little colouring matter of bile. Rother[1] found that the body of a diabetic patient, who had been treated with creosote, smelled of vinegar. The breath of diabetic patients is compared, by Brand,[2] to the smell of apples, and to the breath of persons to whom pure chloroform has been administered. Other authors observed the odour of new hay; and Berndt found the breath of a patient treated with creosote to give first the odour of horses' urine (from the creosote or carbolic acid), and afterwards that of young beer. Petters himself found the odour very peculiar, a mixture of sweet and acid, and compares it, in a concentrated form, to the odour of a mixture of chloroform and acetic ether or aldehyde; when dilute, however, as it always is in the exhalations, he found it more like that of very dilute ammonia,—under all circumstances, however, so peculiar, as frequently to lead the physician to the diagnosis of diabetes. Petters also found that the urine of persons suffering from measles or scarlatina evolved the same odour.

It appears that Dr. Lerch, Director of the Institute for Animal Chemistry at Prague, suggested to Dr. Petters the probability of the odoriferous body in the excretions of diabetic patients being acetone. The latter author succeeded in establishing the presence of acetone in the urine, blood, and most parts of the body of a patient, of whose case the following is a brief outline.

A Jewess, thirty years old, shopwoman, was admitted into the Prague Hospital. She had undergone much privation, and consequent depression of mind, during the last eighteen years. Latterly she had been treated as an out-patient for constipation. Five weeks before admission she was suddenly attacked by violent pain in her stomach, and repeated vomiting. The bowels had been confined during six days. She was relieved by a purgative, and returned a week afterwards, complaining of continued great thirst. She also admitted to pass urine more frequently and in larger quantities. Dr. Grün established the diagnosis of diabetes by the discovery of sugar in her urine. The symptoms now continued to increase in intensity, the pain in the stomach and vomiting returned, and she at last consented to be received into the hospital.

On her arrival she vomited. Her tongue was found a little moist; the saliva had an acid reaction. The breath

[1] 'Preuss. Ver. Zeitg.,' 1844, No. 9.
[2] 'Deutsche Klinik,' 1850, No. 6.

had a strong spirituous odour. The examination of the systems of respiration and circulation revealed no lesion. The urine was straw-yellow, of a strongly acid reaction, and 1·0315 specific gravity, contained 4 per cent. of sugar, much urea, and scarcely a trace of uric acid. Besides the strong peculiar odour, it offered no peculiarities. The patient herself complained of weakness, thirst, and pain in her stomach.

On the morning after her admission she was in a sort of narcotized condition, and gave off a spirituous odour similar to that of chloroform, which was so intense, that after a little time it became perceptible in the whole ward, and was noticed by all other patients. One of the clinical assistants was misled to the opinion that chloroform had been administered to the patient during the night. The patient was almost unconscious, and lay there, the eyes half open, and all muscles relaxed. Her skin was cool (26·4° R., [91·5° F., 33·0° C.,] in the axilla; 26·0° R. in the mouth), as also the tongue, and the strongly smelling breath. The face was slightly flushed, the eyes surrounded by a halo, the looks fixed. The patient was like a person half under the influence of chloroform; her extremities dropped like paralysed on being raised, and a few words could be elicited when her consciousness had been made to return for a moment by questioning with a loud voice. She had a small pulse of 92 beats per minute. The abdomen was meteoristic. As she had passed no water since the night, the catheter was applied, and a pound of urine was withdrawn, which was pale yellow, contained sugar (specific gravity 1·027), and much of the odoriferous principle. Including this quantity, the patient had only passed ninety-three fluid ounces of urine during the last twenty-four hours; the secretion of urine then ceased entirely. The meteoristic swelling of the abdomen increased, she complained of much pain in the stomach in moments of returning consciousness, and died next morning, thirty hours after the beginning of this extraordinary condition.

The post-mortem examination revealed no particular lesion in any organ except the intestinal canal, which was very much distended with gas, the inner surface covered with a thick, grayish-white mucous layer, and the inner membranes very much congested. The contents of the stomach were exactly like those of a fermenting distiller's butt, and consisted of a brownish, flaky mixture, which evolved a spirituous pricking odour, and also the peculiar odour of the other secretions. It had an acid reaction, and gave the tests for grape-sugar. The microscope revealed some fibres

of flesh, some starch-corpuscles in a disintegrating condition, and numerous yeast-cells.

The urine on distillation yielded an alkaline, clear fluid, which had the odour of ammonia, carbolic acid, and an empyreumatic spirituous substance; and after neutralization with dilute sulphuric acid and repeated rectification, allowed the characteristic odour to appear more freely. The distillate was again rectified over chloride of sodium, and afterwards once more for itself in the water-bath, when a colourless, clear fluid, strongly refracting light, of neutral reaction and biting taste, was obtained, which was easily inflammable, and burned with a bright, strongly lighting flame. Though its odour was very much like that of aldehyde, yet it could not be that substance, as it had a neutral reaction. There was therefore only the possibility of its being either methyl-alcohol or acetone left over. Methyl-alcohol was excluded, as the fluid became brown when mixed with sulphuric acid. As caustic potash produced a brown resinous body in the fluid, and solutions of oxyde of silver caused no reduction in it, it could be nothing else but acetone ($C_6H_6O_2$).

The residue of distillation contained nothing besides carbolic acid, which, according to Petters (p. 89) and Städeler, is present in every urine.

The blood had a strong odour of acetone. But its quantity was not sufficient to isolate that substance. It contained sugar, and was faintly alkaline. The watery extract of the lungs, subject to distillation, yielded a neutral distillate, smelling of newly baked bread, which, after repeated rectification, under addition of sulphuric acid, and afterwards of chloride of sodium, lastly after distillation from the water-bath, gave drops which strongly smelled of acetone, yielded the above reactions, and were combustible.

The presence of acetone in the urine and blood was therefore established, and it is most probable that to the anæsthetic effect of this substance, diffused through the whole system as it was, the comatose condition and fatal end of this case were due.

The contents of the stomach did not yield acetone, but alcohol seemed to be present. The mucus of the glandular surface of the stomach, after the latter had been washed with distilled water, was found to possess the property of transforming starch into sugar and gum, and sugar into alcohol and carbonic acid. The contents of the stomach possessed the same power, which is not possessed by normal gastric juice. The influence of saliva was carefully excluded by Dr. Petters, in the experiment with the mucus from the immediate glandular membrane of the stomach.

CHAPTER XXXVII.

INOSITE.

Elements: $C_{12}H_{12}O_{12} + 4HO$.	Carbon . . .	40·00
	Hydrogen . .	6·66
	Oxygen . . .	53·34
		100·00

This hydrocarbon was, in 1850, discovered by Scherer,[1] in the mother-liquor of creatine, obtained from the juice of the muscle of the heart. It was afterwards investigated by Cloëtta,[2] who found it in the parenchyme of most organs, the lungs, spleen, kidneys, and also in the urine of a patient affected by Bright's disease. Vohl[3] found a substance in the unripe fruit of *Phaseolus vulgaris*, which he at first termed phaseomannite, the identity of which with inosite he afterwards demonstrated.

Mode of obtaining Inosite.

When the inspissated juice of flesh (or of the organs mentioned), from which creatine has been obtained, is mixed with strong spirits of wine, it becomes turbid. When put aside, potash salts begin to crystallize, but on further addition of spirits of wine, inosite crystallizes; the mother-liquor is now poured off, the crystals are separated mechanically, and by

[1] 'Ann. d. Chem. und Pharm.' Bd. lxxiii, p. 322; lxxxi, p. 375.
[2] 'Ann. d. Chem. und Pharm.,' Bd. xcix, p. 289. 'Canstatt's Jahresbericht,' über 1856, vol. i, p. 180.
[3] Ibid.

means of a little warm water, which dissolves inosite quicker than the alkaline salts, and deposits it on cooling in crystals.

Physical and Chemical Properties.

Inosite crystallizes in the clinorhombic system, the typical form being most probably a clinorectangular prism. The crystals mostly group together; more rarely they are single, and then become sometimes two eighths to three eighths of an inch long. When exposed to the air they decay by losing water of crystallization. They taste very sweet, are easily soluble in water, little soluble in strong spirits of wine, insoluble in alcohol or ether. From the solution in boiling spirits of wine almost the whole of the inosite crystallizes on cooling in small glistening particles, which are very much like cholesterine.

Inosite is not changed by boiling with dilute sulphuric or hydrochloric acid, or with caustic alkalies.

When heated above 210° C. (410° F.), it fuses into a clear fluid, which, when cooled down rapidly, crystallizes in needles, but, when allowed to cool slowly, becomes a horn-like amorphous mass. When exposed to a stronger heat, inosite burns with a lighting flame, without leaving any residue.

A concentrated solution of caustic potash produces no change of colour on boiling with a solution of inosite; no change takes place when heated with potash and sulphate of copper; with bile and sulphuric acid inosite does not yield the reaction of sugar.

Inosite is not capable of undergoing vinous fermentation. But a solution of it treated with cheese and chalk at a temperature of about 40 C. (104° F.) for some length of time, produces lactic and butyric acid.

If a solution of inosite, or a mixture containing inosite, is evaporated in a platinum spoon to near dryness, and the residue moistened with ammonia and some chloride of calcium, and then again cautiously evaporated to dryness, a vivid rosy colour is produced; this reaction admits of the diagnosis of one fiftieth of a grain of inosite.

CHAPTER XXXVIII.

URERYTHRINE OR PURPURINE.

The *elementary composition* of this substance is unknown. It contains above 60 per cent. of carbon, and about 6 per cent. of hydrogen, the rest being made up of oxygen, and a small quantity of nitrogen.

History.

It was first described by Proust as rosacic acid, and believed to constitute the entire bulk of the lateritious deposits. After uric acid had been found in these deposits, Prout assumed purpuric acid, in combination with ammonia (which purpurate of ammonia he erroneously believed to be identical with the murexide of Liebig and Wöhler), to be an admixture to these deposits. The contemporaneous researches of Vogel, Fromherz, Guggert, Duvernoy, G. Bird, Simon, Scherer, Landerer, and Heller seemed to confirm the opinion of Prout as to the acid nature of purpurine, but the inability of chemists to produce salts of this substance with bases militates against that opinion. The most extensive and also the most productive researches on this substance have been made by Heller.[1] But notwithstanding his most lucid description, little attention has been paid to this substance, and this circumstance, and the various names under which it has passed, have produced some confusion regarding its identity. Thus Virchow[2] erroneously believes G. Bird's purpurine to be identical with cyanurine or uroglaucine.

[1] Ueber das Uroërythrin als Bestandtheil des Harns in Krankheiten, Heller's 'Archiv,' vol. vi, p. 361.

[2] Virchow's 'Archiv,' vol. vi, p. 260.

Occurrence.

Urerythrine occurs in fresh urine generally in a dissolved state, and then imparts to the fluid a fiery reddish-yellow, or yellowish-red colour, sometimes mistaken for blood, or the colouring matter of medicines. It adheres to the amorphous deposits of urates, imparting to them the various shades of colours, but not to deposits of earthy phosphates. It was observed by Landerer[1] in the perspiration from the axilla of a fever patient, an occurrence also observed repeatedly by Heller.

Mode of obtaining it pure.

The deposits of urates with urerythrine adhering, whether formed before or after emission, are collected on a filter and washed with water, until a portion, on being burned on platinum foil, no longer evolves the peculiar odour of burned urine. A considerable loss of substance necessarily occurs with this mode of washing, as also with the subsequent washing with alcohol. After this operation the deposit is digested with warm absolute alcohol, which takes up urerythrine, and, after filtration and evaporation at a temperature not exceeding 50° C. (122° F.), leaves it in the form of a red amorphous residue.

If urerythrine occurs in the urine in solution, it can be obtained therefrom by combining it with an artificial precipitate. On adding to the clear urine a little ammonia or carbonate of ammonia, so that it remains faintly acid, and no precipitate of earths occurs, and, after shaking and letting it stand for several hours, adding a few drops of acetic acid and letting it stand again, a pink deposit will form after the lapse of a short time, which is then treated like the spontaneous deposit (Heller).

On dissolving white and pure urate of ammonia in urine, which by its pink or purple colour indicates the presence of purpurine, it is precipitated on cooling, deeply coloured by the purpurine (G. Bird).

Urerythrine can only be obtained from such precipitates, and never by evaporation of the urine.

[1] Buchner's 'Repertorium,' 1st ser., vol. v, p. 235.

Physical and Chemical properties.

Urerythrine is an amorphous, lobster-red substance. When it shows a radiary or granular crystalline arrangement, it is impure. It has a decidedly acid reaction, and thus adds to the acidity of urine. It is soluble in alcohol, water, and ether, little at the ordinary temperature, more at higher temperatures. The solutions are of a pale reddish-yellow colour, which is never saturated. It burns on platinum foil without exhibiting any particular phenomena, and leaves no residue. Its solution in water is precipitated by acetate of lead, by nitrate of suboxyde and protoxyde of mercury, and by salts of baryta; but the precipitates are only loose combinations, and readily yield urerythrine to boiling alcohol. By dilute acids urerythrine is not decomposed. It dissolves in concentrated sulphuric and hydrochloric acids, and thereby undergoes a change. Alkalies impart to it a yellowish colour.

Diagnosis in Urine.

The pink colour of urine, and the production in it of a *light-pink* precipitate by the addition of a great excess of acetate of lead, ensure the diagnosis. The precipitate produced by acetate of lead in urine destitute of urerythrine, respective in normal urine, is *white*, though containing uræmatine. The filtrate from this precipitate by boiling with hydrochloric acid yields the test for uroxanthine (indican). The presence of the same substance is indicated by the filtrate assuming a violet colour when shaken with concentrated sulphuric acid. When ether is shaken with this acid mixture it becomes red from urrhodine (indigo red); and from the blue residue, uroglaucine (indigo blue) may be obtained by boiling with alcohol.

When an excess of uræmatine is present in urine, the precipitate obtained by acetate of lead assumes a clay colour without any admixture of red. An excess of this colouring matter does, therefore, not prevent the pink colour of the precipitate by lead, due to urerythrine, from appearing, in cases where urerythrine is present. The colouring matter of bile stains the lead precipitate intensely yellow, and then it is difficult to prove the presence of urerythrine.

Urine containing urerythrine, when dropped into concentrated hydrochloric acid, assumes a peculiar yellowish-red colour. But if an excess of uroxanthine (indican) be present, the violet colour produced thereby covers the colour of urerythrine.

For experiment, urine from a case of acute rheumatism is best suited.

The deposits may also be examined for urerythrine by dissolving them in water and treating the solution with acetate of lead. From this precipitate a purer urerythrine with a less considerable loss, is mostly obtained.

In order to ensure the diagnosis of the presence of urerythrine, it is necessary to bear in mind that deposits may be coloured red by the following substances :

1. Only in strongly alkaline urine by
   (*a.*) Urrhodine (colour more violet).
   (*b.*) Precipitates of sennine or rheine.
2. In acid or alkaline urine by
   (*a.*) Urerythrine.
   (*b.*) Blood-corpuscles.

The following reactions ensure the diagnosis of these substances : The deposit, from which the fluid has been removed by decantation or filtration, is shaken with ether, which assumes a violet-red colour when urrhodine is present, and dissolves the entire amount of this substance.

A part of the deposit is acidulated with sulphuric, hydrochloric, or acetic acid ; if the colour is changed into citron yellow, and by the addition of ammonia back again into red, sennine or rheine are indicated.

The presence of albumen or coagulating hæmatoglobuline ensures the diagnosis of blood.

Pathology of Urerythrine.

As urerythrine does not occur in healthy urine, its occurrence is a symptom of disease. It occurs more frequently than any other abnormal substance ; but, notwithstanding, its exact bearing has not as yet been ascertained.

When organic medicines and compounds, drastics, mineral salts, and solvents cause diseases of the intestinal canal or the kidneys, urerythrine does not appear in the urine. Tincture of cantharides, for example, when given in such doses as to cause albumen and blood to appear in the urine, did not make urerythrine appear in the urine. Its occurrence is never observed to accompany diseases of the kidneys.

The case is different, however, with metallic salts ; the compounds of lead, copper, mercury, arsenic, antimony, and others, even when given or ingested accidentally, even in small doses, soon cause urerythrine to appear in the urine.

When taken in large doses, so as to exert poisonous effects, they cause the appearance of large quantities of urerythrine in the urine. As urerythrine frequently appears in the urine in consequence of or in connection with diseases of the liver, independent of metallic poisons, and as the latter mostly exert their first poisonous action in the liver, it becomes likely that the liver is in both cases the place where this substance is produced.

When urerythrine is present in urine, uræmatine is mostly present in larger quantities, as are also urea and uric acid. The quantities of inorganic salts are variable. Any deposits that may occur assume a pink colour.

Uroxanthine is changing, relatively to urerythrine. In urine from cases of acute rheumatism, the quantities of these substances seem to stand in an inverse proportion to each other.

Diseases in which Urerythrine most commonly occurs in the Urine.

1. *Acute rheumatism.*—In this disease it is almost constantly present, but its quantity is often changing periodically. The earthy phosphates appear to be augmented.

Pericarditis.—When this disease sets in, the earthy phosphates mostly undergo a rapid diminution, and during twelve hours may fall from the highest to the lowest figure. Then follows sinking of the chlorides, until they disappear entirely, and some albumen mostly makes its appearance. At this stage the quantity of urerythrine present is very large.

Pneumonia, pleuritis, peritonitis, and acute morbus Brightii, when complicated with acute rheumatism, show the same course of urerythrine and other ingredients of the urine.

2. *Certain diseases of the liver,* such as hypertrophy, induration, granular liver, are accompanied by the largest amount of urerythrine that ever occurs in the urine. Ascites, in consequence of liver disease, gives a large amount. In these cases the quantity of the phosphates is normal, and the amount of uræmatine is mostly increased. The colouring matter of bile is only present in cases which are complicated by obstruction of the gall-duct.

3. *Lead-colic and metallic poisoning.*—In these cases the urine is similar to that in diseases of the liver, but never contains the constituents of bile. Lead and copper, when causing disease, are *always* to be detected in the urine; the other metals in many cases. Earthy phosphates are variable.

4. *Intermittent fever.*—The phosphates are variable; urea is mostly diminished, except during paroxysms.

5. *Diseases of the brain.*—In acute cases of arachnitis and meningitis, the amount of urerythrine in the urine is always increased. The quantities of earthy phosphates and of urea are increased. There is little ammonia and albumen. In chronic diseases of the brain, such as hydrocephalus and tubercles, urerythrine is often present. Typhus also makes urerythrine appear in the urine, together with an excess of earthy phosphates, particularly when brain-symptoms are prevalent.

CHAPTER XXXIX.

UROXANTHINE, OR INDICAN.

UROGLAUCINE, OR INDIGO BLUE. URRHODINE, OR INDIGO RED.

History.

PERHAPS the earliest record of the occurrence in urine of a blue colouring matter is that by Janus Plancus.[1] The first chemical description of a blue or violet colouring matter occurring in urine was given by Braconnot,[2] who termed it cyanourine, and though he found that it had some similarity to indigo, believed it to be a separate organic base. There are several cases on record, where a substance corresponding in character to cyanourine was discovered in urine. The first reliable observation, however, of the occurrence of *indigo* in urine is by Prout.[3] The same substance afterwards also occurred to other observers.

Heller[4] succeeded in extracting from urine a yellow substance, uroxanthine, which by treatment with acids at a higher temperature he could divide into a blue colouring substance, uroglaucine, and a red pigment, urrhodine. Cyanourine was proved by him to have been a mixture of these two bodies. Kletzinsky[5] showed the identity of uroglaucine with indigo blue, and of urrhodine with indigo red. Virchow[6] confirmed the observations of Heller, which had been ignored, doubted, or misrepresented[7] by many authors.

[1] 'Commentarii Instituti Bononiensis,' ad. ann. 1767.
[2] 'Ann. d. Chim. et de Phys.,' xxix, p. 252.
[3] 'On Stomach and Urinary Diseases,' 3d edit., p. xcvi.
[4] Heller's 'Archiv,' 1845.
[5] Ibid., vol. vi, p. 414.
[6] Virchow's 'Archiv,' vol. vi, p. 259.
[7] Heller's observations have been *ignored* by many authors. The latest among them is Neubauer, who, besides his own case of blue matter obtained from urine, takes no notice of hundreds of similar instances observed before him.

Heller's observations have been *doubted* even by such chemists as Robin and

He also found that, when much indigo-producing substance was present, the urine gave the copper-test for sugar. He also obtained uroglaucine from every concentrated urine. Latterly Schunck[1] found indican, identical with Heller's uroxanthine, in urine, which indican he had before discovered to be the chromogen contained in indigoferous

Verdeil. On this indifference Virchow justly remarks in his article quoted above; these authors might have avoided inflicting a great injustice upon Heller by their groundless objections, if they had chosen to satisfy themselves by the experiment. The same applies to Dr. G. Bird, who, in p. 331, expresses himself as follows: "Dr. Heller has lately stated that these curious deposits are merely metamorphosed uroxanthin or yellow colouring matter of urine, and has applied the name of uroglaucine to the blue pigment. He assumes, therefore, that it is identical with what I have described as purpurine, produced by the action of hydrochloric acid upon previously warmed urine. The statements of Heller, however, are mixed up with certain inaccuracies, and can hardly be admitted without more minute investigation." As Hassall, in p. 308 of his last paper in the 'Philosophical Transactions,' has similarly *misrepresented* Heller, I may here correct both errors at once. Heller never stated that uroxanthine was the ordinary, normal, or yellow colouring matter of urine. To that, he applied the name of urophæine. From 1845 to 1857, Heller has always asserted that there is scarcely a trace of uroxanthine in healthy urine, and that its occurrence in urine in any appreciable quantity was strictly pathological. Heller never assumed uroglaucine to be identical with Dr. G. Bird's purpurine; to this substance he applied the name of uroërythrine, and described its properties with the most minute details. He also maintained that uroërythrine was destroyed during the evaporation of urine, while Dr. G. Bird obtained his purpurine, not only from the deposits of urates, but also by extracting with alcohol the residue of the evaporation of urine. Urerythrine and purpurine are consequently only identical, so far as they occur as the colouring principles of deposits of urates. The production of purpurine by the influence of hydrochloric acid upon the normal colouring matter of urine, is Dr. Bird's exclusive property. The names of urophæine and urerythrine, Heller has adopted from Simon. Heller is therefore, in p. 115 of Dr. Bird's work, misrepresented as having applied the name of urrhodine to what Simon had called urerythrine, after Dr. Bird had given it the name of purpurine. Urrhodine may turn out to be identical with purpurine and urerythrine, but Heller kept them distinct. Urerythrine he found ready in the urine; urrhodine he produced from a substance, which he was the first to discover, uroxanthine. The crystals of uroglaucine described by Heller, and stated by Dr. G. Bird (p. 114) and Messrs. Robin and Verdeil, to be uric acid merely tinted by changed colouring matter, are really crystals of indigo, as Virchow also confirms, and as the most trivial experiment can confirm. Uric acid crystals could never be obtained in the manner in which Heller obtained his crystals of uroglaucine.

At p. 115 of the edition of Dr. G. Bird's work by Dr. Birkett, there is, indeed, a foot-note, in which uroxanthine, uroglaucine, and urrhodine are mentioned in succession, and in which it is stated that the experiments regarding uroxanthine and urrhodine were so incomplete as not to admit of any conclusion. Three years ago these experiments were so complete, that the latest discoveries of Dr. Schunck have fully borne them out. It is surprising that on the same page the clearest proved facts should be doubted, where such coin as "sulphur extractive" is taken for good cash.

I hope that my remarks will contribute to put a stop to so general a confusion, in which even Virchow participated, by believing the purpurine of Dr. Bird and rosacic acid of Proust (not Prout) to be identical with cyanourine and uroglaucine.

[1] 'Phil. Mag.,' S. 4, vol. xiv, No. 93, Oct., 1857, p. 288.

plants, and which, under the influence of acids or ferments, yields indigo blue, a peculiar kind of sugar, and a small quantity of other products. Schunck found indican in almost every urine; and his observations strongly support the opinion that indican is a normal ingredient of human urine and the urine of many animals.

UROXANTHINE, OR INDICAN.

The chromogen of indigoferous plants is a peculiar colourless substance, which has been obtained (from *Isatis tinctoria* for example) by extraction with alcohol, precipitation of the extract by acetate of lead, and decomposition of the precipitate, first by carbonic acid, afterwards by hydrothion, when it remained in solution in the filtrate. On evaporation there remains a gum-like mass, indican, which, when boiled with acids, yields indigo blue, a peculiar description of sugar, and a small quantity of other matters.

This indican had long been discovered and described by Heller, who did, however, not observe that sugar was one of the products of its decomposition by acids; but, having discovered the generation of indigo blue and indigo red under the influence of these agents, he shared the error, then almost general, of uroxanthine and the chromogen of the indigoferous plants being white or reduced indigo.

Heller precipitated urine by acetate of lead, and evaporated the filtrate to dryness at a low temperature. He then extracted it with ether, which after evaporation left uroxanthine.

Schunck, having ascertained the peculiar nature of indican, proceeded to obtain evidence of its presence in urine, in the following manner:

When muriatic or sulphuric acid is added to urine, the mixture on being heated becomes brown, and begins to deposit dark-brown flocks, which increase in quantity when the heating is continued. When these flocks are filtered off, washed, and dried, they form a compact, dark-brown mass, from which cold alcohol extracts a resinous matter, leaving undissolved a brown powder, which dissolves, however, in a boiling mixture of alcohol and ammonia. This powder resembles, but is not, indifuscine, one of the products of the decomposition of indican.

If the liquid filtered from these flocks be mixed with a salt of oxyde of copper and an excess of caustic soda, it becomes greenish, and if after being filtered it be heated for

some time, it gradually deposits a tolerably large quantity of suboxyde of copper, which is a proof of the presence of sugar. That the latter has been formed during the process, and did not pre-exist, may be ascertained by previously heating a portion of the urine with a salt of copper and caustic soda, before treating the remainder of it with acid. Samples of urine, which, when tried in this way, afforded very doubtful or no indications of their containing sugar, were found, after being boiled with acid, then filtered and made alkaline, to reduce oxyde of copper in a very marked manner. This reaction proves, that there is contained in urine some body, which by decomposition with acids yields sugar, the brown flocks precipitated at the same time being probably the substance with which the sugar was originally associated in the form of a copulated compound. Schunck found that the composition of these flocks was expressed by the formula $C_{14}H_7NO_4$, which is also that of anthranilic acid, a product of the decomposition of indigo blue.

Indican, or uroxanthine, is soluble in water, alcohol, and ether. By decomposition, under the influence not only of boiling acids, but also of ferments, it yields indigo blue, indigo red, and sugar, as the principal products.

Occurrence of Indican.

According to Heller, uroxanthine is present in the largest proportion in those specimens of urine from patients, which on addition of hydrochloric acid assume a blue tint. Such urine occurs most frequently in diseases of the serous membranes, the kidneys, and the spinal marrow. Schunck has demonstrated the existence of indican in almost every specimen of healthy urine, and thus confirms Virchow, who had already found that indigo blue might be obtained by Heller's process from almost every *concentrated* urine.

Products of the Decomposition of Indican.—Indigo Blue and Indigo Red.

Elements: $C_{16}H_5NO_2$, identical in both substances (Schunck).

Mode of obtaining these substances pure.

a. From the indigo of commerce.—When the indigo of commerce is boiled with dilute acetic acid, *indigo glue* goes

into solution, and may be obtained from it by evaporation, as a yellowish, varnish-like mass, which is soluble in water and alcohol. The substance thus freed of indigo glue is next treated with solution of caustic potash, which dissolves *indigo brown*. This latter substance may be precipitated from the solution in potassa, by the addition of sulphuric acid, in the shape of a voluminous brown mass, which possesses an acid reaction. Indigo thus treated with acid and alkali yields to boiling alcohol a red colouring matter, *indigo red* (indirubine of Schunck), which on evaporation of the alcohol remains in the form of a reddish-brown powder, soluble, with a dark-red colour, in alcohol and ether. On heat being applied to it, it is partly sublimated without decomposition; another part is decomposed, and yields a sublimate of colourless crystals. After the extraction of indigo red there remains *indigo blue*, which constitutes the greater bulk of the substance originally employed. This indigo blue may be further purified in the following manner.

Crystalline indigo blue by sublimation.—Roughly powdered indigo is placed in a shallow china dish, and heated cautiously. On the surface of the fragments there are formed reticular masses of crystals, consisting of pure indigo blue. When heated in a glass tube, indigo evolves purple fumes, which suddenly condense, and settle on the surface of the powder from which they were evolved. It is, however, impossible to conduct the sublimation, so as not to destroy a part of the indigo by overheating. For the production of larger quantities of pure indigo blue, the following process is therefore more profitable.

Crystalline indigo blue by reduction.—On mixing powdered indigo with grape-sugar, spirits of wine, and concentrated solution of caustic soda, and immediately closing the bottle and letting stand for some time, a yellow solution of indigo white, or reduced indigo, in the alkali, results, by the grape-sugar withdrawing one equivalent of oxygen from the indigo blue. If the clear fluid is now decanted, and exposed to the air, the reduced indigo takes up again the lost equivalent of oxygen, and becomes indigo blue, which is slowly deposited in a crystalline form.

Amorphous indigo blue by reduction.—If common indigo is mixed with caustic lime and a solution of sulphate of suboxyde of iron, and, the air being excluded at the same time, is allowed to stand for some time, the suboxyde of iron by withdrawing oxygen transforms indigo blue into indigo white, which latter is soluble in lime. When the clear yellow solution is poured into dilute hydrochloric acid, and

the mixture is exposed to the air, the indigo white rapidly absorbs oxygen, and is precipitated in the form of indigo blue.

Physical and chemical properties.—The crystalline indigo blue forms purple, scaly crystals. The amorphous modification possesses a blue colour with a purple hue, and by friction becomes of a glistening, copper-red colour. In the form of a subtle powder, it is blue. It has neither taste nor flavour, and is insoluble in water, alcohol, ether, and dilute acids and alkalies.

b. Heller's method of obtaining indigo blue and indigo red from pathological urine.—The fresh urine is precipitated by a hot solution of acetate of lead, the filtrate is quickly freed from lead by hydrothion, and the excess of the latter is removed from the filtrate by boiling. This hot fluid is now poured in small portions, under constant stirring, into an equal volume of highly concentrated, fuming, pure hydrochloric acid. The fluid becomes indigo blue, bluish-green, and very dark. If the mixture becomes only violet or red, no deposit of indigo will be obtained. But if it becomes blue, and is allowed to stand for some time, a copper-red, shining, metal-like, dark-blue crystalline pellicle appears. The fluid after twelve hours' standing is diluted with an equal portion of cold water, shaken, and put aside for twenty-four hours. A deposit, frequently inches high, settles towards the bottom; it is separated from the fluid by filtration, washed with boiling water until the washings have a neutral reaction, then washed with some dilute spirits of wine; lastly, it is dried in the water-stove, and over sulphuric acid.

The blackish-blue mass on the filter assumes a copper-red, metallic lustre, when polished by friction with the nail.

The perfectly dry filter is now washed with pure ether, so long as a red-coloured filtrate is obtained; the ethereal filtrates are collected (they have an acid reaction), and on evaporation leave an uncrystallizable, brownish-red resin (pigmento-resinous acid), whose solutions in alcohol and ether present so beautiful a *red* colour, that Heller gave this substance the name of *urrhodine*. If the last portion of ether has left the filter quite uncoloured, a point up to which large quantities of ether, and a corresponding amount of time, are generally required, then the substance on the filter is quite free from urrhodine, and is now dried. All that part of the paper which shows no blue deposit is now cut off; the rest is cut into small pieces, put into a balloon, and

boiled strongly with alcohol of 0·83 to 0·9 specific gravity. The alcohol is poured off as often as it assumes a sky-blue or greenish-blue colour, and the residue is extracted with a new portion of boiling alcohol, until, on protracted and violent boiling, the alcohol remains colourless. In this, as in the above operation with ether, the operator must be prepared for a considerable expense in time and alcohol.

The alcoholic extracts, which have an acid reaction, are filtered while boiling hot, and then evaporated down to about half the bulk, and put aside in a well-closed bottle. After the fluid has become cool, in some cases after protracted standing, *uroglaucine* is precipitated in spider-like, petaloid attempts at crystals. The supernatant alcohol becomes quite colourless.

Both urrhodine and uroglaucine contain a certain quantity of nitrogen; they burn on platinum foil without leaving any residue. Their tests are so stereotyped and unchangeable, even when prepared from the most varied descriptions of urine, that they may be considered as chemically pure chemical individuals.

Heller found, several times, that urine which contained a deposit of uroglaucine produced by spontaneous decomposition of the fluid, and consequently had a greenish-blue tint, became yellow by standing in a well-corked bottle. But, when air was admitted into the bottle, and the urine shaken with it, it became blue again. This process, which appeared very similar to the reduction of indigo in putrefying urine, used in dyeing, was also observed by Kletzinsky in a case of disease of the spine, with paralysis of the bladder. Heller found, that when uroglaucine was boiled with an alcoholic solution of potassa, the solution appeared green; but when the heating was continued during a certain time, and the temperature raised to a certain point, the fluid suddenly became red. On cooling it became green again, and red on heating, and so several times, until at last it permanently lost its colour, a yellow shade being all that remained. These reactions caused Kletzinsky to compare uroglaucine with indigo blue, and the results of his examinations make it evident that *uroglaucine* is identical with *indigo blue*, and *urrhodine* with *indigo red*.

1. Chemically pure indigo blue (obtained from indigo by purifying it with acids, alkalies, and water, and reducing the residue by means of sugar and potash, and oxydizing the reduced indigo in the air) was found soluble in boiling alcohol, with a sky-blue colour, when newly precipitated; and

on cooling and standing, it was deposited in the identical forms of uroglaucine.

2. Uroglaucine, deposited from alcohol, dissolved on trituration in the semihydrate of sulphuric acid $= SO_3 : SO_3 + HO$, and formed a saturated blue solution, which, on immediate dilution with water, deposited traces of a purple substance. The blue solution was left in contact for several hours with sheep's wool, previously freed from fat; after that time, the wool was found coloured blue, and the solution was colourless. The wool remained blue on being washed with soap and water. But on boiling with a hot solution of sesquicarbonate of ammonia, it gave up the blue colour. This is the exact bearing of the coupled acids of indigo and sulphuric acid, namely, sulphindigotic and sulphophenicic acids.

3. Indigo blue obtained as a precipitate by oxydation of reduced indigo, was soluble with a green colour in a hot alcoholic solution of potassa; the solution, at a certain heat, became red, and showed the same changes as described for uroglaucine.

4. Uroglaucine, digested in a closed bottle, either with sugar and potash, or with orpiment, water, and excess of alkali, yielded a solution, which was not blue, but which, on being shaken with air, deposited a bluish ring at the top. The spontaneous reduction in putrid urine is parallel to this. The alcoholic and sulphuric acid solutions of uroglaucine and chemically pure indigo blue have both the property of being transformed, under absorption of hydrogen, into a colourless body (reduced indigo, indigogene), when brought together with hydrochloric acid and zinc. Oxydation on the air restores the blue colour to the pigment, which becomes insoluble.

6. Pure uroglaucine, produced by alcohol, was heated between two watch-glasses; a purple fume arose, which, when inhaled in small portions, caused sneezing and coughing, and condensed in coppery-red microscopic needles, just like sublimated indigo blue.

7. Any solution of uroglaucine, when heated with concentrated nitric acid, yielded a yellow solution, which became orange on the addition of potash; on evaporation on an object-glass, it left microscopical prisms, which deflagrated on heating, and were therefore like pikronitrate of potash. They had a bitter taste.

8. Solutions of uroglaucine and indigo blue became brown when treated with ozonized air, which was passed through by means of a common aspirator. On evaporation they

yielded reddish-yellow microscopical prisms, which became beautifully red with caustic potash (isatine, oxyde of indyl).

9. Sulphurous acid had no effect upon either uroglaucine or indigo blue. Hyposulphites in watery solution, in well-closed bottles, discoloured and reduced both; and, when exposed to the air, both became blue.

10. Indigo red, dissolved in boiling alcohol, was obtained in flakes on cooling: it was soluble in ether, easier than in alcohol; almost insoluble in water and acetic acid; soluble in sulphuric acid, with a yellow colour. These are the properties of urrhodine, with which, moreover, it shares the property of being partially sublimated in colourless masses, perhaps crystals, which become red by nitric acid.

11. The alcoholic solutions of both urrhodine and indigo red bleach in hydrochloric acid and zinc, and become red again when under the influence of air, and shaken with it.

The above tests prove, that uroglaucine and indigo blue have the same physical properties, the same company, the same coupled acids, the same products of oxydation and reduction. There is only wanting the elementary analysis, in order to be quite sure that uroglaucine is $C_{16}H_5NO_2$.

According to Kletzinsky, indigo taken internally does not reappear in the urine, but increases the amount of uric acid secreted.

c. Schunck's method of obtaining indigo blue from ordinary urine.—When acetate of lead is added to urine, it produces a cream-coloured precipitate, which consists of chloride, sulphate, phosphate, and urate of lead, and contains also a little of the extractive (colouring, Th.) matter of urine, which is, as it were, merely mechanically adhering to some of these lead compounds, as it is not precipitated by acetate of lead from a pure watery solution. The urine, which after being filtered from these precipitates is much paler in colour than it was before the addition of acetate of lead, gives with basic acetate of lead a second precipitate of a pale cream colour, which consists of the lead compound of the extractive matter mixed with some basic chloride of lead. Both this and the first precipitate give, when treated with sulphuric or muriatic acid, yellow liquids, which, after being filtered from the sulphate or chloride of lead, and boiled, yield brown flocks exactly like those obtained from urine itself. The liquid filtered from the precipitate obtained with basic acetate of lead is almost colourless. It gives, on the addition of ammonia, an almost white precipitate, the quantity of which

is much less than that of either of the other two precipitates. Now this precipitate contains in most instances, in combination with oxyde of lead, a small quantity of the substance, which, by decomposition with acids, yields indigo blue. For, if the precipitate is decomposed by acids, the filtrate deposits indigo blue on standing.

The following proceeding dispenses with the first precipitation and filtration. The urine having been mixed with basic acetate of lead until no more precipitate is produced, is filtered, and after the precipitate has been washed with water, the liquid is mixed with an excess of ammonia, which always produces more or less of a white or yellowish-white precipitate. This precipitate is collected on a filter, slightly washed with water, and then treated with dilute sulphuric or muriatic acid in the cold. After the whole of the oxyde of lead has combined with the acid employed, the liquid is filtered. When there is much of the indigo-producing body present, the filter acquires a blue tinge, small particles of blue pigment are seen dotting the surface of the sulphate or chloride of lead, and the surface of the liquid, which is of a brownish-purple colour, in a very short time becomes covered with a thin pellicle, which is blue by transmitted, and copper-coloured by reflected light; particles of the same blue substance being at the same time found attached to the sides of the vessel. When there is less of the indigo-producing body present, this pellicle only appears after some time, sometimes not until the next day. After twenty-four hours, however, the action of the acid is always completed, so that if no indigo blue then appears, or can be detected on examination of the deposit, the total absence of the indigo-producing body may be inferred. On the succeeding day, however large the quantity of blue deposit formed may be, the liquid no longer appears purplish, but brown, and, after being filtered and boiled, deposits a dark-brown powder, having exactly the same appearance as that produced by the action of acids on the ordinary extractive matter of urine. The matter left on the filter, after being washed, is treated with caustic soda, which dissolves a portion, acquiring thereby a brown colour. The portion which remains undissolved, after being again collected on a filter and washed, is treated with boiling alcohol. In most cases, the alcohol thereby acquires a bright blue colour. When, however, the quantity of deposit formed is tolerably large, the boiling alcohol first dissolves another substance, which imparts to it a fine purple colour, and which is identical with indigo red (Schunck's indirubine, Heller's urrhodine). That which the boiling

alcohol leaves undissolved is a bright blue powder, having the properties of indigo blue. It dissolves in an alkaline solution of protoxyde of tin, and the solution on exposure to the air becomes covered with a blue film. It is soluble in concentrated sulphuric acid, forming a blue solution, which remains blue even after dilution with water. It imparts to boiling alcohol a bright blue colour, and the solution on cooling and standing deposits blue flocks. When heated in a tube, it gives a purple vapour, which forms on the colder parts of the tube a blue sublimate.

Metamorphoses of Indigo blue.

I have already mentioned the most important metamorphoses of indigo blue, when detailing the modes of obtaining it pure and the evidence of the identity of indigo blue and uroglaucine. It may be well to recapitulate theoretically these metamorphoses, and to add those not yet mentioned.

By the *reduction* of indigo blue, *indigo white* is obtained. This process is effected according to the following formula:

$$\underbrace{C_{16}H_5NO_2}_{\text{Indigo blue.}} - O + \dot{H}O = \underbrace{C_{16}H_6NO_2}_{\text{Indigo white.}}.$$

By the *oxydation* of indigo blue, we obtain in the first instance isatine, which contains two equivalents of oxygen more than indigo blue.

$$\underbrace{C_{16}H_5NO_2}_{\text{Indigo blue.}} + 2O = \underbrace{C_{16}H_6NO_4}_{\text{Isatine.}}.$$

Under the continued influence of oxydizing agents, such as nitric acid, isatine is transformed into nitro-salicylic acid, lastly into picric acid. The compounds obtained from isatine by chemical substitution are very numerous. Under the influence of ammonia it forms a series of remarkable amides.

Under the influence of a concentrated solution of caustic potassa and boiling, giving free access to the air, or adding manganese to the mixture, anthranilic acid is being formed. The substance having the composition of this acid was obtained by Schunck from urine, by the action of strong acids. It remains to be ascertained whether this substance is identical, or only isomeric with anthranilic acid.

The formation of anthranilic acid from indigo blue takes place after the following formula:

$$\underbrace{C_{16}H_5NO_2}_{\text{Indigo blue.}} + 2HO + 4O = \underbrace{C_{14}H_7NO_4}_{\text{Anthranilic acid.}} + 2CO_2.$$

Physiology of Indican.

Schunck has succeeded in obtaining indigo blue from urine in so great a number of instances, that it is probable that indican will in future have to be placed among the normal constituents of urine. It certainly occurs more frequently than any of the abnormal ingredients of urine. Urines containing this substance exhibit no remarkable or peculiar appearance whatever; they are acid, clear, and of the usual colour. Its occurrence, at least if its quantity is moderate, is not to be considered as a pathological phenomenon. Its presence is not attended by any symptoms of ill health, or feelings of discomfort. The state of health and the appearance of the urine do not permit any conclusions to be drawn as to the presence or absence of this indigo-producing substance.

A small number of samples of urine from patients, which Schunck had an opportunity of examining, yielded, with one exception, no more indigo blue than the generality of healthy urines. Heller, however, found more uroxanthine to be present in the urine from persons labouring under diseases of the serous membranes, the kidneys, and the spinal marrow. Perhaps concentration is mainly the condition upon which the success of a search for indigo in urine depends. Virchow could obtain indigo blue from every concentrated urine. Now, as the urine of patients is mostly a fluid of a much higher specific gravity than the urine of healthy individuals, these different observations would herein find a reconciliation.

The physiological quantity of the chromogen in urine must be exceedingly small. By working for several weeks on the urine of two individuals, which contained a comparatively large quantity of chromogen, Schunck obtained one grain of indigo blue.

The urines of forty different individuals, all of whom were apparently in a good state of health, yielded, with one exception only, more or less indigo blue, when examined in the manner described. These individuals belonged to both sexes, and they were of ages varying from seven to fifty-five. The

majority were persons of the working classes. The largest quantity of indigo blue was obtained from the urine of a man above the age of fifty, a publican by trade. The urine of a young man, aged thirty-two, a servant, yielded almost as large a quantity. Among the rest, the urine of a young man, aged twenty-five, an engraver; that of a clerk, aged twenty-three; and that of a girl, aged twelve, who had been a cripple from infancy, were alone remarkable for the amount of indigo blue which they yielded. In all these cases, the indigo blue was accompanied by the substance imparting to alcohol a purple colour, indirubine or urrhodine. The other specimens afforded much less, sometimes mere traces. In all cases, however, in which the urine of the same individual was examined at different times, the amount of indigo blue obtained from it was found to vary exceedingly, it being sometimes considerable, and occasionally dwindling down to a mere trace. It was only very rarely, however, that none was found. In the case of the individual first referred to, the urine gave on one occasion not a trace, and this took place when he was engaged in performing labour, unusual for him both in its nature and amount. In Dr. Schunck's own case, as well as in that of his assistant, the amount varied most capriciously from a tolerable quantity to a mere trace, occasionally even none at all being obtained.

Several experiments with different kinds of diet, in order to ascertain the effect on the amount of indigo blue yielded by the urine, led to no very decisive results.

Of two samples of urine from patients with albuminuria, one gave a small quantity of indigo blue, the other not a trace. Several specimens of diabetic urine yielded it, and one of them a much larger quantity than had been obtained from any other specimen of human urine.

The urine of the horse and the cow, when tried in the same way as human urine, gave comparatively very large quantities of indigo blue, especially that of the horse.

CHAPTER XL.

PHENYLIC OR CARBOLIC ACID.

Formula: $C_{12}H_6O_2$.

History and Occurrence.

Phenylic acid was discovered, by Runge,[1] in tar obtained by the distillation of coal. It is now an article of wholesale manufacture, and passes in commerce by the name of creosote. It occurs in castoreum together with salicine, both substances probably resulting from the barks of poplars and willows, the common food of the beaver (Wöhler). Städeler[2] obtained it in small quantities from the urine of man, the horse, and the cow. After the internal or endermatic application of creosote, or substances containing it, such as tar, phenylic acid appears in the urine. Such urine frequently is black,[3] or deposits a black precipitate of tar-like matter, a part of which may, perhaps, have some relation to indigo.

Mode of obtaining it pure.

a. From coal tar. Coal tar is subjected to distillation, and the products, which pass over at a temperature of from 150° to 200° C. (302° to 392° F.), are collected, mixed with a concentrated solution of potassa, in which phenylic acid is soluble. From this salt the acid is separated by means of hydrochloric acid, and by distillation over chloride of calcium is obtained anhydrous.

[1] 'Poggend. Annal.,' xxxi, p. 69; xxxii, p. 308.

[2] 'Annal. d. Chem. und Pharm.,' lxvii, p. 360; lxxvii, p. 17.

[3] See the cases by Dr. McLeod, 'Medical Gazette,' vol. ii, 1834-35, p. 599. Elliotson, 'Med.-Chir. Transact.,' vol. xix, p. 237. H. M. Hughes, 'Guy's Hospital Rep.,' 3d series, vol. ii, p. 52, where also several observations of Dr. Hermann Weber are quoted.

b. From urine of cows. Städeler obtained phenylic acid from this fluid by first removing hippuric acid in the usual way, with lime and hydrochloric acid. The mother-liquor he subjected to distillation, and the distillate to repeated rectification. The rectified fluid was distilled over hydrate of potassa, the residue was partly saturated with sulphuric acid, again distilled, the distillate rectified by chloride of sodium, and saturated with carbonate of soda. The oily matter thus separated was taken up with ether, the ether evaporated, and the residue again distilled over potassa; the rest of the acid was evolved from the potassa by the addition of bicarbonate of potassa. By continued fractional distillation almost pure phenylic acid was obtained.

c. From human urine, after the endermic administration of tar,[1] or the internal use of creosote. In two cases of psoriasis, tar was rubbed over the whole surface. Three hours after the first inunction, the urine, which before had been clear and straw-yellow, became amber-yellow, and deposited uric acid in colourless plates. The urine which was passed after twelve hours was dark brownish-black, deposited a large sediment of coloured uric acid, and emitted the characteristic odour of tar. These peculiarities the urine retained during the entire course of the tar treatment.

When the brownish-black urine was left to spontaneous decomposition, which generally ensued on the fifth or sixth day, it assumed a dark-green (*lauchgrün*) colour, on the appearance of alkalescence, and then went through all the stages of ordinary decomposition.

The fact of the urine depositing uric acid so completely, that hydrochloric acid did not produce any further precipitate, suggested the probability of the presence of an abnormal acid in the urine. After the addition to the urine of some sulphuric acid, it was subjected to distillation, whereby an acid distillate was obtained, which emitted a strong odour of tar, was milky, but cleared up gradually, and deposited dark-brown drops, which were like creosote. A chip of pine-wood, moistened with hydrochloric acid, and dipped into the clear watery fluid, gradually assumed a bluish-green colour. The addition of chloride of iron to this fluid produced a dark-brown mixture, and an excess of the chloride produced a brown adhering precipitate. Nitrate of silver produced a white precipitate, which, on the addition of ammonia, or simply on warming, was reduced to metallic silver. Neutral acetate of lead produced a white precipitate. When chlorine

[1] Petters, W., 'Prager Vierteljahrschrift,' 1855, vol. iii, p. 126.

gas was passed through the fluid, it assumed an orange colour, and deposited a brown resinous precipitate. The solution on the addition of nitric acid became reddish-brown; sulphuric acid produced a pink, rosy colour at the bottom stratum of the fluid, the supernatant fluid becoming turbid like milk. Under the influence of chromic acid, the solution became black. These tests are characteristic of *carbolic acid.*

After repeated rectification of the original distillate, a pale, yellowish, oily liquid, of the odour of creosote, was obtained, which, on the addition of caustic potash, transformed into a magma of white crystals, which had the smell of mint (*krausemünze*). This potash salt dissolved in water, had a very agreeable odour, and therefore must have contained *eupione*, besides *carbolic acid.* It yielded a pale, yellowish distillate, which after removal of the water by means of chloride of calcium, became clear and colourless, of an oily consistence, and scarcely emitted any odour. It burned with a sooty flame, had a corrosive taste, blistered the skin, began to bubble at a temperature of 203° C. (397 °F.), boiled between 215° and 220° C. (419° and 428° F.), and, with the exception of the first part of the distillate, remained fluid even at a temperature of—25°C. (—13° F.) The elementary analysis of this fluid yielded the following results:

Found,		Calculated,	
C =	68·55	C =	69·90
H =	6·41	H =	6·79
O =	25·04	O =	23·31
	100·00		100·00

From these figures results the formula $C_{12}H_6O_2 + HO$, which corresponds to carbolic acid plus one equivalent of water. This latter, however, was undoubtedly merely an admixture of water, from which the substance could not be freed entirely before the combustion.

When the urine was neutralized with lime, it yielded an ammoniacal distillate, which, after removal of the ammonia by neutralization with sulphuric acid, left a residue from which alcohol extracted a substance having the smell of tar, and depositing in brown flakes on evaporation of the alcohol. The nature of this substance could not be ascertained any closer, as its quantity was too small. A similar substance could be extracted from the fresh urine by means of alcohol. When shaken with ether, the latter extracted from the urine a purple matter, which after evaporation became dark red, and was fusible.

Carbolic acid could only be obtained from the urine after the addition of sulphuric acid. It must therefore have been in combination with a base not ascertained.

Carbolic acid could not precipitate uric acid from its solution, as it is a weaker acid than even carbonic acid, and is driven out of its compounds by the latter. Another acid was therefore present in the urine, and precipitated uric acid.

Dr. Petters is of opinion that most of the constituents of tar may enter the organism, and pass out by the urine. The residue from which the volatile substances had been distilled off, yielded an alcoholic extract, which on evaporation gave a black, tough, tar-like deposit. This, after crystallization of the salts and resolution in alcohol, deposited a substance on the admixture of water, which had the odour of tar, was resinous, and underwent no further changes.

Physiology of Phenylic acid.

Phenylic acid when introduced into the animal economy is, at least in part, excreted unchanged. In case the food of man should contain this acid, its occurrence in human urine would be accounted for. Smoked and dried meat certainly contains a small amount of this acid, together with other substances, the products of dry distillation. There is, however, nothing improbable in the opinion, that phenylic acid may be a collateral product of the oxydation of aliments. For as it is found in the urine of animals feeding on matters which have not been proved, and *à priori* could not be supposed, to contain phenylic acid ready formed, we are driven to the conclusion that it is formed in the body.

Frerichs and Wöhler proved phenylic acid to be a poison. A few drops of it killed rabbits and dogs in a quarter of an hour. Most probably the creosote and tar treatment is only tolerated by patients because these substances are being constantly eliminated by the kidneys. In some of Petters's cases the inunction with tar caused symptoms of poisoning. These substances are the last refuge of despairing empirical therapeutics. Creosote is useful in septic conditions, but the healing effects of tar are mostly of an imaginary nature.

CHAPTER XLI.

DAMALURIC ACID.

Formula : $C_{14}H_{11}O_3 + HO$.

History.

Discovered by Städeler in the urine of man, the horse, and the cow.

Physical and Chemical properties.

Damaluric acid is an oily liquid, of an odour resembling valerianic acid, heavier than water, but somewhat soluble in it. It differs from phenylic acid, in the property of reddening litmus, which phenylic acid has not.

Compounds.

With baryta this acid forms a salt, crystallizing in groups of needles. The salt with silver is a white powder, which does not decompose on exposure to the air. The former is soluble in water, strongly alkaline, does not fuse on heating, and leaves carbonate of baryta on combustion, which retains the original form of the salt. Damaluric acid produces a precipitate in a solution of basic acetate of lead, which under the microscope appears crystalline.

Mode of obtaining it pure.

Städeler distilled the urine of the cow with sulphuric acid, and thereby obtained an acid distillate, which was decomposed by means of carbonate of soda. The solution of the soda salts thus obtained was freed from phenylic and taurylic acid by means of ether, evaporated, and, after addition of

sulphuric acid, again subjected to distillation. From the distillate the baryta salt was obtained, which contained 39·18 per cent. of baryta. The silver salt contains 49·36 per cent. of oxyde of silver.

Städeler distinguishes further damolic and taurylic acids as ingredients of human or animal urine. Without doubting in the least the correctness of his observations, it is just to say, that the existence of these acids is not, as yet, sufficiently established for me to describe them at full length in this treatise.

CHAPTER XLII.

OXALIC ACID

Formula: $2HO \cdot C_4O_6 = \left.\begin{matrix} C_4O_4 \\ H_2 \end{matrix}\right\} O_4 = C_4H_2O_8$.

Composition of one equivalent in 100 parts:

Carbon	= 24·0 . .	26·667
Hydrogen	= 2·0 . .	2·222
Oxygen	= 64·0 . .	71·111
	90·0 . .	100·000

History and Occurrence.

The sal acetosellæ had been known and used for a long time, when, in 1784, Scheele[1] described a proceeding of separating oxalic acid from it by acetate of lead, and also discovered the identity of this oxalic acid with the acid found by Bergmann[2] to be the principal product of the oxydation of sugar by means of nitric acid.

Oxalic acid is one of the most frequent products of the oxydation of organic matter by artificial processes. Its compounds are very frequent in plants, where the acid represents most probably the first stage of the reduction of carbonic acid. Thus, binoxalate of potash was formerly manufactured from certain species of oxalis, in which, as in certain species of rumex, it is found in considerable quantities. The parallel soda salt is found in certain plants familiar at the seashore, or in the neighbourhood of salt-works, salicornia and salsola; the latter, like "lucus a non lucendo," termed salsola kali. Oxalate of lime enters largely into the construction of many

[1] 'Opusc.,' vol. ii, p. 187.
[2] Ibid., vol. i, p. 251; vol. iii, pp. 364, 370.

species of lichen, growing on rocks of limestone; it frequently amounts to one half of their weight.[1] Such lichens are found in great beauty on Chiswick Bridge. Most higher plants contain smaller or larger quantities of the calcareous oxalate. For study, rhubarb and onion peel are useful. In the animal organism oxalic acid is rarely met with, except in the insoluble form of the oxalate of lime when taken in vegetable food. Oxalic acid occurs free in urine, when large quantities of oxalic acid or oxalates are taken in repeated doses. After the ingestion of these substances, the urine also contains oxalate of lime in form of a precipitate.

Oxalic acid, mostly in form of the oxalate of lime, occurs in the urine in the course of certain diseases. It is at present unknown whether the oxalic acid in these cases is a product of the organism itself, and, like the acid after ingestion into the stomach, is carried by the blood to the kidneys to be there secreted, or whether the acid is the product of a certain and peculiar decomposition of urine in the urinary passages.

Normal human urine, after some standing, mostly deposits microscopical traces of oxalate of lime, not approachable by quantitative analysis. The normal urine of herbivorous animals mostly contains a more appreciable quantity of the oxalate.

Mode of producing Oxalic acid.

One part of sugar is heated with six parts of nitric acid of 1·3 spec. grav., until red vapours are no longer evolved. The fluid on evaporation on the water-bath yields oxalic acid in crystals, amounting to one third of the weight of the sugar employed.

Physical and Chemical properties.

From its watery solution oxalic acid crystallizes in monoclinometric prisms, containing four equivalents of water of crystallization, and hence having the composition $C_4H_2O_8 + 4HO$. In dry air it loses the whole of the water of crystallization, and transforms into a white powder. It is soluble in nine parts of cold water, much more soluble in boiling water or alcohol.

[1] Braconnot, 'Ann. de Chim. et de Phys.,' xxviii, p. 318.

Decompositions.

It fuses by heat, and on the temperature being raised to from 110° to 130° C. (230° to 266° F.) it is decomposed into carbonic acid, carbonic oxyde and water, and formic acid.

$$C_4H_2O_8 = 2CO_2 + C_2H_2O_4$$

$$\underbrace{C_2H_2O_4}_{\text{Formic acid.}} = 2CO + 2HO.$$

When heated with concentrated sulphuric acid, oxalic acid is decomposed into equal volumes of carbonic acid and carbonic oxyde. By oxydizing agents oxalic acid is transformed into carbonic acid: this is effected slowly by nitric acid; quicker by chlorine water, peroxyde of lead, or manganese; rapidly by a solution of permanganate of potash.

Compounds.

Oxalic acid being a very strong acid, displaces many weaker acids from their combinations. With two equivalents of oxydes of metals it forms neutral salts of the formula

$$C\,O_6 + 2MO, \text{ or } \left.\begin{matrix} C_4O_4 \\ M_2 \end{matrix}\right\} O_4.$$

and with one equivalent of any oxyde it forms acid salts, having the composition

$$C_4O_6 + HO\,.\,MO, \text{ or } \left.\begin{matrix} C_4O_4 \\ H\,.\,M \end{matrix}\right\} O_4.$$

The quadroxalates have the composition $C_4O_6 + HO\,.\,MO + C_4H_2O_8 + 4HO$.

The salts of the alkalies are easily soluble in water, and insoluble in alcohol. The salts of the alkaline earths are quite insoluble, so that lime and oxalic acid constitute the best precipitants for each other. It was Bergmann who first employed the oxalate from oxalis as the reagent for lime salts. The oxalates of oxydes of metals are mostly insoluble, or little soluble, in water.

Oxalate of Lime. $C_4O_6 + 2CaO + 4HO$.

This salt is obtained by mixing solutions of chloride of calcium and any oxalate of an alkali, in the form of a white crystalline powder, which may be shown to consist of crossed prisms

of the quadratic system. Exposed to dry air it loses one half of its water of crystallization; the other half may be removed by heating to 180° C. (356° F.) It is necessary to keep the salt covered during the drying process, as, at the temperature of 150° C. (302° F.), it becomes very electrical, so as to be thrown out of the dish by the slightest touch. It is insoluble in water and acetic acid, soluble in hydrochloric and nitric acid. From solutions in the latter acids it may sometimes be obtained in crystals by slow evaporation. From the solution in hot concentrated hydrochloric acid a double salt of chloride of calcium and oxalate of lime, of the composition $(C_4O_6+2CaO)+2CaCl+14Aq$, is sometimes obtained in crystals. Free oxalic acid is also obtained in crystals from this solution. The double salt, when brought into contact with water, is decomposed into chloride of calcium, which dissolves, and oxalate of lime, which remains as an insoluble powder. If the oxalic acid have not been removed by alcohol, no chloride of calcium is obtained after resolution of the crystals, as it is immediately decomposed by the oxalic acid.

The oxalate of lime, constituting the quadratic crystals found in plants, contains six equivalents of water of crystallization.

Physical characters of Oxalate of Lime.

Of these I shall treat at some length, in order to clear up some errors in the literature of the day.

I have had several cases of severe disorder under my care, in which there occurred deposits of oxalate of lime in the well-known octahedra, and others in which the reputed dumb-bells were present. In two of these cases the octahedra and dumb-bells occurred promiscuously; and in one the crystals of both descriptions were of so exquisite a beauty of definition, and of so large a size, as seemed to be particularly favorable to examination. This examination was repeated frequently, and under a variety of circumstances, and seemed to have for its result that the octahedra of oxalate of lime presented a certain degree of polarizing power, and that they appeared mostly as oblong squares. This result differed from the opinion almost generally received, at least among gentlemen of the medical profession, namely, that the octahedra of oxalate of lime do not polarize. They were not to polarize because they crystallized in the regular or cubic system, a position which was considered as proved. On the other hand, it was explained, that these crystals must belong to the cubic system, because they did not polarize. Our

knowledge upon this point evidently moved in a circle, not in the spiral line of progress.

In looking over the literature, I found that what had been seen had been rightly seen and figured, I may say, very faithfully, but not always very intelligibly. But the appearances had been misinterpreted, disregarded, or explained away.

How this was possible, will not be easily intelligible hereafter. One saw a square, with cross lines, suggesting the shape of an octahedra. Dr. G. Bird, using a word, which no doubt conveyed more than it was intended to convey, styled them cubes. He says, at p. 212, § 215, "If the light is very bright, these crystals generally resemble cubes marked with a cross, the point of intersection of the two arms corresponding to one of the apices of the octahedron." Now, on putting squares for cubes the sentence is literally correct, and fits his fig. 39, to which he refers. To cubes, however, this figure has no resemblance. In a similar sense, we must explain the word cubes on two different places, where it is equally misapplied (p. 212, second line from below, and p. 215, eighth and tenth lines from above).

However that may be, there can be no doubt that Dr. G. Bird believed the oxalate of lime to crystallize in the cubic system. In three editions of his work the dumb-bells and ellipsoid bodies, occurring along with or alternately with the octahedra of the oxalate, pass as oxalate of lime. It is only in the fourth edition that the difficulty arises from the dumb-bells and octahedra exhibiting different appearances in polarized light. He says, at p. 216, § 220, *et seq.*: "These dumb-bell and oval crystals, although I have always described them as oxalate of lime, have always presented a very serious difficulty to their being thus regarded, in consequence of the peculiarity of their optical characters. It is well known that all crystals referable to the cube or regular octahedron never possess double refraction, and hence scarcely exert any influence upon a plane polarized ray of light. In accordance with this law, the ordinary crystals of oxalate of lime do not in the slightest degree exhibit the phenomena of colour when examined in the polarizing microscope; merely in the slightest degree, if lying in a favorable position, appearing illuminated when the polarizing prisms are crossed. On the other hand, the dumb-bell crystals, as I long ago stated, exhibit a beautiful series of coloured rings traversed by a black cross." In consequence of this supposed difference between dumb-bells and octahedra of the oxalate, Dr. G. Bird submitted the former to an investigation, the result of which was, however, not

very decisive. He wanted to prove by the chemical test that the dumb-bells did not consist of mere oxalate of lime, "because their powerful action on polarized light was quite incompatible with their being composed exclusively of this salt" (p. 219). His five chemical experiments detailed under A, B, C, D, E, at pp. 217 and 218, failed entirely to establish any difference between these bodies and the common oxalate, as did also the experiments of Dr. Bacon, quoted at pp. 220 and 221. The results of Dr. Bacon's experiments, according to his own words, are as follows: "That the dumb-bell crystals consist of a salt of lime containing either oxalic, oxaluric, or perhaps some other organic acid easily converted into oxalic acid, but the exact nature of the acid remains to be ascertained by future investigation." From this sentence it follows clearly that the dumb-bells may after all be oxalate of lime, supposing that their optical properties can be brought to harmonise with that opinion; at least it has not been proved by any chemical experiment that they are not oxalate of lime. After Dr. G. Bird had condemned his former statements, his new opinion was generally adopted, but upon optical grounds only, or rather upon no grounds at all, as we hall hereafter see.

Some of the authors who have followed Dr. G. Bird in his opinion regarding these crystals, are not very accurate in their statements, a circumstance which we must suppose to have increased the confusion already existing. Dr. Beale, at p. 217 of his work on the microscope, when speaking of the dumb-bells, and mentioning that they might be composed of the oxalurate of lime, and had the power of polarizing light, says that "substances which crystallize in the octahedral form do not possess this property." Now, if Dr. Beale had closely adhered to Dr. G. Bird's statement already quoted, namely, that all crystals referable to the cube or regular (!) octahedron never possess double refraction, and if he had not been so modest as to allow authority to prevail over the result of his own observations, he would not have put down the octahedral form generally as not polarizing, which he seems to have been compelled to do, from the fact of his distinctly stating that his octahedra were of the quadratic system, inasmuch as one of their axes was much shorter than the other two. Unless, therefore, he put all octahedra down as non-polarizing, his octahedra ought to have been polarizing ones, because all crystals except those of the regular system do polarize. If Dr. Beale had attended to the relation of the crystallographical axes of his crystals, his ten drawings (fig. 185 in the 'Microsc. in Clin.

Med.'), otherwise so correctly executed, could not have failed to urge upon him the conviction that the oxalate of lime crystallizes in the quadratic and not in the cubic system.

There is sufficient evidence to show that other authors were aware of the fact, that the system in which the oxalate of lime crystallizes, is not the regular or cubic system. In the third edition of Dr. Prout's work on 'Stomach and Urinary Diseases,' plate i, fig. 6, there is a diagram, to which there is the following explanation on the next page: "Fig. 6 represents a flat octahedron; the form stated by Wollaston and others to be that most frequently assumed by crystallized oxalate of lime. According to the recent observations of Mr. Brooke, however, some natural crystals of the oxalate of lime, containing one proportion of water, presented the form of an oblique rhombic prism. Whether the salts thus appearing in two different forms are the same in composition, or whether the octahedral form has been erroneously assumed, is not ascertained." See 'Lond. and Edinb. Philos. Mag.,' vol. xvi, p. 449 (1840). Funke, in pl. i of his 'Atlas der physiologischen Chemie,' figures some oxalate of lime. The (artificial) crystals were small. He saw some octahedra with one of their lateral angles towards the observer, similar to the four lower diagrams of Dr. Beale's fig. 185, and concluded that they were quadratic octahedra—an opinion which is certainly justified by the more common appearances; and, moreover, that they were of the variety in which the vertical axis is the longest, which is wrong. It is wrong for the following reason: If the vertical axis is longest, the other two axes must be equal, which they are not. On making the two equal axes the horizontal ones, the shortest axis becomes the vertical.

Dr. G. Bird, at p. 221, quotes an experiment of the American physician already mentioned, Dr. Bacon, of Boston, by which this observer obtained *four-sided prisms of pure oxalate of lime*. The experiment runs thus, § 225: "Dr. Bacon examined the effects of the different acids upon artificially prepared oxalate of lime. He ascertained that when dissolved in hydrochloric acid . . . and allowed to evaporate spontaneously, a mixture of transparent rhomboidal plates, minute octahedra, and four-sided prisms, often arranged in rosettes, with zeolitic crystals, were obtained. The rhomboids and zeolite groups acted powerfully on polarized light, the prisms less strongly, and the octahedra not at all. On submitting these crystals to analysis, the rhomboids were found to contain hydrochloric acid, but the prisms and octahedra were pure oxalate of lime." Now the occurrence of

these prisms is perhaps the strongest possible reason that could be advanced why the oxalate of lime cannot crystallize in the cubic system, leaving dimorphism out of the question for the present. The cubic system, by the nature of its axes, three axes of equal length, and at right angles to each other, precludes the possibility of a prism or column ever occurring in it. Besides, even had it been possible for the prisms to be in the regular system, they could not have polarized.

It is a matter of great surprise that Dr. G. Bird should have overlooked the incompatibility of the prism with the regular or cubic octahedron. Whether his fig. 40, representing the "square prisms with a four-sided pyramid at each end, forming a dodecahedron" (a term quite unusual in crystallography for this combination, which certainly has twelve planes, but not equivalent ones, a requisite for a dodecahedron), is drawn from specimens under his own observation, is not stated. Perhaps they are given after Dr. Bacon. Here we must, however, state that the crystals obtained from a solution of oxalate of lime in hydrochloric acid, do not at once permit a conclusion to be drawn upon the primary crystallizing form of the oxalate of lime, inasmuch as they may be a mixture of the above-described double-salt of chloride of calcium and oxalate of lime, plus water of crystallization, and of oxalate of lime and oxalic acid.

Prismatic crystals of oxalate of lime were first observed by Brooke as already mentioned. They were then described by C. Schmidt ('Ann. d. Chem. und Pharm.,' lxi, p. 304), who says that he measured them, and found them to belong to the fifth system of crystallization, the oblique, or monoclinoedric (Naumann), or hemiorthotype (Mohs), viz., the system in which two of the axes are at right angles to each other in an horizontal plane, and the third inclined but in a vertical plane passing through either of the other two. It is, however, most improbable that these measurements were correctly made, inasmuch as nobody has ever since observed any oxalate of lime in the oblique system. In the urine, prismatic crystals of oxalate of lime were first observed by Dr. F. W. Beneke ('Zur Physiologie und Pathologie des phosphorsauren und oxalsauren Kalkes,' 1850). He described them as quadratic prisms, with pyramidal terminations, and gave good drawings of all the forms of oxalate of lime on the first table appended to his publication. According to Ch. Gerhardt, ('Lehrbuch der organischen Chemie,' 1854, German edition by R. Wagner, Nürnberg, vol. i, p. 285,) oxalate of lime occurs in plants in the shape of quadratic or pyramidal octahedra, which are frequently combined

with the quadratic prism. The quadratic octahedron may be the primary one (P: P = 46° 28′), or an obtuse one P: P = 119° 34′) (123° 19′ Rose). The measurements seem to be those of Schmidt, adapted to the pyramidal system. They can therefore not be relied upon. It is very doubtful whether the primary octahedron does ever occur.

Oxalate of lime is represented as crystallizing in quadratic octahedra by E. von Gorup-Besanez, p. 182 of the second edition of his 'Anleitung zur zoochemischen Analyse,' 1854. He says, that the long or pointed octahedra are of rare occurrence. Robin and Verdeil, pl. vi, figs. 2 and 3, of their 'Atlas' represent pyramidal octahedra.

Preparation of objects for microscopical observation.—It is perhaps well to mention here, that all precipitates of the oxalate of lime used for any experiment were carefully washed until they yielded no more traces of their soluble components, so that no crystallization could have taken place under the influence of the evaporation of the water surrounding the object on the slide. The oxalate of lime has very little affinity for water, and any preparation of it not permanently mounted gets dry very fast; for this reason I always take a flat cell of Brunswick black for every specimen, which not only allows a larger amount of fluid to remain with the crystals, but can also be converted into a temporary mounting, simply by warming it a little, and pressing the circular thin glass cover gently against the cell, whereby it closely adheres to the latter, and precludes evaporation. The object may be mounted permanently if desired, by surrounding the cell with Brunswick black. A little preserving fluid should therefore always be put into the cell, if the observer has the intention to make permanent objects.

Crystals of the oxalate of lime are obtained from the urine of children a few hours after a meal of rhubarb. The sediment after being washed consists of numerous crystals of all sizes, the large ones being particularly favorable for examination. Mixed with these are in most cases numerous ellipsoid bodies, more rarely some dumb-bells. It is partly on specimens of this description that the following observations on the polarizing power of the oxalate of lime were made. The oxalate which occurs in the urine pathologically, be it produced in the kidney, bladder, or after emission of the urine, is generally of a smaller size, and mixed with other matter, and therefore is not so favorable an object for microscopical examination. Very large crystals occur in the urine of the horse, but here they are mixed with a large

quantity of stellar crystals of the carbonate of lime. The latter is best dissolved in dilute acetic acid, which leaves the oxalate undissolved.

Artificial oxalate of lime is best prepared by mixing a solution of an oxalate—for example, oxalate of ammonia—with a soluble and dissolved preparation of lime—for example, chloride of calcium, lime-water, or phosphate of lime (in the urine). Precipitated from concentrated solutions, the oxalate of lime appears in seemingly amorphous lumpy masses, as they are described by most writers; by taking, however, very dilute solutions, and mixing them at a higher temperature, close imitations of the urinary crystals may be obtained. The admixture of a soluble oxalate to urine gives a great variety of crystals, some of which are described in the following pages.

On submitting the crystals to the microscope, it is necessary to use a sufficiently high power. Though a half-inch object-glass is quite sufficient for recognising the characteristic crystals, yet the quarter-inch is stereoscopically better, that is to say, because under a higher power fewer points are in focus at a time, and the observer becomes more conscious of the relations of the different points, sides, edges, and angles of the crystals, because they have more relief, and appear as bodies, and not as flat markings, as they do under lower powers. The crystals obtained from plants, such as the cuticle of the onion and others, are generally much larger than those obtained from animal fluids, and therefore require lower powers, though under higher powers they are seen to great advantage.

Pure artificial oxalate of lime, from oxalate of ammonia and chloride of calcium.

Experiment 1.—To a boiling concentrated solution of oxalate of ammonia, a concentrated solution of chloride of calcium was added, whereby a copious white precipitate was produced. Under the microscope, this precipitate consisted apparently of irregular lumpy masses, but on the application of higher powers, and on taking single particles for examination, it was seen that these were composed of four smaller roundish particles each, so as to represent a cross with rounded-off angles. Mixed with these were small squares, and crosses lying on squares. When the test had cooled by standing over-night, prisms with pyramidal ends could be discovered here and there. The lumpy masses polarized white

light; the prisms red, blue, and violet. See the small crossed and large coloured prisms on the right side of fig. 4, Pl. V.

Experiment 2.—To a concentrated solution of oxalate of ammonia of ordinary temperature, a solution of chloride of calcium was added. The precipitate obtained consisted of the same particles as in the first experiment, but they were rather larger and better defined. There were, however, no prisms in this precipitate, which polarized light between two Nichol prisms without variegation of colour.

Artificial oxalate of lime from water.

Experiment 3.—The water of the New River Water Company, with which my house is supplied, contains in solution, like most water, a certain proportion of carbonate of lime. I therefore thought it suitable for an experiment with the oxalate of ammonia. As I wanted crystallization to go on as slowly as possible, I did not take a solution of the oxalate of ammonia for precipitating the lime, but dropped a crystal of about two grains in weight in about an ounce of water contained in a test-tube, and allowed it to stand over-night. I obtained a white thin deposit, consisting of innumerable crosses, being prisms with pyramidal ends crossed at right angles.

The appearances are represented in fig. 4, Pl. V, on the left of the coloured prisms. Some prisms were single; in other cases a great many prisms were crossed at various angles. But the crosses with right angles were the ground form. All the crystals polarized light without much colour.

This experiment gave me the key to the explanation of the nature of the bodies found in the first two experiments. The lumpy masses with four indentures are in fact nothing but crossed prisms, whose ends, however, are irregular, round, sometimes thickened; the angles are frequently so much filled up, that a round body is produced, which it would be difficult to give an account of, but for the other crystals. Here we have then in the first instance crossed prisms, the angles and edges of which become rounded off, and the corners filled up, and that the more, the more the formation of the crystals is hastened, and the more concentrated the solutions are out of which they form. The roundest body from an oxalate of lime precipitate will, on careful examination, yet exhibit four points corresponding to the places where under more favorable circumstances there would have

been four open angles. This is a satisfactory explanation of the so-called tuberose (*knollig*, in German) appearance of artificial precipitates of the oxalate of lime.

Even regular crystals may become tuberose by apposition of new matter. So in the first deposit I found a crystal to the four pyramidal sides of which round masses were apposited. When these masses get larger, they form a sort of cap on each side of the prism, which when still larger makes them much like dumb-bells, with which indeed they are identical. Crossed dumb-bells (see centre of fig. 6, Pl. V) are large tuberose crystals.

Artificial oxalate of lime from urine.

Experiment 4.—To urine, which had just been emitted from the bladder, a solution of oxalate of ammonia was added. In the precipitate a great variety of crystalline forms were observed.

a. Small prismatic crystals, gradually rounding off into—

b. The ellipsoid and dumb-bell forms, the latter less prominent.

c. Squarish, flat bodies, with several indentures on two opposite sides. They appear as if formed by a number of ellipsoid bodies joined together with their flat sides.

d. Almost regular octahedra, the lateral edges not quite straight.

e. Crossed prisms or crossed octahedra. The types of all these crystals are represented in fig. 5 of Pl. V.

On standing in water for some weeks the crystals seemed to decay, particularly on their thin edges, which became much corroded. The development of vegetable growths made the formerly white precipitate green and dirty looking.

Experiment 5.—In this experiment not a single well-defined octahedron was obtained. The deposit consisted of granules of different shapes and sizes, the largest not exceeding $\frac{1}{6\,3\,0\,0}$ of an inch in their longest diameter. There was a tendency to straight, square outlines, in some cross markings were present. The deposit polarized as usual, white light being produced by the bodies. This urine was very acid, and the addition of the acid salt caused uric acid to crystallize in well-defined, large, four-sided rhombic plates, with right angles, polarizing in dark colours. This is the only instance in which I observed almost regular rhombic plates of uric

acid to crystallize out of urine, of a size and beauty equal to that of the finest artificially prepared uric acid.

Experiment 6.—The entire deposit consisted of octahedral crystals, with their angles and corners cut off, so as to make their outline to appear eight-sided; fig. 4, Pl. V, below coloured prisms. Most of the crystals were square; viz., their horizontal sides were equal, in some all eight sides were equal, in others the four secondary sides were shorter. In few specimens only two corners were cut off. Whether the new plane was one plane, or two forming an obtuse angle, I could not ascertain. In some apparently square crystals there was an octagonal marking, corresponding by four parallel sides to the original four sides of the octahedral form. In some it appeared as if the crystal had been divided by a plane falling through the four lateral edges, and one half had been turned upon the other half in an angle of 45° round an axis perpendicular upon the plane just described, representing a tropia, or turn, of the value of one eighth of the circle. The long axis (c) was $= 2$, taking the short one (b) as $= 1$. The crystals were very dark, and the cross was faintly illuminated.

Experiment 7.—The crystals obtained were long, crossed octahedra. The centre of the twins was occupied by octahedra of the ordinary appearance, and by crossed octahedra described in the former experiment. Assuming each octahedron to be a twin by crossing, there were here four or six crystals arranged round one common principal axis, each set being turned round the common axis in an angle of 30°, so that none of the horizontal axes of any one twin crystal coincided with the horizontal axes of the next one, but was distant from the secondary and ternary axes in the angle described. Four crystals crossing frequently formed eight-rayed stars. Of the four secondary rays, sometimes only one, two, or three were present, giving the crystal an unsymmetrical appearance. Mixed with these regular crystals was a large proportion of roundish bodies polarizing in colours, attempts at ellipsoids, dumb-bells, and so on, many of which were twin crystals.

Experiment 8.—After the addition of oxalate of ammonia to urine some caustic ammonia was added, until the fluid was alkaline. After standing over-night, a sediment had formed, and a thin crust was swimming on the fluid, consisting of radiated, zeolitic balls, baked together, which were of a yellowish colour and not affected by acetic acid.

They seem, therefore, to have been uric acid. The sediment was of a filmy nature, and consisted of numerous irregular prisms of ammonio-phosphate of magnesia, often crossed by two or three, and taking all the fitful appearances of this salt. Mixed with these were octahedra of oxalate of lime and other irregular polarizing undefinable bodies.

Experiment 9.—In this deposit many regular and irregular octahedral crystals were present, many simple twins, double twins; the corners sometimes very little prominent, or rounded off: there were small crossed prisms. But the most regular crystals were large simple prisms, with apparently pyramidal terminations. The prisms, when seen edgeways, were flat, about one fourth or one fifth of their width in thickness. The dark ends on the prisms, when seen edgeways, corresponded to the planes terminating the plate; but on the large planes no octahedral planes were to be distinguished, so that the prisms could not be explained otherwise than as being prismatic plates, terminated by a horizontal prism.

Oxalate of lime occurring in urine spontaneously.

Observation 10.—*Urine of a slightly dyspeptic man.*—I put a sample of urine, which came acid and a little cloudy out of the bladder, to stand over-night. After sixteen hours a dense mucous cloud had settled at the bottom of the vessel, and, besides, a dense pink deposit of urate of soda had settled all over the cloud, and on the sides of the vessel. The mucus showed minute granules disposed all over its surface, distinct from the urate. There were many oxalate of lime crystals, but all only fragments of octahedra, mostly halves, and, when lying on their sides, showed the edge cut off by a prismatic plane, which latter reflected light when well focussed. These halves were most common. Then there were crystals with one edge regular, one corner cut off parallel to an octahedral edge, or parallel to an octahedral diagonal. There were irregular conglomerations of crystals of all shapes and sizes, from a roundish body to a regular hedgehog-like mass.

The irregular parts of the crystals seemed to have been those with which they were attached to their basis, which, most likely, was the mucus.

Case of so-called oxaluria.

Observation 11.—A gentleman, thirty-five years of age,

during the spring of 1856, had suffered from boils on various parts of his body, with some eczema now and then upon his arms. He had taken the sulphates of iron and magnesia, which, though they seemed to be borne badly by his digestive organs, improved his skin and general health so far that the boils disappeared. About the latter end of June, 1856, he became dyspeptic, his tongue got covered with a fur, and excoriations broke out along its sides, which he ascribed to the influence of the iron. His bowels became irregular, his mind depressed, his general health impaired. He then remarked a cloud in his urine a few hours after passing it; and, on examination, the cloud consisted of mucus with numerous octahedra of the oxalate of lime.

When he presented himself to me, he suffered from all the subjective symptoms described as characteristic of oxaluria. On inquiry, I found that he had read the description of that disease in Dr. Bird's work on 'Urinary Deposits,' at Mr. Pillischer's Microscope Rooms, which he used to frequent as an amateur of the microscope.

On August 21st, I examined the urine from twenty-four hours. It was yellow, acid, and quite normal. The cloud at the bottom contained many octahedra imbedded in the mucus, in which a great number of thread-like vibriones were moving about, particularly at the borders of the mucous masses, where the medium was more dilute, and therefore seemed to allow of their more free movements. They seemed to have a connection with beginning decomposition of the mucus.

Average length of sides of octahedra $= \frac{4}{600}$ of an inch. (See Pl. II, fig. 4, crystals on the upper left.)

Experiment 12.—A part of the urine from the foregoing case was filtered, and some oxalate of ammonia added to it. The deposit obtained after six hours' standing was made up of octagonal crystals. They were more or less regular, became irregular with rough edges and rough surfaces, and then baked together in irregular rough masses. Mixed with those octahedral and irregular crystals were numerous prisms, some with double outlines, some very thin, and others very short. These prisms were very much like those in the first experiment with chloride of calcium. The whole deposit polarized in even so weak a light as that of a composite candle reflected from the mirror of the microscope, and, as usual, the more regular a crystal was, the less did it polarize.

Oxalate of lime in decomposing urine.

Observation 13.—A sample of ordinary yellow, acid urine, from a man enjoying average health, was put in an open beaker, and allowed to stand in my laboratory during six days of cool August weather. After the lapse of that time the cloud, which had settled on the day after it was passed, and had not been microscopically examined, had increased in density; and the urine had become turbid, and covered with a skim, in which there were some vegetable growths perceptible.

The sediment, which was pulverulent, after being shaken, always settled quickly to the bottom of the beaker. It consisted of octahedra of the oxalate of lime, of very small dimensions indeed, so that their true outline was only distinctly visible when perfectly in focus. Mixed with the octahedral forms were irregular small prisms, and few crossed prisms. The crystals frequently appeared as if one side or edge had been eaten out, or had not been perfectly formed. Others were roundish, and corresponded to the lumpy masses of pure artificial oxalate. Some small ellipsoidal bodies were present. Very minute animalculæ, or monads, were in constant motion through the fluid, and appeared as gray, dark points.

On seeing the oxalate sitting firmly on the particles of mucus, as if it had been formed out of them, and seeing only the free sides (planes, angles, and edges) perfectly developed, the other portions turned towards the mucus however always irregular, I could not help thinking that the mucus might have a share in the production of the oxalate.

Crystals of Oxalate of Lime from Urinary Calculi.

Though the greater proportion of the oxalate of lime calculi have an amorphous or only crystalline texture, there are some not very rare specimens, which on their surface are covered with the most perfect crystals. Mr. Quekett kindly afforded me an opportunity of closely examining several such calculi contained in the museum of the Royal College of Surgeons.

C. 34. Presented by Mr. Luke. A reddish brown calculus, is covered with white glistening crystals. They are octahedra, the principal axis of which is not much shorter than the two horizontal ones. The principal axis of the crystals averages in length from about one fortieth of an inch to one eightieth of an inch.

C. 35. Presented by Mr. Luke. In this specimen the

greenish octahedra are very flat, so that the principal axis is not longer than about one third of one of the secondary axes. The sides of the longest crystals measured one eighth of an inch. They are so arranged on the surface of the calculus as to present their lateral edges, the bodies of the crystals being buried in the calculus.

C. 1. Presented by Sir E. Home. This spherical calculus consists throughout of crystallised oxalate of lime. The crystals are smaller, and some octahedra present appearances as if their substance had been arranged in layers horizontal to the principal axis. Here and there the crystals are flattened in the direction of the principal axis, and present the appearance of square plates, sharpened at each of the four sides by two octahedral planes.

Oxalate of lime from plants and animals coincides in its crystallographical characters with the specimens described in the foregoing. All varieties of crystals which I have as yet met with may be brought under one of the following forms:

Quadratic octahedron.—Primary axis always shorter than secondary axes.

Crossed octahedra, or tropias, imitating the appearance of crossed octahedra.

Quadratic octahedron and prism combined.—The same combination, to which a second prism is added.

Crossed prisms.

Triple twins, with tropia.

Modifications of crossed octahedra by a secondary twin tropia, affecting the points of the octahedra.

Contortions and anomalies.—Dumb-bells, being prisms with apposition of irregular matter to both octahedral ends, the prismatic sides frequently to be distinguished.

Polarization of Oxalate of Lime.

I have already remarked that pure oxalate of lime can readily be ascertained to possess the power of polarizing light. But the ordinary oxalate of lime, the octahedra, have a very faint polarizing power, which can only be brought out fully by reflecting a ray of the sun through the crystal lying between the two Nichol prisms, and excluding from the eye every other light but that coming from the crystal in the microscope. In Pl. V, at the bottom of fig. 4, I have represented a large crystal, as it appeared in polarized light. The reader has only to supply by his imagination a bluish-black field round the crystals in order to complete appearances. The figure at the right-hand side represents the large

crystal seen edgeways. The explanation of the fact that the ordinary octahedra polarize very faintly seems to be that, as they are very flat, their principal axis is mostly standing almost perpendicular. Now as a crystal polarizes the less, the more parallel with its principal axis are the rays of polarized light passing through it, it is probable that the octahedra polarize only little because the polarized light passing through them is almost parallel to their principal axis. This may be one reason, though no doubt others co-operate in obscuring the polarization of light by these crystals when ordinarily illuminated.

It is now clear that there is no optical reason for assuming octahedra and dumb-bells to be made up of different materials. And as there is not a shadow of chemical evidence for the supposition that the dumb-bells consist of oxalurate of lime, they must for the present continue to be ranged under the oxalate, with which, indeed, Dr. G. Bird proved them to be identical by the five experiments intended to show that they were oxalurate of lime.

Mode of determining the quantity of Oxalic acid in Urine.

Oxalic acid, which may be present in the urine in a free state, is transformed into a precipitate, by first adding to the urine, previously neutralized by ammonia, some acetic acid, and then a salt of lime, for example chloride of calcium. The precipitate, after several hours' or days' standing, is separated by decantation and filtration. The oxalate of lime thus obtained may be transformed into the sulphate in the manner described at p. 199, or it may be analysed by Hempel's method, given at p. 200.

Pathological indications.

The presence of oxalic acid or any of its compounds in urine may indicate that oxalic acid or any of its compounds has been introduced into the stomach, as an ingredient of food, as a medicine, or as a poison. Though Wöhler had long ago proved that oxalic acid, when taken into the stomach, might reappear in the urine, Schmidt and Lehmann[1] both denied that such was the case. As their doubts could not be allowed to supersede the proofs of Wöhler, Buchheim[2] repeated the experiments of the latter chemist, and had the satisfaction of obtaining their confirmation in every instance.

[1] 'Physiol. Chem.,' Cavend. Edit., i, p. 45.
[2] 'Archiv f. physiol. Heilkunde,' 1857.

In the following I have given the original experiment of Wöhler, and the extensive analyses of Piotrowsky and Buchheim, as illustrations of the manner in which researches on this and other subjects should be conducted.

Wöhler made a middle-sized dog eat two drachms of powdered oxalic acid mixed with meat and bread. After the dog had been killed eight hours later, there were found three ounces of urine in the bladder, which did not appear to be more acid than usual. On the urine becoming cool, there was deposited a considerable quantity of a white powder, consisting of small crystals very much like triple phosphate. On mixing the decanted clear urine with a solution of nitrate of lime, another precipitate of a similar description, and in the same quantity as the first spontaneous one, was obtained. Both precipitates on examination were proved to be pure oxalate of lime. They transformed into carbonate of lime mixed with some charcoal, on exposure to red heat, did not evolve any ammonia by heat or fusion with potash, were quietly soluble in nitric acid, and again precipitated in a crystalline state by ammonia. When heated with a solution of carbonate of ammonia, carbonate of lime was formed, and the filtrate on evaporation yielded a crystalline salt, having all the properties of oxalate of ammonia. Besides these ingredients, the urine contained a considerable quantity of albumen. The precipitate obtained by nitrate of lime most probably contained some phosphate of lime.

Piotrowsky, under Buchheim's directions, has repeated these experiments upon himself. In order to ascertain the degree of accuracy with which oxalic acid in urine could be determined quantitatively, the urine of twenty-four hours, amounting to 987·8 grammes, was mixed with a solution of 1·0 gramme of crystallized oxalic acid, which had before been neutralized by ammonia. The mixture was evaporated to one sixth of its original bulk, strongly acidulated with acetic acid to keep phosphates in solution, and then had some chloride of calcium mixed with it. The precipitate, after standing for several days, was collected on a filter, pressed between bibulous paper, and dissolved in hydrochloric acid; from the solution uric acid was removed by filtration; the filtrate was neutralized with ammonia, and again acidulated with acetic acid. The oxalate of lime thus obtained after filtration and drying, at a temperature of 120° C. (248° F.), amounted to 1·087 grammes, corresponding to 0·931 grammes of crystallized oxalic acid. The same proceeding was adopted in the following experiments:

A. *Free oxalic acid.*—I. Five grammes of crystallized oxalic acid, in doses of 1 gramme each, were taken in the course of five hours, and the urine was collected during twenty-four hours from the beginning of the experiment. It was very turbid after a few hours. When filtered it did yet contain some salts of lime, showing that all the lime was not combined with oxalic acid. The total quantity from the twenty-four hours was 1588·5 grammes, and yielded 0·418 grammes of anhydrous oxalate of lime, corresponding to 0·4115 grammes of crystallized oxalic acid, being 8·23 per cent. of the quantity taken.

II. Seven grammes of oxalic acid were taken in the course of six hours. The thick, neutral urine, whose quantity was 1443·4 grammes, contained the oxalate of lime almost exclusively in the shape of dumb-bells. After it had been evaporated, acidified, and left standing for several days, the filtrate gave no evidence of the presence of lime, but the addition of chloride of calcium produced a fresh precipitate. The first precipitate, free from water, amounted to 0·735 grammes, the second to 0·241 grammes, together corresponding to 0·961 grammes of crystallized oxalic acid, being 13·72 per cent. of the quantity taken.

III. Seven grammes of oxalic acid were taken, as in Exp. II. The urine amounted to 1380·2 grammes; the first precipitate to 0·766 grammes, the second to 0·157 grammes, together corresponding to 0·909 grammes crystallized oxalic acid, or 12·98 per cent. of the quantity taken.

IV. Eight grammes of oxalic acid were taken in the course of several hours. The quantity of the acid turbid urine was 1513 grammes: that of the first precipitate 0·878 grammes; that of the second 0·302 grammes, corresponding to 1·162 grammes of oxalic acid, or 14·52 per cent. of the quantity ingested.

B. *Oxalate of soda.*—V. Seven grammes of oxalic acid were neutralized with carbonate of soda, and the solution was evaporated to dryness. The salt thus obtained was taken in six doses in the course of several hours. The quantity of acid turbid urine voided in the subsequent twenty-four hours was 1678·6 grammes. The spontaneous precipitate amounted to 0·759; the second, artificially produced one to 0·296 grammes, corresponding to 1·039 grammes of crystallized oxalic acid, equal to 14·84 per cent. of the quantity taken.

C. *Acid oxalate or binoxalate of soda.*—VI. Four grammes of oxalic acid were neutralized with carbonate of soda. To the

solution four grammes of oxalic acid were added, and the fluid evaporated to dryness. The residue was taken in several doses. It created considerable thirst, and the quantity of urine rose in proportion to the amount of water drunk, to 2976·3 grammes. The first precipitate weighed 0·883 grammes, the second 0·324 grammes, together corresponding to 1·188 grammes of crystallized oxalic acid, being 14·85 per cent. of that taken.

D. *Oxalate of lime.*—VII. Seven grammes of oxalic acid were neutralized with ammonia, and precipitated with chloride of calcium. The dried precipitate was taken by an individual who had not served for any experiments with oxalic acid. The urine amounted to 1215·4 grammes, was acid, somewhat turbid, and made only a slight deposit, which, under the microscope, consisted of crystals of oxalate of lime, and amounted to 0·105 grammes, corresponding to 0·1034 grammes of oxalic acid, being 1·477 per cent. of the amount ingested. The urine did yet contain some lime in solution. In the normal urine of the same person, which was collected a few days afterwards, and amounted to 1264·4 grammes, no appreciable quantity of oxalate of lime could be detected.

VIII. A second experiment was made with another individual, whose urine under the microscope exhibited a few scattered crystals of oxalate of lime, which could, however, not be determined by weight; seven grammes of oxalic acid, in the form of oxalate of lime, were taken. The urine was more turbid than in the former experiment, and yielded 0·118 grammes of oxalate of lime, corresponding to 0·1162 grammes of crystallized oxalic acid, or 1·659 per cent.

The specimens of oxalate obtained in the last two cases were each exposed to red heat, dissolved in dilute hydrochloric acid, and treated with some chloride of barium. In both an insignificant turbidity ensued, so that they could have contained only very small quantities of gypsum.

The experiments show that large quantities of oxalic acid may be taken with impunity if taken in hourly, or otherwise divided, doses. They do not militate against the fact that oxalic acid, taken in doses of half a drachm to one or two drachms *at a time*, is a deadly poison. They also prove that a part of the oxalic acid in any form, taken in larger and repeated doses, makes its reappearance in the urine, partly as oxalate of lime, partly as a soluble oxalate; but the larger proportion of the oxalic acid taken disappears in the system, without appearing in the urine as carbonate, in cases where the acid

or neutral salt has been taken. The quantity of oxalic acid passing into the urine is not different, if oxalic acid be taken as such, or in combination with alkalies. But if taken in combination with lime, only a small per centage of the oxalic acid reappears in the urine, because the greater part of the oxalate of lime passes unchanged through the intestines, and is discharged with the fæces, as was proved by Magawley and Buchheim[1] in two experiments. In two experiments with oxalate of magnesia, this salt seemed to be decomposed in the intestinal canal in larger quantity than the lime salt. The quantity of lime in the urine after ingestion into the stomach of oxalic acid, or its salts, is neither increased nor diminished.

The following table perspicuously exhibits the results of the above observations:

No. of experiment.	Form in which Oxalic Acid was taken.	Quantity of Oxalic acid taken. ($C_4H_2O_8 + 4HO$.)	Per centage in the Urine of Oxalic acid taken.	Spontaneous precipitate of Oxalate of Lime, anhydrous.	Lime from spontaneous Oxalate.	Oxalate of Lime from soluble Oxalate.
I.	$C_4H_2O_8 + 4HO$.	5·0	8·23	0·418		
II.		7·0	13·72	0·735	0·322	0·241
III.		7·0	12·98	0·766	0·335	0·157
IV.		8·0	14·52	0·878	0·384	0·302
V.	$2NaO, C_4O_6$.	7·0	14·84	0·759	0·332	0·296
VI.	$\left.\begin{matrix}NaO\\HO\end{matrix}\right\} C_4O_6 + 2HO$.	8·0	14·85	0·883	0·386	0·324
VII.	$2CaO, C_4O_6 + 4HO$.	7·0	1·477	0·105		
VIII.		7·0	1·659	0·118		

The presence in the urine of any considerable quantity of oxalic acid, in any form, for a longer period of time, during which the ingestion of oxalic acid, in any form, into the stomach was excluded, indicates the existence of a disorder, the nature of which is, at present, entirely unknown. This disorder, to which the names of oxalic acid diathesis and oxaluria have been applied by systematic ontologists, has a great tendency to the production of oxalate of lime concretions in the urinary passages. It is not ascertained whether the oxalic acid in these cases is formed in the circulation, or only in the urinary passages, by a peculiar kind of fermentation of some normal or abnormal ingredient of the urine.

[1] Loc. cit., p. 240. See further on this subject, Orfila, 'Toxicologie gén,' 1843, i, 187.

Oxalate of lime is frequently found, in not very small amounts, in the urine of patients recovering from severe diseases.[1] Thus, Kletzinsky[2] examined the first urine, after the attack, of three cholera patients, and every specimen contained oxalate of lime. Its quantity was ascertained by collecting the deposit of oxalate and any precipitate produced by a lime-salt on a filter, and, after washing, dissolving it in hydrochloric acid. To the solution chloride of gold was added, and the mixture boiled, until no further reduction took place. From the weight of the brownish-violet, dicroic precipitate of metallic gold, the quantity of oxalic acid present in solution was calculated upon the basis of $31\,Au = 30\,(C_2O_3 + HO)$.

The first urine of the first patient measured 457 cub. cent., and contained 278 milligrammes, or 0·6 per mille, of oxalic acid.

The first urine of the second patient measured 460 cub. cent., and yielded 58 milligrammes of oxalic acid, or 0·125 per mille. Thirteen ounces of urine contained three quarters of a grain of oxalic acid.

The first urine of the third patient, 463 cub. cent., yielded 117 milligrammes, or 0·25 per mille, of oxalic acid. Thirteen ounces contained a grain and a half of the acid.

The presence in urine of such small microscopical traces of oxalate of lime, that their quantity cannot be estimated by quantitative analysis, is of no practical or pathological importance. The question after their origin is one of the greatest difficulty and the smallest use, and therefore I do not propose here to discuss it.

The presence of oxalate of lime in the urine may indicate disease of the kidney, with which it is not rarely associated. The relations between the oxalate and the kidney disease are, however, most uncertain. For, whereas the experiment of Wöhler shows that large quantities of oxalic acid passing the kidneys may so irritate them as to produce the appearance of albumen in the excretion, it is not unreasonable to think that, in some cases of disease or poisoning, a similar relation might exist. But these investigations are surrounded with many difficulties, which make speculation more than ordinarily dangerous.

The following case is one in which considerable quantities of oxalate of lime were present in albuminous urine of a patient, who succumbed to disease of the kidneys.

[1] Walsh, 'Month. Journ. of Med. Science.,' Jan., 1849.
[2] S. H. Flamm, 'Cholera und Vergiftung,' Wien, 1856, p. 4.

R. D—, æt. 30, the wife of a policeman. She had been for some time under the treatment of Dr. Smiles, and improved considerably. Her illness she dates from the time of her last confinement, which was very severe, and caused prolapsus uteri. About six weeks ago, the urine became turbid, and she got very weak and thin; her feet swelled, her body emaciated, and the emaciation was the more apparent as she was pregnant in the sixth month. She had an abscess at the outer side of the middle of her left thigh.

Her tongue was very foul, covered with a thick, white fur, and yellowish-brown in the middle. She had little appetite, and could not fancy anything. Her bowels were regular. She was very thin indeed; abdomen very prominent; her feet were excessively swollen, particularly so over the instep. The urine was turbid on making, and became still more so on standing. She said it was dark, and like blood sometimes. The abscess discharged a thin pus.

Urine of May 15th.—Loaded with the urate of ammonia. Reaction decidedly acid. Specific gravity, at the temperature of the body, 1017. It did not become clear, but made a sediment, which became more apparent, and subsided more readily to the bottom when the urine was mixed with twice its bulk of warm water, and allowed to stand in warm water. The deposit, when examined under a power of 400 diameters, consisted of an immense number of small crystals of octahedral oxalate of lime, with which there was a certain proportion of small and large dumb-bell-shaped crystals or bodies mixed up. Epithelial scales and granular casts of the tubules of the kidneys were present in numbers. (See Plate V, fig. 6.)

A part of the urine was then filtered and warmed, whereupon it became perfectly clear. On being now heated, it became slightly turbid, and on the addition of a few drops of nitric acid, the fluid became of a dark colour, and the turbidity assumed the appearance of flakes.

℞ Mist. Ferri c. Quinin., ter die.

She states the quantity of urine to have been very small a few weeks ago, only one or two table-spoonfuls having been passed at a time, and that not very frequently.

May 19th.—I was summoned this morning to the patient, who during the night had been attacked by sickness and vomiting. I found her perfectly prostrate, crouched up in her bed, throwing her clothes about in a restless manner. She complained of pain at the back of her head and neck, of pain in her stomach, and particularly across her loins. She was incoherent in her replies, grasping the hand which was approached to feel her pulse. The latter was excessively weak, respiration frequent, evidently blood-hunger, viz., there was more air in the lungs than the heart could drive blood into them to absorb. The vomiting had been very severe, and the retching had continued for several hours from two o'clock last night. I saw the colour of bile on her night-gown.

In the afternoon she had got worse, being apparently unconscious, and only at intervals recognising her relatives. Her limbs were in a constant spasmodic action, like severe fidgets, and the levatores angulorum oris were in that peculiar spasmodic action, which constitutes a feature of the sardonic grin, or of incipient tetanus. Pulse weak, irregular; extremities cold.

She had twice made water that day. Both specimens intensely acid, contained abundance of octahedra and dumb-bell crystals, casts, and albumen.

She died in the evening.

Post-mortem examination, May 20th, afternoon.—I was assisted by Mr. J. Paul, the resident medical officer of the St. Pancras Royal General Dispensary. The emaciation of the body was extreme, a skeleton covered with parchment. Abdomen very prominent; dry sore at the outer side of the middle of left thigh; feet somewhat œdematous, particularly over instep. Slight rigor mortis.

The pericardium, which contained some serum, was then opened. All the blood-vessels going from or to the heart were then ligatured twice. The heart was then removed, and both sides were emptied of their contents in such a manner as to keep venous and arterial blood separate. Both were fluid, and of a dark crimson-lake colour. There were some fibrinous coagula in the cavities

of the heart, having the appearance and colour of the yellow fat of hot roast-beef. The heart itself was excessively thin and flabby, brownish-red, and the tissue in a sort of broken-up condition, a degeneration in which the muscular fibres divide into the elementary fibrils, which appear at the broken end of a fibre like the hair on the end of a painting brush. There was some fatty and some other granular matter, besides numerous nuclei deposited in the substance of the fibres; the heart was very tearable. The lungs were then taken out, after the blood from their veins and that from the upper cava had been collected separately, being taken with spoons out of the pericardium. This too was very thin, and perfectly fluid. The lungs appeared sound in structure, with the exception of a few hard nodes on the tops, particularly the left top, which appeared like contracted scars of healed-up cavities. Some few small tubercles were present. With these exceptions, the lungs themselves were sound in structure; but they adhered to the thorax. The thoracic aorta was somewhat filled with fluid blood.

The stomach contained some medicine, port wine, and mucous matter; the small and large intestines presented nothing peculiar. The liver was large, and showed signs of hepatic venous congestion (nutmeg liver). It was taken out with all its vessels ligatured, to retain the blood in the organ. The spleen and pancreas showed nothing particular. The kidneys were of ordinary size, perhaps, a little thicker than usual. In the pelvis, they contained a smeary mass, covering the pyramids and lining, consisting of tubular epithelium and casts, fatty matter, and softened epithelium of the calyces. But no trace of oxalate of lime crystals, either in dumb-bells or octahedra, could be discovered. On a section of the kidneys being made, they exhibited several of their pyramids in fatty degeneration and atrophy, an appearance which was verified by the microscope. The tubular epithelium was fatty. The Malpighian corpuscles were normal in size and condition, and their numbers did not seem to be diminished, except, perhaps, over the fibrous parts, where they could not be detected.

The womb contained a fœtus of four months. Some of the liquor amnii was collected, as also some of the blood of the fœtus.

There was no stone in the bladder, of which also there had been no symptoms during life.

The blood showed a degree of leukocythosis, a large excess of white blood-corpuscles being present. After two days' standing in the corked bottles it coagulated, and permitted the clear serum to be decanted from the cake. This fact deserves attention, for the cases in which fluid blood is found in the great vessels (heart included) not being rare, and there being frequently no opportunity for letting a sample of the blood stand for a day or two, in order to test it upon its coagulability, the blood may easily be put down as absolutely not coagulable, while the coagulation is only delayed by the peculiar condition of the fluid, and takes place much as usual, only after a certain lapse of time.

The decanted serum was dried in the water-bath, and preserved in a well-corked bottle for future examination. Another quantity of blood, that contained in the ascending cava, the hepatic veins, and the portal vein, was mixed with water before it had time to coagulate; this contained fibrine, serum, and blood-corpuscles in solution. This was immediately subjected to chemical analysis.

The bile, gall-bladder, or its mucus and mucous membrane, showed no traces of oxalate crystals, even after several days' standing, and repeated examinations.

There were no crystals in the liquor amnii, nor in the mucus from the surface of the child, the inner surface of the womb, nor in the meconium, which had passed into the liquor amnii. In short, in no part of the body (bladder unexamined) were any crystals detected. I was induced to this examination by u statement of C. Schmidt, who found the oxalate octahedra in the womb and gall-bladder of certain cases.

The analysis of the blood, which was conducted with great care, and which it would serve no purpose here to detail, *yielded no evidence of the presence of oxalic acid.*

Concretions of Oxalate of Lime.

Sand and gravel.—Small concretions of oxalate of lime of the size of uric acid sand (see p. 110), are rarely, if ever met with. But there is a variety of oxalate of lime concretions, of small size, pale colour, and smooth surface, and usually containing some urate of soda. They are most frequently found in the calyces of the kidneys, and being many in number they exhibit the effects of prolonged attrition. These concretions, termed *hemp-seed* calculi, or gravel, are not seldom passed by elderly persons after severe nephritic attacks characterising the passage through the ureters of concretions.

Renal concretions of oxalate of lime are frequently of a very large size, particularly when uric acid has supervened. According to Prout, the pain and derangement caused by oxalate concretions in the kidneys usually assume different characters from the pain and derangement attending lithic acid concretions. The pain is generally of a more acute character; and though principally referred to a particular spot over the region of the kidney, is often discursive, and shoots in the direction of the ureter, epigastrium, or shoulder.

The same author observed, that renal hæmorrhage, referable to concretions, had become very much more frequent after two epidemics of cholera in London. It remains to be ascertained, whether the occurrence of oxalate of lime in the urine of cholera patients had any share in the production of these concretions.

Calculi of Oxalate of Lime.

The purest concretions of oxalate of lime are the white crystallized variety, of which I have already noticed three specimens preserved in the Museum of the Royal College of Surgeons. Such a calculus is represented by Prout, on Plate V, fig. 7*. The mode in which the large crystals are deposited on these calculi, leaves no doubt of their having been formed in the bladder from a solution of oxalic acid and lime. On a section, these and the crystalline calculi exhibit peculiar crystalline fibres, running from the centre in irregular curved lines towards the periphery, and mostly ending in the projections which give these calculi their peculiar uneven surface. Though layers may be distinguished,

yet they are not so distinct, nor so regular, as in the uric acid concretions.

The peculiar tuberculated surface of the smaller variety of the oxalate of lime concretions has caused the name of *mulberry calculi* to be applied to them.

The colour of those oxalate of lime calculi which are of more frequent occurrence than the white crystallized variety is generally deep brown, sometimes approaching to very dark olive-green. This olive-green shade is also exhibited by most microscopical crystals. In some calculi the colour becomes brownish-black. These calculi are mostly very hard.

Layers of Oxalate of Lime in alternating and mixed calculi.

The most simple alternating calculus to be here considered is an oxalate of lime stone, with a crust of phosphate of lime, or mixed phosphates. This phosphatic crust is the produce of the decomposition of urine caused by the presence of the calculus in the bladder, it is the consequence of mechanical disease. Calculi, in which a nucleus of the oxalate, however large, is surrounded by a body of uric acid, suggest a different history. Here, the condition of the urine, which gave rise to the oxalate concretion, must have changed into the acid fermentation. The reverse is the case in calculi having a uric acid nucleus, and one or more layers of oxalate of lime. A nucleus of oxalate of lime may be surrounded by a mixed body, generally consisting of oxalate of lime, uric acid, and urates, rarely of cystine and phosphates. Most mixed calculi, or mixed layers of alternating calculi, contain smaller or larger quantities of oxalate of lime.

Chemical characters of Oxalate of Lime concretions.

The powder of such a concretion is not affected by acetic acid; dilute mineral acids, however, dissolve it without effervescence. From the latter solution it is precipitated by an excess of ammonia. A small piece of the concretion heated before the blowpipe, at first becomes black, from the admixture of a variable, but always small, quantity of organic matter, mostly urates and epithelium. It then becomes white, and ultimately leaves a bulky residue, which when moistened with water exerts an alkaline reaction on red litmus paper, and effervesces with acids. The residue is therefore carbonate of lime, with an admixture of caustic lime.

Statistics of Oxalate of Lime concretions.

The general proportion of calculi into the nucleus of which oxalate of lime largely enters, in all the museums, is as 1 : 4⅓; which is equivalent to saying, that if a mulberry stone had not been formed and detained in the bladder, two persons out of about nine who suffer from calculus would not have been troubled with that affection. The general proportion of calculi consisting essentially of oxalate of lime to all other calculi is as 1 to 15. The ratio in which in alternating calculi the oxalate of lime succeeds to uric acid, is as 1 to 15⅔; on the contrary, the ratio in which uric acid succeeds to oxalate of lime is as 1 to 13⅔. Hence the alternation of the two ingredients may be considered as nearly equal. The oxalate of lime succeeds to the urate of ammonia more frequently than to uric acid. Thus the ratio in which the oxalate of lime succeeds to the urate of ammonia is 1 to 9⅝. On the contrary, the ratio in which the urate of ammonia succeeds to the oxalate of lime, is only as 1 to 38; a very striking distinction. The phosphates succeed to the oxalate of lime in the proportion of 1 to 7½, and the proportion in which the oxalate of lime succeeds to the phosphates is as 1 to 253⅓ only. (Prout.)

CHAPTER XLIII.

LACTIC ACID.

Formula: $2HO . C_{12}H_{10}O_{10}$, or $C_{12}H_{10}O_8 \left.\begin{matrix}\\ H_2\end{matrix}\right\} O_4$.

Composition in 100 parts:		
	Carbon . .	40·00
	Hydrogen .	6·67
	Oxygen . .	53·33
		100·00

Occurrence.

The name of this acid is derived from its occurrence in sour milk. It is found in the juice of the muscles of man and animals. It has been found in the urine under various circumstances by Lehmann; other chemists, however, *e. g.*, Liebig, Pelouze, and Gregory, have never been able to find it in urine. Under certain conditions it is formed during the fermentation of sugar, and consequently is found in many fermented acid liquids, particularly the juice of sauer-kraut, or fermented cabbage, a dish which is peculiar to the Germans.

Mode of obtaining it pure.

Lactic acid may be produced from alanine, by treating this artificial base with nitrous acid.

$$\underbrace{2(C_6H_7NO_4)}_{\text{Alanine}} + 2NO_3 = \underbrace{C_{12}H_{12}O_{12}}_{\text{Lactic acid.}} + 4N + 2HO.$$

By the artificial fermentation of sugar, lactic acid may be obtained in large quantities. The following prescription of Bensch[1] is very profitable: 6 parts of cane-sugar, $\frac{1}{16}$th part

[1] 'Ann. d. Chem. und Pharm.,' lxi, p. 174.

of tartaric acid, 8 parts of sour milk, ½ part of old cheese, and 3 parts of levigated chalk, are mixed with 26 parts of water and exposed to a temperature of 32° C. (90° F.) In the course of ten or twelve days the mixture is transformed into a semisolid mass of lactate of lime. This is boiled with 20 parts of water and $\frac{1}{16}$th part of caustic lime; the mixture is filtered while boiling hot, and then gently evaporated. From the concentrated solution lactate of lime in granules is obtained after some days' standing. The salt is collected in a calico bag, and pressed in several folds of linen, to free it from the mother-liquor. It is then again dissolved in twice its weight of water, and decomposed with $\frac{7}{32}$ parts of sulphuric acid. The precipitated gypsum is removed by filtration, and the acid fluid saturated with $\frac{3}{10}$ths of carbonate of zinc. The crystallized zinc salt is then decomposed by sulphuretted hydrogen, and the filtrate is evaporated by heat, lastly in vacuo. The lactic acid thus obtained may be further purified by solution in ether.

Liebig's method of obtaining lactic acid from the juice of flesh.—The mother liquor from which creatine has crystallized, is evaporated a little more, and then gradually mixed with small portions of alcohol, until it assumes a milky turbidity. After a few days' standing the inosinates have crystallized. The mother-liquor from this crystallization is again evaporated in the water-bath, and the residue treated with alcohol, which dissolves all the lactates. The solution is separated from the insoluble syrup, and the alcohol is evaporated to a syrupy consistence. This syrup is now mixed with an equal volume of dilute sulphuric acid (composed of one volume of concentrated acid and two volumes of water), or with a solution of oxalic acid of equal strength; of the latter so much must be added that a crystalline precipitate ensues. The mixture is immediately treated with three or four times its volume of alcohol. The sulphates and oxalates are thereby precipitated, lactic acid remaining in solution. To this solution ether is added, until the addition of a new portion does not produce a fresh turbidity. The precipitate is separated from the fluid by filtration, the filtrate freed from alcohol and ether by distillation and evaporated on the water-bath to a syrupy consistence. This syrup is mixed with half its volume of alcohol, and then five times its volume of ether is added, whereby an almost pure solution of lactic acid in ether is obtained. The ether is evaporated, the residue is treated with milk of lime; the lactate of lime obtained after filtration and evaporation is washed with alcohol, and by re-crystallization, and, if necessary, treatment with

animal charcoal, is obtained perfectly pure. From it lactic acid may be obtained as above.

Mode of ascertaining the presence of Lactic acid in Urine.

The urine is evaporated on the water-bath to a syrupy consistence, and the residue treated with an alcoholic solution of oxalic acid. Oxalate of lime, potash, soda, and urea, are thereby precipitated; the solution contains hydrochloric, phosphoric, and oxalic acids, and, if any be present, lactic acid. This solution is now treated with an excess of hydrated oxyde of lead, and the precipitate of chloride, phosphate, oxalate, and the excess of the oxyde of lead is separated from the fluid by filtration. The fluid, containing lactate of lead, is treated with hydrothion, and the filtrate after boiling with oxyde of zinc and filtration, on evaporation and standing, yields crystals of lactate of zinc. From this different salts, or the acid itself, may be prepared.

In consequence of the extremely minute quantities of lactic acid to be obtained from the animal fluids, Lehmann adopts the following method, with a view of studying the forms of the different salts under the microscope. The impure lactic acid from the alcoholic extract of the matters treated with sulphuric or oxalic acid, is treated with baryta water, and the excess of the baryta removed by carbonic acid; the solution of lactate of baryta is evaporated to the consistence of a syrup, treated with alcohol, filtered, again evaporated, and then allowed to stand for some time, in order that any other baryta salts may crystallize. If butyric acid were present in the urine, it would at this stage be obtained from the solution. The filtrate, or, if there was no crystallization, the fluid, is dissolved in water, and decomposed with a solution of gypsum; the fluid from which the sulphate of baryta has been removed by filtration is strongly concentrated, and, on examining it under the microscope, the double brushes of lactate of lime may be easily distinguished from the crystals of gypsum. On dissolving these crystals of lactate of lime in alcohol, and adding sulphate of copper to the alcoholic solution, the fluid, after standing for some time (in order that the excess of sulphate of copper and the gypsum that is formed may separate as completely as possible), is evaporated so as to crystallize, and the crystals of lactate of copper are then microscopically examined. If, by the above process, we do not obtain distinct and measurable crystals,

we must dissolve the residue in a little water, and, after boiling it to remove any butyric acid that may yet remain behind, filter and concentrate it. Into this concentrated solution of lactate of copper a small bar of zinc is placed. The zinc soon becomes covered with crystals of lactate of zinc, which may be identified under the microscope. If an accurate crystallometric investigation cannot be instituted, we must precipitate the solution of the zinc salt with a boiling solution of protochloride of tin, and allow it to stand for some time; on then making a microscopical examination, we shall find clusters of crystals, in groups of thick rhombic plates, lying close upon each other. The demonstration of the different salts may thus serve to show the presence of lactic acid. If there be sufficient material, the atomic weight may be determined. But where all the above proofs are present, an elementary analysis will hardly be required.

Physical and Chemical properties.

Lactic acid is a colourless, syrupy liquid, of a strongly acid taste. Its specific gravity is 1·215. It is soluble in any proportions in water, alcohol, and ether. When its solution in water is heated, a part is volatilized with the vapours of water; the greater part of the acid, however, remains, and, at a temperature of 130° C. (266 °F.), loses two equivalents of water, and is thereby transformed into the anhydrous modification, which on cooling solidifies into a firm, yellowish mass. This fuses already at a temperature below 100° C. (212° F.); when boiled with water, it becomes again converted into the ordinary hydrated lactic acid. If the acid is heated to 260° C. (500° F.) the loss of four equivalents of water transforms it into *lactide* ($C_{12}H_8O_8$). This substance occurs as a sublimate, and from its alcoholic solution crystallizes in white, glistening, rhombic plates. When kept in contact with water for some time, it is also converted into lactic acid. On being heated rapidly, lactide is decomposed into aldehyde and carbonic oxyde, according to the formula

$$C_{12}H_8O_8 = 2(C_4H_4O_2) + 4CO.$$

This has led to the conclusion, that lactic acid might be a copulated compound of aldehyde and formic acid, according to the formula

$$C_{12}H_{12}O_{12} = 2(C_2H_2O_4 + C_4H_4O_2).$$

When lactic acid salts are left in contact with putrefying bodies at a temperature of from 30° to 35° C. (86° to 95° F.)

the acid is transformed into butyric acid under evolution of carbonic acid and hydrogen, according to the formula

$$2CaO \cdot C_{12}H_{10}O_{10} + HO = CaO \cdot C_8H_7O_3 + CaO \cdot CO_2 + 4H + 3CO_2.$$

Compounds.

With bases lactic acid forms neutral salts of the composition

$$2MO \cdot C_{12}H_{10}O_{10}, \text{ or } \left.\begin{matrix} C_{12}H_{10}O_8 \\ M_2 \end{matrix}\right\} O_4,$$

and acid salts of the composition

$$MO \cdot HO \cdot C_{12}H_{10}O_{10}, \text{ or } \left.\begin{matrix} C_{12}H_{10}O_8 \\ HM \end{matrix}\right\} O_4.$$

There are also some basic salts.

Lactate of lime, $2CaO \cdot C_{12}H_{10}O_{10} + 10\,HO$, crystallizes in granular masses, which under the microscope present a radiary arrangement of needles, and are little soluble in cold water and alcohol, but soluble in all proportions in these fluids at the boiling heat.

Lactate of zinc. $2ZnO \cdot C_{12}H_{10}O_{10} + 6HO$.—This salt is soluble in 58 parts of cold and 6 parts of boiling water. From such a concentrated hot solution it crystallizes easily on cooling in form of four-sided prisms, with oblique terminal planes.

Lactate of copper. $2CuO + C_{12}H_{10}O_{10} + 4HO$.—It crystallizes in sky-blue little warts, and is soluble in water and alcohol.

The lactates obtained from the juice of flesh exhibit some differences from the lactates obtained by other proceedings, which has led to the conclusion that there are two modifications of lactic acid present in the respective salts, the one from flesh being a monobasic, the other, obtained by the fermentation of sugar, being a bibasic acid. It has been suggested that the former might be composed according to the formula $C_6H_6O_6$.

Lactate of lime from the juice of flesh is very similar to the ordinary lactate of lime in its external appearance. It contains, however, only 8 equivalents of water of crystallization. It is also less soluble in water than the ordinary salt.

Lactate of zinc from the juice of flesh contains only 4 equivalents of water, and is much more soluble in water and alcohol than the ordinary lactate of zinc.

Pathological indications.

I have already mentioned the most important circumstances, normal and pathological, under which lactic acid is found in various parts of the economy. Its occurrence in urine is extremely variable, according to Lehmann,[1] upon whose researches I have mainly relied in this paragraph.

In all cases where the supply of lactates to the blood is very great,—whether this depends on an excess of acid being formed in the muscles, or on the use of a diet tending to produce it, or an imperfect process of oxydation in the blood,—lactic acid may be detected in the urine. Hence in the urine of the same individual, lactic acid may on one day be present, and on another absent. In the urine of many persons, no lactic acid can be detected; and in the urine of others again (especially of persons who, in consequence of repeated catarrhs, suffer from partial relaxation of the pulmonary tissue), it is constantly present. Stall-fed animals, living on amylaceous fodder, excrete lactic acid by the kidneys, while under other conditions this acid cannot be detected in their urine. In most febrile diseases lactic acid may be recognised in the urine.

Urine containing a considerable quantity of oxalate of lime almost always contains some lactic acid at the same time. Scherer[2] and Marchand[3] have sometimes observed a considerable amount of lactic acid in the urine of rachitic children, and Lehmann noticed it in the osteomalacia of adults.

If urine is to be examined for lactic acid, it must be quite fresh. For, since it has been shown by Scherer that, on exposure of urine to the atmosphere, there occurs a gradual augmentation of the free acid, which is mostly lactic acid, it might be possible to mistake a produce of the first stage of the acid fermentation of urine for a produce of the organism. Diabetic urine produces lactic acid very quickly and in large quantities. Now, as all urine contains indican, which under certain circumstances may be transformed into sugar and other products, the formation of lactic acid in any urine is possible; in this way also, the occurrence of acetic acid in all putrefied urine seems to find an explanation. It is also probable that the butyric acid found once or twice in urine was a product of the further decomposition of a lactate.

[1] 'Physiol. Chemistry,' Cavendish Soc. Edit., vol. i, p. 92, et seq.
[2] 'Untersuchungen zur Pathologie,' p. 74, et seq.
[3] 'Lehrbuch der Physiologischen Chemie,' p. 105.

The presence of lactic acid in fresh urine may indicate that acid fermentation is taking place in the urinary passages. In these cases there may be a deposit of uric acid, either already formed in the kidneys or bladder, or produced soon after emission.

CHAPTER XLIV.

UROPHANIC ORGANIC ACIDS.

Under this head I wish to bring to the notice of the reader a series of organic acids which never appear in the urine as products of the organism, but as substances simply passing through the body without undergoing destruction. Of some acids only a small proportion reappears in the urine, after the ingestion of large doses into the stomach. The same acids when introduced in small quantities are entirely oxydized in the body, and their salts appear in the urine as the carbonates of the respective bases. In this sense, oxalic and lactic acid, as we have already seen, may sometimes be called urophanic acids. But as they may be products of a morbid process of the organism as well, they do not exclusively belong under this class, and have therefore been treated of separately. Besides the acids which may be totally oxydized in the body, or of which a small proportion only may appear in the urine, we have to notice acids of which the entire amount appears either unchanged, or partially changed, or combined. Gallic acid seems to pass unchanged through the body; tannic acid is transformed into gallic and pyrogallic acid; salicylic acid, imitating benzoic acid, combines with glycocoll, and appears in the urine as salicyluric acid. The occurrence of these substances in urine is mostly accidental, and dependent upon the inspiration of some experimenter, only one or two being administered as medicines.

It would be exceeding the limits of usefulness of this treatise, were I to give the chemical properties of all the acids in detail, together with the methods by which they are detected in the urine. The older facts are therefore summarily given; the newer ones, however, I have given a little more extensively when relating to substances of importance. These remarks I wish also to apply to the manner in which

the other chapters on urophanic substances have been treated.

The first extensive researches on the changes which substances introduced into the stomach undergo or not undergo before they reappear in the urine, were instituted by Wöhler.[1] Many urophanic substances were investigated by Wöhler and Frerichs[2] conjointly, and by Heller and Kletzinsky, who contributed many papers in the six volumes of Heller's 'Archiv.' The rest of the observations were made by sporadic observers, whom I shall have an opportunity of quoting under the several articles.

1. SUCCINIC ACID.

Formula: $2HO \,.\, C_8H_4O_6$, or $\left.\begin{matrix} C_8H_4O_4 \\ H_2 \end{matrix}\right\} O_4$.

Succinic acid was found by Wöhler in the urine of a dog, to whom he had given half a drachm of the acid. Kletzinsky[3] also found succinic acid in the urine when he had taken a salt of it. Buchheim, on the contrary, could never find any trace of succinic acid in the urine, no matter whether it was taken in the form of salt or free, and in large quantities. The amount of hippuric acid was, however, found to be considerably increased, an observation also made by Dr. W. Kühne.[4]

2. MALIC ACID.

Formula: $2HO \,.\, C_8H_4O_8$, or $\left.\begin{matrix} C_8H_4O_6 \\ H_2 \end{matrix}\right\} O_4$.

Magawly took 30 grammes of neutral malate of lime, and in another experiment the same quantity of a mixture of neutral and acid malate of lime. In both cases the urine was normal and acid, and contained no trace of malic acid.

[1] Tiedemann and Treviranus, 'Zeitschrift für Physiologie,' vol. i, p. 125.
[2] 'Ann. d. Chem. und Pharm.,' lxv, p. 335.
[3] Heller's 'Archiv,' vol. vi, p. 95.
[4] Virchow's 'Archiv,' vol. xii, 1857, p. 400.

3. TARTARIC ACID.

Formula: $2HO \,.\, C_8H_4O_{10}$, or $\left.\begin{matrix} C_8H_4O_8 \\ H_2 \end{matrix}\right\} O_4$.

Occurrence.

This acid occurs in young wines in the form of potash salt. As it is never a product of the organism, it can only occur in the urine after ingestion into the stomach. It is therefore a merely accidental ingredient of urine, without any pathological significance. Its physiological bearing is however important, and I therefore thought it useful to record the following experiments on its reappearance in urine after ingestion.

Experiments on the reappearance of Tartaric acid in Urine after ingestion into the stomach.

Wöhler caused a dog to eat two drachms of powdered tartaric acid, mixed with bread and meat. The dog was killed six hours later. The bladder contained four ounces of urine, which on cooling deposited a large quantity of small white crystals, similar to oxalate of lime in the first experiment, with oxalic acid. By precipitation of the urine by means of nitrate of lime, another quantity of the same precipitate was obtained, which, together with the first one, amounted to more than half a drachm. On exposure to red heat the precipitate evolved the peculiar odour of burning tartrates, and left a residue of carbonate of lime mixed with some charcoal. Having observed oxalic acid pass into the urine, Wöhler believed the tests just detailed to be sufficient evidence of the presence of tartaric acid, in the form of tartrate of lime. The urine was more than usually acid, and contained no albumen.

Of the tartrates, Wöhler experimentalised with tartrate and bitartrate of potassa, tartrate of potassa and boracic acid, tartrate of potassa and soda, or Seignette salt, all of which, when taken in doses from one to three drachms, made the urine alkaline. When cream of tartar had been taken, the urine contained no tartaric acid while it was alkaline, but on again becoming acid, the acid could easily be detected by adding to the urine some nitrate of

lime, which would cause a precipitate of tartrate of lime to be recognised as a tartrate by the peculiar odour on burning.

The precipitate obtained by Wöhler must have contained phosphate of lime. The test for tartaric acid by the odour of the burning salt is also not always sufficiently characteristic, being masked by the odour of adhering urinary matters. For this reason, Buchheim adopted the following proceeding for discovering tartaric acid in urine. A day's urine, amounting to 1010·3 grammes, was mixed with one gramme of tartaric acid, previously neutralized by ammonia, and the mixture treated with chloride of calcium and ammonia. The precipitate formed hereby was quickly removed by filtration. It consisted of phosphate of lime, and did not contain any tartrate of lime. The filtrate was evaporated to $\frac{1}{10}$th or $\frac{1}{12}$th of its bulk and put aside for six or eight days. The precipitate which had formed after the lapse of that time was separated by filtration, washed, dissolved in dilute hydrochloric acid, which left the greater part of the sulphate of lime undissolved; the solution was next neutralized with ammonia and acidulated with acetic acid until the precipitate produced by the ammonia had disappeared. After the lapse of six or eight days, the tartrate of lime, which is very little soluble in acetic acid, had crystallized in large and small crystals. They were dried at 100° C. (212° F.) and weighed, and in this case amounted to 1·212 grammes, corresponding to 0·699 grammes of crystallized tartaric acid, instead of 1·0 gramme originally added to the urine.

A. Free tartaric acid.—I. Buchheim took repeated two- or three-gramme doses of tartaric acid, at intervals of half an hour each. After having taken about ten grammes, borborygmi made their appearance, and when 19·6 grammes had been used a fluid motion of the bowels occurred, followed by two others a little later. The fluid fæces contained alkaline carbonates, but no tartaric acid. The urine from twelve hours amounted to 1047·6 grammes, and yielded 0·604 grammes of tartrate of lime, corresponding to 0·349 grammes of crystallized tartaric acid, or 1·78 per cent. of the amount taken.

II. Piotrowsky took 20·0 grammes of tartaric acid in the course of twelve hours. There were borborygmi, but no motions. The urine from twenty-four hours amounted to 996·2 grammes, and yielded 0·653 grammes of tartrate of lime, corresponding to 0·377 grammes of crystallized tartaric acid, or 1·88 per cent.

III. The same gentleman took 30·0 grammes of tartaric acid in the course of fifteen hours. The urine had quite the ordinary appearance, and amounted to 1241·7 grammes. After removal of the phosphates, some crystals of tartrate of lime appeared on evaporation. The total of tartrate of lime obtained amounted to 1·138 grammes, or 3·79 per cent.

IV. 30·0 grammes, taken in larger doses and at shorter intervals, caused relaxation of bowels. The fæces were as in Experiment I. The urine, 1140·3 grammes, was of ordinary condition, and yielded 1·702 grammes of tartrate of lime, corresponding to 0·982 grammes of tartaric acid, or 3·27 per cent.

V. Another individual took 10·0 grammes of tartaric acid. The urine amounted to 2123·6 grammes, and was as usual. The quantity of tartrate of lime found was 0·254 grammes, corresponding to 0·147 grammes of tartaric acid, or 1·47 per cent.

VI. A woman, forty-five years of age, suffering from erysipelas of the right forearm, took 10·0 grammes of tartaric acid in several doses. The normal urine weighed 851·2 grammes, and yielded 0·496 grammes of tartrate of lime, corresponding to 0·286 grammes of tartaric acid, or 2·86 per cent.

VII. Piotrowsky took 5·0 grammes, divided in three doses. The urine, 963·4 grammes, had a strongly acid reaction. It yielded 0·164 grammes of tartrate of lime, or 0·095 grammes of crytallized tartaric acid, or 1·89 per cent.

VIII. Of 2·0 grammes of the acid taken in small doses in the course of ten hours no trace reappeared in the urine.

Bitartrate of potash.—IX. 45·0 grammes of bitartrate were taken in three portions, at intervals of four hours. The urine became alkaline only after the last dose, and so strongly alkaline as to cause violent burning in the urethra on being passed. The total quantity of urine amounted to 1251·7 grammes, and was strongly alkaline, so as to effervesce on the addition of acids. There were obtained 0·623 grammes of tartrate of lime, equal to 0·359 grammes of tartaric acid, or 1·0 per cent.

X. 60·0 grammes of the bitartrate were taken in doses of 15 grammes, in the course of nine hours. The urine became alkaline in three hours and a half, and amounted to 2039·0 grammes. It yielded 1·535 grammes of tartrate of lime, corresponding to 0·886 grammes of tartaric acid, or 1·85 per cent.

Neutral tartrate of potash.—XI. Piotrowsky took 30·0 grammes of neutral tartrate in three doses. Soon afterwards diarrhœa ensued, but the fæces contained only carbonic, no tartaric acid. The urine became soon alkaline, and effervesced with acids; it amounted to 1279·3 grammes, and yielded 0·561 grammes of tartrate of lime, corresponding to 0·324 grammes of tartaric acid, or 1·63 per cent.

XII. A few days afterwards the same experiment was repeated. From 1340·0 grammes of strongly alkaline urine, 0·549 grammes of tartrate of lime were obtained, equal 0·317 grammes of tartaric acid, or 1·59 per cent.

XIII. After ingestion of 45·0 grammes of the neutral salt, 2585·0 grammes of urine yielded 0·843 grammes of tartrate of lime, or 0·486 grammes of tartaric acid, or 1·63 per cent.

Tartrate of soda and potash.—XIV. 45·0 grammes of this salt made the urine soon alkaline. It amounted to 1301·5 grammes, and yielded 1·374 grammes of tartrate of lime, equal to 0·793 grammes of tartaric acid, or 3·32 per cent.

XV. On repetition, the urine came to 1088·3 grammes, and there were obtained 1·937 grammes of tartrate of lime, equal to 1·118 grammes of tartaric acid, or 4·68 per cent.

XVI. 60·0 grammes were taken in four doses, at intervals of three hours. The urine, 1473·0 grammes, alkaline, yielded 2·840 grammes of tartrate of potash, corresponding to 1·638 grammes of tartaric acid, or 5·14 per cent. In neither of these three cases the bowels became relaxed.

Tartrate of iron and potash.—XVII. Of this preparation, containing 26·0 per cent. of iron, 10·0 grammes were taken in one dose. The urine, 984·0 grammes, was strongly acid, and did not contain any tartaric acid. The fæces were soft, and blackish-green. The ashes of the urine contained no increased quantity of iron.

Tartrate of suboxyde of nickel and potash.—XVIII. Wöhler found nickel in the urine of a dog, to which he had given half a drachm of the salt. The urine was made brown by sulphuretted ammonium, and gradually deposited dark brown flakes. A green solution of this salt was obtained by adding carbonate of suboxyde of nickel to a boiling solution of bitartrate of potash. Of this solution, which contained 0·64 per cent. of metallic nickel, 164·4 grammes (= 1·052 grammes of nickel) were taken in six doses by Piotrowsky. The urine

was 1260·0 grammes. The ashes of the urine yielded a small amount of nickel. No tartaric acid could be found in the urine. The urine of the next days contained no trace of nickel. The fæces, which were of the usual consistence, contained no nickel on the first day, but considerable quantities on the second and third. They were dark brown, from the sulphuret of nickel, which is dark brown, when finely divided, and not blackish-green, like sulphuret of iron.

The experiments show that of large quantities of tartaric acid and its salts, ingested into the stomach, a small per centage may reappear in the urine. The great bulk is transformed into carbonates.

The following table exhibits the results of the above experiments:

Form in which the Acid was taken.		Grammes of Acid taken. $C_8H_4O_{10}+2HO$.	Per centage of Acid found in Urine.
$C_8H_4O_{10}+2HO$ . . .	I.	19·6	1·78
	II.	20·0	1·83
	III.	30·0	3·79
	IV.	30·0	3·27
	V.	10·0	1·47
	VI.	10·0	2·86
	VII.	5·0	1·89
	VIII.	2·0	
$\left.\begin{matrix}KO\\HO\end{matrix}\right\}C_8H_4O_{10}$ . . .	IX.	35·0	1·00
	X.	47·82	1·85
$2KO,C_8H_4O_{10}$	XI.	19·88	1·63
	XII.	19·88	1·59
	XIII.	29·81	1·63
$\left.\begin{matrix}KO\\NaO\end{matrix}\right\}C_8H_4O_{10}+8HO$.	XIV.	23·90	3·32
	XV.	23·90	4·68
	XVI.	31·87	5·14

Of the salt with potash and soda, a larger per centage appears in the urine.

Of tartaric acid, a much smaller per centage reappears in the urine than of oxalic acid.

Wöhler believed that free tartaric acid passed unchanged

into the urine, but did not do so when taken in combination with bases. This error has given rise to the theory, that the presence of alkalies in the blood was necessary for oxydation, and that by increasing the amount of alkali in the blood we could favour this process. Mialhe's treatment of diabetes, already found practically useless,[1] and experimentally made improbable by Lehmann[2] and Poggiale,[3] thus loses its last foundation. Dr. Parkes was of opinion, that by the medicinal use of alkalies the quantity of sulphuric acid in the urine, which was to be considered as the product of oxydation of albuminous substances, became augmented. But the experiments of W. Clare[4] do not support that opinion, so that the alleged use of the alkalies has become more than questionable.

4. CITRIC ACID.

Formula: $3HO, C_{12}H_5O_{11}$, or $\left.\begin{matrix} C_{12}H_5O_8 \\ H_3 \end{matrix}\right\} O_6$.

The experiments of Morichini, quoted by Wöhler, on the passage of citric acid into the urine, are related with so many improbabilities, that we must leave them out of consideration. The only experiments worth noticing, previous to those of Buchheim, are by Gilbert Blane, who found that citrate of potash appeared in the urine as carbonate.

In eight different experiments by Buchheim, in which repeated and large quantities of free citric acid were taken, the urine was quite normal, and contained no trace of citric acid. The citrates with three equivalents, one-and-a-half equivalents, and one equivalent of soda, respectively, taken in three different experiments, made the urine alkaline; but no trace of citric acid was found in the urine. The citrates with three equivalents and one equivalent of magnesia, respectively, caused diarrhœa, the fæces containing carbonate of magnesia. The urine was acid, and free of citric acid.

[1] Garrod, Gulston Lect. on Diabetes, 'Assoc. Med. Journ.,' 1857.
[2] 'Lehrbuch d. Physiol. Chemie,' 2d edit., Leipzig, 1853, vol. iii, p. 205.
[3] 'Comptes rend.,' t. xlii, p. 198.
[4] Loc. cit.

5. TANNIC ACID.

Elements: $C_{54}H_{22}O_{34} = 3HO, C_{54}H_{19}O_{31}$.

Wöhler and Frerichs gave to a dog pure tannic acid, in doses gradually increasing from 0·5 to 6·0 grammes. The animal remained well, but the fæces gradually ceased to be discharged, though the appetite remained the same. The urine, in the beginning of the experiment, showed the normal yellow colour, which, however, gradually changed into a dark, lastly intensely brown colour, until at last it became brownish-black, and impervious to transmitted light.

The brown urine yielded a blackish-blue precipitate with salts of oxyde of iron, but no precipitate was produced in it by a solution of gelatine. Tannic acid, consequently, in its transit through the body, had become transmuted into gallic acid.

Salts of the suboxyde of iron produced a bluish-black precipitate in the urine, indicating the presence of pyrogallic acid. As this acid, in presence of ammonia, is easily transformed into humine-like bodies, it is reasonable to explain the black colour of the urine by the further decomposition of the pyrogallic acid, for which the ammoniacal condition of the urine afforded the opportunity. The dark colour and peculiar reactions of the urine continued for two days after tannic acid had ceased to be administered.

By the action of acids, alkalies, or ferments, tannic acid, taking up water, is transformed into gallic acid and sugar, according to the following formula:

$$\underbrace{C_{54}H_{22}O_{34}}_{\text{Tannic acid.}} + 8HO = 3\underbrace{(C_{14}H_6O_{10})}_{\text{Gallic acid.}} + \underbrace{C_{12}H_{12}O_{12}}_{\text{Sugar.}}.$$

It is probable that the metamorphosis of tannic acid in the human body takes place in a similar manner.

6. TOLUYLIC ACID.

Elements: HO, $C_{16}H_7O_3$, or $\left.\begin{matrix} C_{16}H_7O_2 \\ H \end{matrix}\right\} O_2$.

Kraut[1] took toluylic acid in doses of several grammes. He

[1] 'Ann. d. Chem. und Pharm.,' xcviii, p. 360.

felt no effect from it; the urine which was voided afterwards had a strongly acid reaction. It was evaporated to the consistence of a syrup, and extracted with alcohol. The extract was treated with oxalic acid, and again evaporated, and the residue extracted with ether containing some alcohol. This left, on evaporation, a yellowish, crystalline mass, mixed with oxalic acid. It was boiled with carbonate of lime, when from the filtrate a lime-salt crystallized. This, after repeated crystallization, and decomposition with dilute warm hydrochloric acid, yielded, on the fluid cooling, a crystallized acid (*toluric acid*) which, after recrystallization from boiling water, was obtained pure in crystalline colourless plates. The solution in alcohol on spontaneous evaporation deposited large rhombic crystals. This acid has the composition $C_{20}H_{11}NO_8$. It forms salts with baryta, and oxyde of silver, and the alkalies, which are more soluble in hot than cold water. In cold fuming hydrochloric acid, toluric acid is soluble. If the solution, after short ebullition, is allowed to cool, toluric acid crystallizes from it unchanged. But when this solution is boiled during several hours, the hydrochloric acid being replaced as it evaporates, and is lastly evaporated to dryness, a residue remains, which may be separated in two by treatment with water. This fluid leaves an amorphous substance undissolved, which may be recognised as toluylic acid, and transformed into the silversalt; the solution, after saturation with ammonia, evaporation, and addition of alcohol, leaves a precipitate, which is glycocoll. It may be identified by its property of dissolving oxyde of copper in watery solution, in which alcohol produces a precipitate of oxyde of copper glycocoll.

Toluylic acid, therefore, like benzoic acid, combines with glycocoll in the animal economy, water being eliminated.

$$\underbrace{C_{14}H_6O_4}_{\text{Benzoic acid.}} + \underbrace{C_4H_5NO_4}_{\text{Glycocoll.}} - 2HO = \underbrace{C_{18}H_9NO_6}_{\text{Hippuric acid.}}.$$

$$\underbrace{C_{16}H_8O_4}_{\text{Toluylic acid.}} + \underbrace{C_4H_5NO_4}_{\text{Glycocoll.}} - 2HO = \underbrace{C_{20}H_{11}NO_6}_{\text{Toluric acid.}}.$$

The third acid of the benzoic series, cuminic acid, does not exhibit this copulative property.

7. SALICYLIC ACID.

Elements: $C_{14}H_6O_6$, or $\left.\begin{matrix}C_{14}H_4O_4\\H_2\end{matrix}\right\}O_2$.

Bertagnini took about 6 grammes of this acid in hourly doses of 0·25 grammes. On the first day there was no inconvenience attending the experiment; on the second day, however, he suffered from continued noises in his ears, and a sensation of being narcotized. The same symptoms occurred in a second experiment, in which about 7·5 grammes were taken in successive doses. Already, an hour after the injection of the first dose, the urine gave a violet reaction on the addition of salts of iron, a peculiarity which continued during the entire duration of the experiment, and was yet present, though faintly, for forty-eight hours after the last ingestion of salicylic acid. The acid urine was evaporated down to a small bulk, and put aside for crystallization of the salts. The decanted liquid was strongly acidified with hydrochloric acid, and repeatedly digested with ether. The ethereal solutions, on evaporation, left a strongly acid fluid, which, on further evaporation, deposited crystals. These were purified by pressing between paper, recrystallization, and treatment with animal charcoal. The substance so obtained was a mixture of small needles, and large, glistening, needle-shaped crystals, which latter appeared to be volatile on being heated. The separation of the two substances was effected by heating the mixture to from 140° to 150° C. (284° to 302° F.) in a current of air. The volatile body proved to be salicylic acid: the body which remained after recrystallization contained nitrogen, had the composition $C_{18}H_9NO_8$, and the properties of an acid. It dissolved in warm hydrochloric acid, and on cooling crystallized from the solution. By protracted boiling of this solution in hydrochloric acid, it was decomposed, and from the mixture, after neutralization of the hydrochloric acid by means of carbonate of lime in pieces, ether extracted salicylic acid. In solution there remained glycocoll.

$$\underbrace{C_{14}H_6O_6}_{\text{Salicylic acid.}} + \underbrace{C_4H_5NO_4}_{\text{Glycocoll.}} - 2HO = \underbrace{C_{18}H_9NO_8}_{\text{Salicyluric acid.}}.$$

From the analogy to hippuric acid, Bertagnini was induced to give the name of salicyluric acid to this new copulated acid.

From its solution in hot water, salicyluric acid crystallizes in concentric groups of thin glistening needles. It has a bitter taste and a strongly acid reaction. It is easily soluble in boiling, little soluble in cold water, easily soluble in alcohol, less in ether. These solutions impart a violet colour to salts of oxyde of iron, which colour disappears under the influence of concentrated acids. It fuses at 160° C. (320° F.) without loss of weight, and, on cooling, solidifies into an indistinctly crystalline mass. Towards 170° C. (338° F.) it begins to get brown, and is decomposed, salicylic acid being volatilized. If heated rapidly, it swells up, evolves ammonia, and leaves charcoal, which is combustible without leaving any residue.

When to a boiling solution of the acid in water carbonate of lime or baryta is added, an evolution of carbonic acid takes place, and the solution contains a salt of the acid with the respective oxyde. These salts are little soluble in cold water. There is also an insoluble lime-salt obtained by the addition of small portions of milk of lime to a hot solution of the acid, until the mixture solidifies into a mass of glistening scales. From this, Bertagnini believes salicyluric acid to be a bibasic acid.

Salicylous acid reappears in the urine unchanged. (Wöhler and Frerichs.)

8. CAMPHORIC ACID.

Elements: $C_{20}H_{16}O_8$, or 2HO, $C_{20}H_{14}O_6$, or $\left.\begin{matrix} C_{20}H_{14}O_4 \\ H_2 \end{matrix}\right\} O_4$.

Bertagnini[1] took 12 grammes of this acid in doses of about 0·5 grammes, distributed over two days, without experiencing any inconvenience. The urine which was passed during that time was strongly acid, and contained unchanged camphoric acid. It was condensed to one third of its original volume; and, after addition of some hydrochloric acid, a crystalline deposit ensued. When the mother-liquor was shaken with ether, the latter, after evaporation, deposited another quantity of brown crystals. These were treated with milk of lime, whereby a soluble lime-salt was obtained, which was decomposed by hydrochloric acid, whereupon a white crystallized substance was obtained, having all the properties and the composition of camphoric acid.

[1] 'Il nuovo Cimento,' i, 363. 'Ann. d. Chem. und Pharm.,' xcvii, p. 248.

9. ANISIC ACID.

Elements: $C_{16}H_8O_6$.

Bertagnini took about 6 grammes of anisic acid in the course of two days. It caused a sensation of heaviness in the stomach. The urine had a strongly acid reaction; and, after evaporation, addition of hydrochloric acid, and shaking with ether, anisic acid was obtained from the latter by evaporation, and identified by elementary analysis.

10. CUMINIC ACID.

Elements: HO, $C_{20}H_{11}O_3$, or $\left.\begin{matrix}C_{20}H_{11}O_2\\H\end{matrix}\right\}O_2$.

When Kletzinsky[1] took a salt of cuminic acid, he could find it again in the urine. Hofmann and Kraut both found cuminic acid to reappear unchanged in the urine.

[1] Heller's 'Archiv,' vol. vi, p. 95.

CHAPTER XLV.

UROPHANIC ORGANIC BASES.

The substances here to be considered may be innocuous matters, or medicines, or poisons. In respect of these two latter classes, the analysis of the urine becomes of peculiar importance as a key to the knowledge of the mode of action of medicines in the system, or as a guide to the discovery of the nature of a poison, under the influence of which an individual is labouring, or has died. Thus the analysis of the urine may lead to the prevention of some of the most hideous crimes, with which the annals of toxicology have been filled of late. The merest trace of strychnia administered in any form makes its reappearance in the urine. Arsenic and antimony, when administered as slow poisons, as has been ascertained to have been the case in several notorious instances, may in every case be detected in the urine. Thus to the watchful medical practitioner an almost infallible source of information is afforded in cases where the ordinary sources of symptomatology leave him in the dark, or at the best in doubt.

1. QUININE AND QUINIDINE.

Elements of Quinine: $C_{40}H_{24}N_2O_4$.
Elements of Quinidine: $C_{36}H_{22}N_2O_2$.

Dr. Herapath[1] has discovered a process by which it is possible to obtain demonstrative evidence of the presence of quinine in urine, in quantities so exceedingly minute, that they would be perfectly inappreciable by any other process.

[1] 'Quarterly Journ. of Micros. Sc.,' No. v, October, 1853, p. 13.

The same method (by a slight modification) has also enabled Dr. Herapath to prove the fact, that quinidine, like quinine, escapes from the system by the kidneys in an unaltered state.

The subject furnishing the urine for examination, was a man suffering from tetanus, in consequence of an injury to the great toe. Amputation was performed at the Bristol Infirmary, by Mr. Morgan. The tetanic symptoms were at first treated by the exhibition of five grains of the disulphates of quinine and quinidine, with half a grain of cannabis indica, every three hours. He consequently took forty grains of the mixed disulphates in the period of twenty-four hours.

The urine had a greenish-yellow appearance, and, upon standing, deposited a brownish-yellow sediment; it possessed a slightly acid reaction, and had a specific gravity of 1·032. The sediment examined by the microscope, showed prisms and lozenges of uric acid, together with amorphous urate of ammonia. The fluid urine was cautiously decanted from the amorphous and crystalline deposits.

a. Half a pint of this urine was treated with liquor potassæ until decidedly alkaline; it was then repeatedly agitated with pure washed ether; the ethereal solution having had time to separate by repose, was carefully removed by a pipette; and having been transferred to a counterpoised test-tube, it was evaporated to dryness in a warm water bath; the residue weighed 0·79 grain after being kept at 212° F., until no further loss of weight occurred. (Method of Stas.)

b. A magma of phosphates and adherent alkaloid still remained above the urinous substratum; this was also removed by a pipette, and transferred to a porcelain capsule, evaporated to dryness at 212° F., and this residue exhausted by ether, the ethereal solution evaporated to dryness by a warm water bath as before, and the residue dried at 212°, gave 0·61 grain additional alkaloid. Therefore, 0·79 + 0·69 = 1·4 grains of alkaloids were obtained by these two operations from the eight fluid ounces of urine.

Now, to determine if it contained quinine, the following process was adopted:

Test fluid. To a mixture of three drachms of pure acetic acid with one drachm of alcohol, six drops of diluted sulphuric acid (one acid to nine water) were added.

One drop of this test-fluid is to be placed on a glass slide, and the merest atom of the alkaloid added; time given for solution to take place; then, upon the tip of a very fine glass rod, a very minute drop of tincture of iodine added: if quinine be present, the first effect is the production of the yellow

or cinnamon-brown coloured compound of iodine and quinine, which shows itself as a small circular spot, whilst the alcohol separates in little drops, which, by a sort of repulsive movement, drive the fluid away; after a time the acid liquid again flows over the spot, and the polarizing crystals of sulphate of iodo-quinine are slowly produced in beautiful rosettes; this experiment succeeds best without the aid of heat.

To render these crystals evident, it merely remains to bring the glass slide upon the field of the microscope (having half-inch objective and lowest power eye-piece), with the selenite stage and single tourmaline beneath it: instantly the crystals assume the two complementary colours of the stage; red and green, supposing the pink stage is employed, or blue and yellow, provided that the blue selenite is made use of—all those crystals at right angles to the plane of the tourmaline producing that tint, which an analysing plate of tourmaline would produce when at right angles to the polarizing plate; whilst those at 90° to these educe the complementary tint, in the same manner as the analysing plate would have done if it had been revolved through an arc of 90°. (*Vide* Plate VI, fig. 3.)

Not only do these peculiar crystals act in the way just related, but they may be easily proved to possess the whole of the optical properties of that remarkable salt of quinine, so fully described by Dr. Herapath, in the 'Phil. Mag.' for March, 1852; the chemical analysis of which was published in the number for September of the same year. In fact, these crystals are perfectly identical with the sulphate of iodo-quinine, and have the composition

$$C_{40}H_{24}N_2O_4 \cdot I_2 \cdot 2(HO \cdot SO_3) + 10HO.$$

To test for quinidine it is merely necessary to allow the drop of acid solution to evaporate spontaneously to dryness upon the glass slide (before and without the addition of iodine), and to examine the crystalline mass by two tourmalines crossed at right angles, and without the selenite stage; immediately little circular disks of white, with a well-defined black cross very vividly shown, start into existence, should quinidine be present even in minute quantities. (Plate vi, fig. 4.) This figure was drawn from a slide prepared by Dr. Herapath, from the urine of the same patient; about one twentieth part of a grain of the ethereal extract was used by him in the manner described.

Quinidine is generally found in the urine if "hospital qui-

nine," or that of the British Alkaloid Company, has been employed; these drugs severally contain a very large per centage of quinidine; the former at least 50, the latter about 20 per cent. But Howard's disulphate of quinine scarcely contains 5 per cent. of quinidine. These substances are easily separated, in consequence of the much greater solubility of the disulphate of quinidine in cold water, thus—

One part of disulphate of quinine requires 740 parts water, at 60°.

One part of disulphate of quinidine requires 340 parts water, at 55°.

So that the latter salt is more than twice as soluble as the former.

If we employ the selenite stage in examining this object, depicted at fig. 4 of Plate vi, the black cross at once disappears, and is replaced by one which consists of two colours, being divided into a cross with a red and a green fringe, whilst the four intermediate sectors are of a rich orange yellow; these appearances alter upon the revolution of the analysing plate of tourmaline. When the blue stage is employed, the cross will assume a blue or a yellow hue, according to the position of the analysing plate.

These phenomena are analogous to those exhibited by certain crystals of boracic acid, and also by the circular disks of salicine (prepared by fusion by Mr. John Thwaites), the difference being that the salts of quinidine have more intense depolarizing powers than either of the other substances; and the mode of formation effectually excludes these from consideration. Quinine prepared in the same manner as the quinidine has a very different mode of crystallization; but it occasionally presents circular corneous plates, also exhibiting the black cross and white sectors, but not with one tenth part of the brilliancy, which of course readily enables us to discriminate the two.

Dr. Herapath having shown in his previous papers that none of the vegetable alkaloids, when treated with sulphuric acid and iodine, possess the power of forming crystalline compounds of similar properties, and these artificial quinine tourmalines being pre-eminent in their action on light, it follows that the existence of these crystals is a *demonstration* of the presence of quinine.

The above patient was taking 40 grains of the disulphates of quinine and quinidine; there were found 1·4 grains of alkaloids, which would be equivalent to 1·884 of the disulphate; and if the patient voided three pints of urine in twenty-four hours, we should only account for 11·304 grains

of the remedy employed, leaving a deficiency of 30 grains nearly, either to be assimilated by the body, or to be destroyed in its transit through the vascular system, or lost from other causes.

It would be interesting to undertake a series of experiments to determine whether other excretions of the patient contain this remedy, and also to discover what length of time elapses after ingestion, before all evidence of its elimination by the kidneys ceases: this being done, we may be in a position to say what the *medical equivalent* of quinine may be in a given disease.

2. STRYCHNINE.

Elements: $C_{42}H_{22}N_2O_4$.

Strychnine, when introduced into the animal economy in any noteable quantity, per example, in the ordinary medical doses at from one tenth to one twentieth of a grain, repeated at intervals, reappears in the urine. The analysis of the urine may therefore be useful for discovering attempted, or effected poisoning by strychnine.

The diagnostic properties of strychnine are, its bitter taste, even in extremely dilute solutions, and the violet and blue, or purple reaction, under the influence of bichromate of potash and sulphuric acid. It is little soluble in water, alcohol, or ether, more soluble in boiling alcohol, and crystallizes from this solution on cooling. Its acid salts, however, are easily soluble in water and alcohol, and may by means of that property be extracted from organic substances. The residue of this extraction by water and alcohol, containing the acid salts, having been made alkaline by caustic potassa, yields all its strychnine to ether, which, after evaporation, leaves it more or less pure. (Method of Stas.)

Mode of obtaining Strychnine from Urine.

In order to obtain strychnine from urine, it is only necessary to evaporate this fluid to the consistence of a thin syrup, to make it strongly alkaline by caustic potassa, and to shake it with large and repeated quantities of ether. The ethereal solution, which is only obtained after some standing, and sometimes only after the addition of some alcohol, is evaporated, and the residue treated with concentrated sul-

phuric acid on the water-bath. After several hours' digestion the acid is neutralised by carbonate of soda, the fluid is then made alkaline, and again extracted with ether, which after evaporation will leave strychnine, to be tested by the taste, and by the reaction with bichromate of potassa and sulphuric acid. This latter reaction is best effected in the following manner. The solution in water of the supposed alkaloid is placed in a small china dish, and after evaporation to dryness, at a low temperature, is dissolved in a drop or several drops of sulphuric acid. This solution is now spread over the space of about a four-penny piece. A small granule of bichromate of potash is now dropped into the solution. On moving the fluid, by giving the china dish different inclinations, violet streaks are perceived to flow from the granule of bichromate, and on moving the crystal to and fro in the fluid, by means of a glass rod, the entire solution soon assumes a fine purple colour. (Otto.)

One grain of a solution of strychnine, containing one forty-thousandth part of a grain of solid strychnine, yielded this test quite clearly. Five drops of the same solution brought upon the tongue, had a decidedly bitter taste; on some occasions two or three drops would permit the bitterness to be recognised.

3. SANTONINE.

Elements: C_5H_3O, or $C_{30}H_{18}O_6$.

When santonine is administered internally, the normal urine does not appear to have undergone any change when afterwards passed. If the urine be, however, by any accident alkaline, it has a fine red colour. In the acid and unchanged urine passed after the ingestion of santonine, this red colour may be produced by ammonia, and the fixed alkalies and earths, also by the carbonates, tribasic phosphates, and borates of the alkalies. The phosphates, which are thereby precipitated, are coloured red by adhering pigment. If this alkaline red urine is left to stand, it sooner or later becomes yellow again, and the red colour cannot again be produced by either acids or alkalies. The red colour of urine, produced in common acid yellow urine passed after ingestion of santonine, may be made to disappear quickly by shaking with oxygen gas, or by passing ozone through it, which latter is perfectly absorbed during its passage.

Kletzinsky took santonine in doses increased gradually

from one half to three grains. Fifteen grains had besides a slight diuretic, no other, effect. Twenty hours after ingestion, the last traces of the urinary pigment produced by the santonine could be perceived in the urine.

This observer dissolved santonine in a hot solution of caustic potassa in alcohol, and passed ozonized air through the solution, which was kept hot in a water-bath. The solution became red, but afterwards the colour changed into yellow, which did not undergo any further modification. The ozonized air now passed through the solution. The alkaline solution after neutralization with acetic acid was evaporated to remove the alkohol, and after dilution with water precipitated by an excess of neutral acetate of lead. The yellow flaky precipitate was washed with boiling water, removed into a flask, suspended in alcohol, and treated with hydrothion. The filtrate was freed from hydrothion, treated with animal charcoal, until it was colourless, and lastly evaporated. The residue was acid, and left colourless rhombic prisms, which burned on platinum foil without residue, under evolution of vapours, having an irritating influence upon the air-passages. Their solution was neutralised by ammonia; in this neutral solution, salts of iron produced a brownish-yellow precipitate, salts of manganese no reaction. It was therefore probable, that the prisms were an acid of the succinic group. The lead salt yielded 66·225 per cent. (calcul. 66·18) of oxyde of lead. The crystals of the acid yielded by combustion with oxyde of copper, figures equal to 5 equivalents of carbon, 3·9 equivalents of hydrogen, and by deficit 4 equivalents of oxygen, which corresponds to the formula $C_5H_4O_4$, or $C_5H_3O_3 + HO$, being the hydrate of lipinic or pyrotartaric acid.

Between santonine, C_5H_3O, and lipinic acid, $C_5H_3O_3$, a substance may be supposed to exist of the formula $C_5H_3O_2$, lipinous acid, urophanic pigment of cinna, being perhaps the red pigment in alkaline urine after ingestion of santonine. The direct proof of this assumption is, however, yet wanting. Like sennine, rhamnine, and rheine, this urophanic santoneine is a pigmento-resinous acid, and one of a group nearly related to the succinic series. Santonine from this may be considered as oxyde of lipine, $C_5H_3 + O$.

The equivalent of santonine has been determined to be $C_{30}H_{18}O_6$ from its compound with soda,

$$NaO . C_{30}H_{18}O_6 + 8\,HO.$$

The newest formula for pyrotartaric acid is $2\,HO . C_{10}H_6O_6$. If santonine is to be transformed into this acid without any

further changes than the accession of oxygen, 12 equivalents of this latter and six of water would have to join one equivalent of santonine, and this compound by separation would form three atoms of pyrotartaric acid. It is scarcely necessary to state that this metamorphosis requires further confirmation.

CHAPTER XLVI.

UROPHANIC INORGANIC SUBSTANCES.

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1. IODINE.

IODINE is frequently used as a medicine, sometimes rather indiscriminately. In other cases, its effects are irregular, though it has been given with a due regard to experience. It is necessary to ascertain the reasons of this variable action; and for this purpose the analysis of the urine will best serve. For one of the principal reasons why iodine and its preparations are borne very well by some, and have injurious effects in others, is the varying length of time required for its removal from the body. Thus Lehmann found that, when several persons had each taken a dose of 10 grains of iodide of potassium, some would immediately begin to excrete it in their urine, which after the lapse of twenty-four hours no longer contained any trace of the iodide. In others, however, the iodide could frequently be found even after the lapse of three days. Supposing the daily dose of 10 grains to have been administered for a length of time to these two classes of people, the first class would most probably never have at one time more than 10 grains of the iodide in their body, while the latter might have 30 or 40 grains in their body at one time. Not only, therefore, would the action of the drug, in these latter cases, go parallel to the quantity present, but also it would last much longer; and in this way equal doses at equal intervals might in the latter class produce four times the effect they would produce in the first class. In some cases, therefore, where an explanation of an extraordinary mode of action of iodine or iodides may be necessary or desirable, the analysis of the urine will be the chief source for information on this point,

due consideration being given to other excretions, by which iodine is removed from the economy.

Volumetrical analysis of Iodine in the Urine. Kersting's Method.

This method[1] is based upon the fact, that a very dilute solution of iodine or an iodide yields all the iodine by distillation with sulphuric acid. In the distillate, the amount of iodine is determined by a solution of chloride of suboxyde of palladium of known strength. In the performance of this analysis, care must be taken never to have an *excess* of the solution of iodine mixed with the solution of palladium, as in that case the fluid does not get clear very quickly, and the precipitate of iodide of palladium adheres to the walls of the glass. But when the solution of palladium is present in slight excess together with a little hydrochloric acid, and the mixture is warmed to from 60° to 100° C. (140° to 212° F.), and agitated, the iodide of palladium, after a few seconds, separates in black, cheesy flakes, and the supernatant fluid is perfectly clear and colourless. In performing the analysis, therefore, to a known volume of the solution of palladium of known strength, such a volume of the solution of iodine to be analysed is added, as is just sufficient to precipitate the entire amount of palladium in solution. This analysis is so accurate, that $\frac{1}{300}$th milligramme of iodine may be determined by means of the palladium, and $\frac{1}{100,000}$th milligramme of palladium by means of iodine. The method is therefore, in one sense ten thousand times more delicate than chemical scales of the highest order. The chemical balance which I employ, one by Liebrich, at Giessen, will turn with $\frac{1}{10}$th milligramme, when loaded with 100 grammes on each side. It therefore indicates one millionth of the weight which it is capable of carrying. The balance has therefore a disadvantage when compared with volumetrical analysis, in not being so able to combine quantity with accuracy; the dilution of tests enables us to produce a delicacy regarding quantities, which we might in vain endeavour to attain by mechanical appliances.

Preparation of Solution of Iodide of Potassium of known strength.

This solution is to be so graduated that every part of it contains $\frac{1}{1000}$th part of iodine. For that purpose 1·308

[1] Kersting, 'Ann. d. Chem. und Pharm.,' Bd. 87, p. 21. See also Neubauer, loc. cit., p. 120.

grammes of dry iodide of potassium, perfectly free from iodate of potash, are dissolved in water, and the solution is diluted until amounting to one litre. 1 c.c. of this solution contains 1 milligramme of iodine, as 1·308 grammes of iodide of potassium contain 1 gramme of iodine.

$$(126{\cdot}88 : 165{\cdot}99 = 1 : x = 1{\cdot}308.)$$

Solution of Chloride of Suboxyde of Palladium of known strength.

We prepare a solution of palladium of unknown strength, and graduate it by means of the solution of iodide of potassium, just described. 1 gramme of the metal is dissolved in aqua regia, with the aid of heat, and evaporated to dryness on the water-bath. After solution of the residue in 50 c.c. of concentrated hydrochloric acid, water is added to the amount of about 2000 c.c. The exact amount of palladium contained in a given volume is now determined by means of the solution of iodide of potassium of known strength, in the following manner. 10 c.c. of the solution of palladium to be graduated, are put into a balloon of about 200 c.c. capacity. The balloon is closed by a cork-stopper, and warmed in a water-bath, to near boiling heat. From a burette, the graduated solution of iodide of potassium is now added, the mixture shaken, and warmed again. Four minutes will suffice to separate the mixture into a precipitate, which subsides towards the bottom of the vessel, and a clear supernatant fluid. Of the latter, two portions are each put in a test-tube. To the one portion, a few drops of the solution of iodide of potassium are added; and, by comparison with the other test-tube, we find whether a brownish tint has been produced by the iodide. In case a brownish precipitate has been produced, the two portions are again poured back to the main bulk of fluid, to which some more solution of the iodide is added under agitation, and warming, and so on, until in a fresh portion of the clear supernatant fluid no discoloration is produced by the addition of the iodide test fluid. At this stage of the proceeding, the fluid is separated from the precipitate by filtration; and, if a sample of it is not tinted brown by either solution of palladium or iodine, the fluid does not contain a trace of excess of either substance, and the analysis is completed. From the equivalent of the iodine used, the amount of palladium contained in the 10 c.c. used for analysis, may be found by calculation. 1 milligramme of iodine is equivalent to 0·42

milligrammes of palladium, which is therefore the quantity indicated by every cubic centimetre of the graduated solution of iodide of potassium.

Supposing the 10 c.c. of solution of chloride of palladium required for the complete precipitation of palladium contained in it, 11·9 c.c. of graduated solution of iodide of potassium, containing 11·9 milligrammes of iodine, then the amount of palladium contained in the 10 c.c. of solution was 11·9 × 0·42 milligrammes = 4·998 milligrammes. The same volume of solution of palladium would therefore require such an amount of solution of iodine of *unknown* strength, as would exactly contain 11·9 milligrammes of iodine. From the amount thus used, the amount of iodine contained in the entire bulk of fluid is ascertained by calculation.

Application to the Urine.

100 c.c. or more of urine are mixed with 20 c.c. of concentrated sulphuric acid, and kept in a cold water-bath during the first violent evolution of heat. The balloon containing the mixture is then connected with Liebig's cooler, and the distillation proceeded with. It is continued until, in the neck of the balloon, white vapours of sulphuric acid begin to appear. If, however, the urine contains only a very small amount of iodine, any measured quantity, after addition of an excess of caustic potash, may be concentrated by simple evaporation of the water, and only then distilled with sulphuric acid in the manner described.

The distillate thus obtained contains iodurettted hydrogen, all volatile acids of the urine, with carbonic, sulphurous, and sulphuric acids. The sulphurous acid must be oxydized, before the fluid can be subject to further analysis. This is effected in the following manner:—To the distillate are added one or two drops of solution of starch (made of 1 part of starch, $\frac{1}{10}$th part of sulphuric acid, and 24 parts of water), and after that a saturated solution of chloride of lime in drops, until the fluid just begins to get blue. The blue colour is then again made to disappear by one or two drops of a dilute solution of sulphurous acid in water. The volume of the entire solution is now measured, and the necessary quantity of it filled into a Mohr's burette, and from this added to the 10 c.c. of solution of chloride of palladium in the manner above described, until the entire amount of palladium is precipitated.

Thus, if 100 c.c. of urine yielded 96 c.c. of distillate, and if of this distillate 12 c.c. were required for precipitating the

4·998 milligrammes of palladium from the 10 c.c. of solution, then the 12 c.c. contain 11·9 milligrammes of iodine. (53·24 : 126·88 = 4·998 : x.) The 96 c.c. of distillate therefore, corresponding to 100 c.c. of urine, contain 8 × 11·9 milligrammes = 95·2 milligrammes, = 0·0952 grammes of iodine.

2. ARSENIC AND ANTIMONY.

In cases where these metals, or either of them, should be present in urine in any considerable quantity, they would be precipitated as sulphides by a current of hydrothion conducted through the acidified liquid. But mostly their quantities are very small, not so much because those poisons are sparingly eliminated by the kidneys, as because (in cases of poisoning), the urine containing the largest proportion is mostly not to be obtained.

When these substances have been administered to any person, either in medicinal doses, or by accident or criminal design, the urine of the patient voided some time afterwards, almost always contains some arsenic or antimony, so that Orfila was induced to recommend a diuretic treatment in cases of poisoning by either of these substances.

Reinsch's Method of obtaining Arsenic and Antimony from Urine.[1]

The urine is evaporated to a small bulk, and then from one sixth to one seventh of its volume of pure hydrochloric acid is added to it. It is boiled; and while boiling, a small piece of thin copper foil, freshly brightened by rubbing with some oxalic or hydrochloric acid and paper, or a piece of fine copper-gauze, is introduced. Sooner or later, according to the quantity present, antimony, or arsenic, or both, are deposited on the copper, producing a blackish grey, or grey deposit, with a reddish-violet, or purple tint, if antimony in small quantities is deposited; but an iron grey or black tint, if antimony in large quantities, or arsenic, are deposited. If no deposit is observed at first, the whole of the liquid must be boiled down on the copper, before the inference is drawn, that arsenic or antimony are absent. If the copper be removed without any metallic tarnish or deposit upon its surface, there is no antimony or arsenic present. If it has ac-

[1] Taylor, 'Guy's Hosp. Rep.,' October, 1857.

quired a metallic deposit, then, after well washing, and drying it, the following steps must be resorted to in order to determine the nature of the metallic coating.

Diagnosis of Arsenic and Antimony.

The copper foil is placed in a tube, which is closed at one end, and heated. A grey or dark metallic ring deposited at the cold part of the glass tube, consists of arsenic. A white sublimate deposited beyond the black ring, and seen under the microscope to consist of cubes and octahedra, is arsenious acid.

Antimony is not sublimed under these circumstances.

The copper foil is placed into a concentrated alkaline solution of hypochlorite of soda; the metallic deposit of arsenic is immediately or slowly dissolved. The presence of small quantities of antimony does not interfere with this reaction, any further than that the antimony remains undissolved.

If the copper foil, after having undergone the above tests, still retains a metallic coating, it is boiled in a weak solution of potash, the metal being partly exposed to air by drawing it out of the alkaline liquid, and then again returning it. In this way the antimony is oxydized by the air in contact with an alkaline solution, and antimoniate of potash is formed. In about five or ten minutes, the copper will have lost the deposit, and the liquid may then be filtered, acidulated with hydrochloric acid, and treated with sulphuretted hydrogen. The persulphide of antimony, of its characteristic colour, is orange-red thrown down, either immediately, or on allowing the liquid to stand for a short time. (Watson).

3. LEAD.

Kletzinsky's Method[1] *of obtaining Lead from the Urine of patients labouring under Lead poisoning.*

It is necessary to employ not less than one day's urine for this operation, which is the more likely to be successful, the larger the quantity of urine employed.

The urine, after being made alkaline by caustic potassa, is mixed with two per cent. of its weight of nitrate of potassa, and evaporated to dryness. The residue is now transferred into a small china capsule, and exposed to red heat, when a

[1] 'Wien. Med. Wochenschrift,' 1857, No. 42, 44, 45.

slow deflagration destroys the whole amount of organic matter present. On cooling, there remains a white slaky mass, not adhering to the capsule, and containing all the inorganic fixed ingredients of the urine together, with the lead that may have been present. This slake is powdered finely, and boiled for some time with a half-saturated solution of neutral tartrate of ammonia, to which some caustic ammonia has been added. The decoction is freed from the residue by filtration; the filtrate contains all the lead in solution. It is acidulated by means of hydrochloric acid, and a current of sulphuretted hydrogen is allowed to pass through it. A brown discoloration, or a black precipitate, indicates the presence of a poisonous metal, which from the history of the case may be supposed to be lead. The precipitate is allowed to deposit for twenty-four hours, washed by decantation, redissolved in warm *dilute* nitric acid, and the filtrate from the precipitate of sulphur, after neutralization, is tested by means of chromate of potassa and sulphuric acid. The chromate yielding a yellow, the sulphuric acid a white precipitate, excludes any doubt as to the black precipitate having been sulphuret of lead.

In fourteen cases of distinct lead poisoning examined in this manner, Kletzinsky succeeded only in two, in proving the presence in the urine of lead by the latter tests. In the twelve remaining, the presence of lead was only indicated by the brownish colour produced in the acid solution by hydrothion.

A plumber, æt. 34, was admitted into St. Mary's Hospital, under the care of Dr. Chambers, on the 7th of January, 1857. He had had colic three or four times previously, but had experienced no symptoms of saturnine paralysis. On the 7th of January, he was suddenly attacked with epileptic fits. He had a succession of fits, which lasted for thirty-six hours. When Dr. Sieveking saw him, on the 14th of January, he stated that he had no recollection of anything that happened from the time of his admission into the hospital to the 12th of January; that he woke up with severe headache, occupying the entire head, with vertigo, and found that he had lost the power of moving the left leg and the right arm; the left arm and the right leg continued normal both in regard to sensation and motion. There was decided diminution of sensation in the affected limbs, and the right hand was in a permanent semi-flexed condition, with very little power remaining of opening or closing the fingers. On first recovering consciousness, the people in the ward seemed to him as small dolls, and the opposite side of the room seemed to be sunk forty feet below its own level. These erroneous impressions he was conscious of at the time, and they disappeared in four days. The urine was very scanty. There was a marked blue line round the margin of the upper and lower gums. There had been a susceptibility to pain in the paralysed parts, which remained after the ordinary tactile sensibility appeared to be restored. On the 10th of January, the patient had 10 grains of iodide of potassium administered to him three times a day. A rapid improvement was perceptible. The amount of urine rapidly increased; but although on two occasions after commencing the iodide of potassium, the urine of at least twelve hours was tested for lead, none was found.

The fact that Dr. Bernays, the able chemical lecturer at St. Mary's Hospital, kindly charged himself with these analyses, will be a sufficient guarantee that no lead was present. Dr. Sieveking again ordered the urine to be collected from the 20th to the 21st of January, and although probably only about one half of the urine secreted had been preserved, owing to the remainder having been discharged in defecation, he obtained 860 c.c., of a reddish-yellow hue, and turbid. This was evaporated down nearly to dryness, and the residue was boiled with nitro-hydrochloric acid, and filtered. The filtrate, on the addition of sulphide of ammonium, or of sulphuretted hydrogen, gave a copious precipitate of the sulphuret of lead.—Dr. Sieveking, '*Med. Times and Gaz*,' Feb. 14, 1857.

4. MERCURY.

The urine is treated on the water-bath with chlorate of potash and fuming hydrochloric acid, until the chlorate and organic matters are entirely destroyed. The fluid is then evaporated to dryness, and the residue extracted with ether, until this solvent does not take up anything more. The ethereal solution, on evaporation, leaves dry mercury in the form of chloride, or corrosive sublimate. The watery solution of this latter is precipitated yellow by caustic potassa, and the precipitate is insoluble in an excess of the alkali. Iodide of potassium produces a fiery red precipitate of iodide of mercury, soluble in an excess of the iodide of potassium.

In all cases, where the urine contains mercury, there is at the same time a peculiar albuminous substance present in it, which with nitric acid gives a faint reaction of albumen. A substance is also present, having the reactions of sugar.

Not in all cases of mercurialism has it been possible to detect the metal in the urine. In some cases, the metal only appeared in the urine at intervals, even where the symptoms had undergone no remission. In other cases, the reappearance of the metal in the urine was accompanied by a decided increase in the severity of the mercurial symptoms.

5. COPPER.

The urine[1] is treated on the water-bath with chlorate of potash and fuming hydrochloric acid, until the organic matters and the chlorate are entirely destroyed. The pale yellowish solution is now made alkaline by an excess of ammonia, whereby its colour changes into brown, with a smoky hue. Any precipitate that may ensue is removed by

[1] Kletzinsky, 'Wien. Med. Wochenschrift,' 1857, No. 43.

filtration. The filtrate is evaporated on the water-bath to perfect dryness, the residue moistened with nitric acid of 1·5 specific gravity, and exposed to red heat in a china capsule. The ashes, which must not contain any charcoal, are dissolved in hydrochloric acid, and this solution is boiled under addition of little nitric acid, in order to ensure the highest possible oxydation of the metals, iron and copper, of which the former is always present in urine. This acid solution is now treated with excess of ammonia, whereupon a precipitate of hydrated oxyde of iron falls down, which must be removed by filtration. If the filtrate has a bluish colour, and after being acidulated with acetic acid, yields a reddish turbidity or reddish-brown precipitate with ferrocyanide of potassium, the presence of copper is proved. This proof may be further strengthened by acidulating the alkaline solution by hydrochloric acid, and conducting a current of sulphuretted hydrogen through it; a brownish turbidity, soluble in sulphuretted ammonium, with a brown colour, is indicative of copper. Another test consists in putting a piece of blank iron foil, surrounded by a spiral wire of platinum, into the solution, acidulated by hydrochloric acid. After several hours, the iron is covered by a red hue, if copper is present in the solution.

In six cases of poisoning by copper compounds, noticed by Kletzinsky, this metal could be found in the urine as long as any symptoms remained about the patients. When the symptoms ceased, the copper disappeared from the urine, but continued to be discharged with the fæces. The fæces of healthy persons mostly contain some copper; healthy urine, however, does not contain any traces of this metal.

Of other inorganic substances introduced into the system; the following have been found to make their appearance in the urine:

Bromine (Heller), and bromides.
Ammonia, mostly as such, a small quantity transformed into nitric acid. (Bence Jones.)
Carbonates, Silicates, Chlorides, Borates, } of alkalies. (Wöhler).
Sulphocyanide, or rhodide, Ferrocyanide, Ferricyanide changed into ferrocyanide, } of potassium. (Wöhler.)

Rhodalline, as sulphocyanide of ammonium. (Wöhler and Frerichs.)

Chlorate } of potassa. (Wöhler.)
Nitrate }

Sulphuret of potassium reappears partly as such, partly as sulphate of potassa. (Wöhler.)

Chloride of barium. (Wöhler.)

ADDENDA.

1. TRIMETHYLAMINE.

When large quantities of human urine are distilled, a distillate is obtained, having a strong smell of ammonia, and also of sea-fish. When a little over-saturated with hydrochloric acid, it assumes a reddish colour, owing to the presence of one of the acids discovered by Städeler. By crystallization, a large amount of chloride of ammonium is separated; the mother liquor is evaporated to dryness, the residue extracted with alcohol, and the alcoholic solution is mixed with bichloride of platinum. After several crystallizations, fine crystals of the double salt of trimethylamine and bichloride of platinum are obtained, containing 37·17 Pt., and 40·22 Cl, and having the formula $C_6H_{10}NCl_3$ Pt.

Sixty-five litres of fluid, being previously condensed urine, gave 2200 grammes of chloride of ammonium, and only 17 grammes of the double salt of trimethylamine, corresponding to only 3·7 grammes of free trimethylamine.[1]

2. SARKINE.

Since the printing of the chapter on "Sarcine," for which I provisionally proposed the name of Carnine, the above spelling of the original word has been introduced in Germany. I have no hesitation in adopting it, as effecting in a preferable manner the object which I had in view when proposing a new synonym, namely, distinction from *Sarcina ventriculi*.

Mode of obtaining Sarkine from Human Urine.

The urine is neutralized with milk of lime, and treated with a solution of chloride of calcium, so long as a precipitate

[1] Dessaignes, 'Ann. d. Chem. und Pharm.,' c, p. 218. 'Comp. Rend.,' xliii, p. 670.

is thereby produced. The filtrate is evaporated to half its bulk, and while hot, is treated with a solution of acetate of copper, until a precipitate ceases to be produced. The precipitate, at first bluish, and very voluminous, quickly becomes flaky, and though still voluminous, assumes a light brown colour. The fluid, which has exchanged its alkaline reaction for an acid one, is now set aside, and after the precipitate has settled, is removed by decantation, or, what is preferable, the syphon. The precipitate is washed several times with water, and the latter is removed by decantation with the syphon; it is lastly collected on a filter, and washed with water, until the washings begin to get turbid. If the precipitate is now analysed, it is found to contain oxyde of copper, lime, uric acid, and sarkine. To separate these substances, the precipitate is washed from the filter into a narrow-necked bottle, and suspended in a large amount of water. Sulphuretted hydrogen is now passed through it, until the fluid, after shaking in the stoppered bottle, smells strongly of the hydrothion. The sulphide of copper is allowed to deposit in a warm place, the supernatant liquid is removed by the syphon: the precipitate is thrown on a filter and washed with water containing hydrothion, and the filtrates are united with the decanted fluid. This solution in the cold quickly becomes turbid, and deposits urate of lime in needles and crystalline masses. It is cleared up by warming it on the sand-bath, and a solution of oxalic acid is added to it, until it ceases to produce a precipitate, and the fluid has assumed a strongly acid reaction. The mixture is now allowed to stand on the sand-bath for twenty-four hours, and stirred frequently. After that time, all uric acid is deposited in crystals, mixed with the oxalate of lime. The deposit is separated by filtration, and the filtrate is freed of oxalic acid by treatment with pure carbonate of lime. When the boiling fluid shows an alkaline reaction, it may be filtered, and evaporated to a small bulk. On cooling, sarkine is precipitated in the form of a light, amorphous, granular mass. The mother liquor, which is very brown, is separated by filtration, and the precipitate on the filter is washed with cold water, until almost white, and until the washings are quite colourless. What remains on the filter is pure sarkine. The mother liquor, by repeated evaporation, and standing, deposits the greater part of its sarkine, which may be obtained pure like the first portion.

My experience has led me to avoid hydrated oxyde of lead as a purifying agent for sarkine, or the dark mother liquor. The quantities of sarkine which it retains are very large, and

the sarkine obtained is not purer than that procured by the above proceeding.

The sarkine is now dissolved in a large quantity of hot water, and a dilute solution of nitrate of silver is added to it. A voluminous greyish-white precipitate thereby produced is a compound of sarkine and nitrate of silver. The fluid must be stirred and kept hot, while the last portions of the nitrate, necessary for the complete precipitation of the sarkine are added, as the bulky, gelatinous precipitate would otherwise enclose mechanically a considerable amount of uncombined nitrate, which it would be difficult to remove by washing. The precipitate becomes a little darker by boiling, but is not blackened like the precipitate which nitrate of silver produces in acid urates. When the precipitate of sarkine and nitrate of silver is collected on a filter, it must be washed for a length of time, and then dried over sulphuric acid in the vacuum. When dried in the water-bath, some silver is easily reduced, and the precipitate becomes black. During the process of drying, the large and bulky precipitate shrinks to an insignificantly small compass.

The bulky wet precipitate may be removed from the filter, and dissolved in concentrated fuming nitric acid. The assistance of heat quickens the solution, and lessens the amount of acid necessary. The dried precipitate may be dissolved in ordinary nitric acid, gently warmed, or boiling, if less concentrated. The solution, which is perfectly clear, and somewhat yellow, on cooling and standing deposits groups of microscopical rhombic plates, and needles, of the sarkine and nitrate of silver compound. When they are left in the acid mother liquor for some time, they become so long and thin as to resemble bundles of long hair emanating in curls from one invisible centre towards all directions. This appearance is very characteristic, and I have never seen anything resembling it.

3. SARCINA VENTRICULI (*Goodsir.*)

Synonym : Merismopœdia punctata (Meyen).

This alga, which by Goodsir, was discovered in vomited matters, belongs according to Nägeli, to the natural order of the Palmellaceæ. It consists of particles in a peculiar cubic arrangement; there are generally not less than eight particles united within a structureless membrane, forming a cubic package, which looks like a bundle tightly bound by crossed strings. If these bodies multiply, the increase is

not cubic, but simply quadratic. In this manner, four primary bundles, of eight particles each, are arranged into a square, presenting to the eye sixteen particles, but in reality being made up of thirty-two.

The particles themselves are of a greenish, or greenish-brown colour, of an irregular, roundish shape, and frequently present a dark point in their centre, from which Meyen derived the adjective given by him to the alga.

The sarcina occurring in human urine, and which undoubtedly may be developed in the bladder, has a more irregular arrangement than the alga occurring in the stomach. The specimen represented in fig. 2 of Plate VI, I purchased from Mr. Norman, the microscopical mounter, who informed me that it came from a case under Mr. Hilton's care, in Guy's Hospital. The algæ, though mounted in creosote water, did yet show their peculiar movements for weeks after their confinement in the glass cell. This specimen is now in the hands of my friend Dr. H. Welcker, of Giessen, from whose pen we may shortly expect a practical paper on the subject of sarcina in the urinary passages of man.

The first observations of sarcina in urine were made by Heller, who has reported three cases. Three cases have been recorded by Mackay and Johnson. Beale[1] observed a case himself, and mentions one brought under his notice by Mr. Brown, of Lichfield. Hilton's and Welcker's cases further swell the number. Several cases, hitherto unpublished, were also mentioned at the late meeting of Naturalists at Bonn.

In the cases lately observed in Germany, chronic dyspepsia was a prominent collateral feature.

4. UROSTEALITH.[2]

A young man, æt. 24, was admitted into the general hospital, at Vienna, suffering from the symptoms which usually attend the presence of concretions in the urinary organs. There was pain in the region of the left kidney. On examination, a calculus was discovered to be present in the bladder. During several days he passed some concretions, not larger than hempseeds; on a subsequent occasion, the concretions

[1] 'The Microscope,' &c., p. 176.

[2] Heller, 'Heller's Archiv,' 1845, p. 1. See also Simon's 'Animal Chemistry,' Syd. Soc. Edit., vol. ii, pp. 326 and 452. Another case has been published by W. Moore, 'Dublin Quart. Journ. of Med. Sc.,' March, 1854, p. 373. See also Heller's 'Archiv,' vol. vi, p. 423.

had a bloody surface; sometimes he passed small coagula of blood, at others crystals of triple phosphate. After the nature of the calculus had been made probable by the analysis of the concretions, which consisted of urostealith, the patient was treated with carbonate of soda, when urostealith was found dissolved in the urine, and the phosphatic crusts of the calculus were passed by the urethra, in a broken up condition.

Chemical properties of Urostealith.

A fragment of a calculus placed on platinum foil, and heated, remains solid at first, then begins to fuse and swell up, and gives off a pungent odour, resembling that of shellack and benzoine. The substance next takes fire, and burns with a clear yellow flame; a voluminous charcoal ultimately remains, which, when thoroughly burned, leaves a small amount of ash, principally lime.

When boiled in water, urostealith becomes soft, but does not dissolve. It dissolves with difficulty in warm alcohol, easily in ether, and on evaporation is again obtained in an amorphous condition. If kept at a gentle heat for some time, it assumes a violet colour. It readily dissolves in a hot solution of caustic potassa, forming a brown soap, which, by treatment with an acid, again separates into urostealith, and the salt of the acid. When heated with nitric acid, it yields a colourless solution, a slight quantity of gas being evolved. If this solution is evaporated, the residue, when treated with ammonia or potassa, assumes a dark yellow colour.

It is by no means clear, whether urostealith is a resin or a fat. Its elementary composition is entirely unknown, even qualitatively.

TABLE I.

AVERAGE COMPOSITION OF THE NORMAL URINE FROM TWENTY-FOUR HOURS.

Average quantity from 24 hours, 1400 to 1600 cubic centimetres, 49 to 56 fluid ounces.
Average specific gravity, 1·020.
Mean amount of solids 55 to 66 grammes, or 850 to 1020 grains.

Water	1345 to 1534 grammes.		
Urea	30 to 40	„	463 to 617 grs.
Uric acid	0·5	„	or 7·5 „
Creatine	0·3	„	or 4·5 „
Creatinine	0·45	„	or 7·0 „
Sarkine, Uræmatine, Uroxanthine	undetermined.		
Hippuric acid	0·5	„	or 7·5 „
Chlorine	6 to 8	„	92 to 123 „
(or Chloride of sodium	10 to 13	„	154 to 200 „)
Sulphuric acid	1·5 to 2·5	„	23 to 38 „
Phosphoric acid	3·66	„	56 „
Potash and soda, Lime and magnesia	undetermined.		
Earthy phosphates	1·28 grammes,		19 „
Iron	undetermined.		
Ammonia	0·7 grammes,		10 „
Trimethylamine, Carbonic acid, Phenylic acid, Damaluric acid	undetermined.		

The minor estimates account for 48 out of 55 grammes of solids, the larger estimates for 62 out of 66 grammes of solids.

TABLE II.

TABLE FOR DISCOVERING THE NATURE OF URINARY DEPOSITS BY CHEMICAL REAGENTS.

1.	Deposit, white		2.
	,, coloured		5.
2.	,, dissolves by heat		Urates.
	,, insoluble by heat		3.
3.	,, soluble in liquor ammoniæ		Cystine.
	,, insoluble in ,,		4.
4.	,, soluble in acetic acid		Earthy phosphates.
	,, insoluble		Oxalate of lime.
5.	,, visibly crystalline		Uric acid.
	,, amorphous		6.
6.	,, pale, readily soluble by heat		Urates.
	,, deeply coloured, slowly soluble by heat		,, stained by purpurine.

TABLE III.

TABLE FOR THE MICROSCOPICAL CHEMICAL EXAMINATION OF URINARY DEPOSITS.

1.	Deposit, amorphous	2.	
	,, visibly crystalline	3.	
2.	,, soluble in liq. potassæ		Urates.
	,, insoluble		Phosphate of lime.
3.	,, crystals in well-defined octahedra		Oxalate of lime.
	,, not octahedral	4.	
4.	,, in six-sided tables, soluble in ammonia		Cystine.
	,, not tabular, nor soluble in ammonia	5.	
5.	,, soluble in acetic acid	6.	
	,, insoluble in ,,	7.	
6.	,, in prisms, or simple pennæ, or foliaceous stars		Triple phosphate.
	,, in radiated globules, soluble with effervescence in acetic acid		Carbonate of lime.
7.	,, in dumb-bells		Oxalate of lime.
	,, in lozenges, or compound crystals strongly coloured		Uric acid.
	,, in spherical masses		Urate of soda.

The above tables are Dr. G. Bird's ('Urin. Dep.,' 4th edit., p. 19, 20), slightly condensed, by the exclusion of bibasic triple phosphate and oxalurate of lime, for the existence of which substances in urine no proof has been afforded to us. In Dr. Birkett's edition these tables are spun out excessively, and thereby have lost much of their original perspicuity.

TABLE IV.

TABLE FOR THE CONVERSION OF THE CENTIGRADE THERMOMETER SCALE INTO THAT OF FAHRENHEIT, AND VICE VERSA.

$n°$ Fah. $= {}^{5}/_{9}\,(n° - 32°)$ C.

$n°$ C. $= {}^{9}/_{5}\,(n° + 32)$ Fah.

1° Fah. = 0°55 C. 0°1 Fah. = 0°055 C.

Fahrenheit.	Centigrade.	Fahrenheit.	Centigrade.	Fahrenheit.	Centigrade.
+ 140	60·00	+ 99	37·22	+ 58	14·44
139	59·44	98	36·67	57	13·89
138	58·89	97	36·11	56	13·33
137	58·33	96	35·55	55	12·78
136	57·78	95	35·00	54	12·22
135	57·22	94	34·44	53	11·67
134	56·67	93	33·89	52	11·11
133	56·11	92	33·33	51	10·55
132	55·55	91	32·78	50	10·00
131	55·00	90	32·22	49	9·44
130	54·44	89	31·67	48	8·89
129	53·89	88	31·11	47	8·33
128	53·33	87	30·55	46	7·78
127	52·78	86	30·00	45	7·22
126	52·22	85	29·44	44	6·67
125	51·67	84	28·89	43	6·11
124	51·11	83	28·33	42	5·55
123	50·55	82	27·78	41	5·00
122	50·00	81	27·22	40	4·44
121	49·44	80	26·67	39	3·89
120	48·89	79	26·11	38	3·33
119	48·33	78	25·55	37	2·78
118	47·78	77	25·00	36	2·22
117	47·22	76	24·44	35	1·67
116	46·67	75	23·89	34	1·11
115	46·11	74	23·33	33	+ 0·55
114	45·55	73	22·78	32	0·00
113	45·00	72	22·22	31	— 0·55
112	44·44	71	21·67	30	1·11
111	43·89	70	21·11	29	1·67
110	43·33	69	20·55	28	2·22
109	42·78	68	20·00	27	2·78
108	42·22	67	19·44	26	3·33
107	41·67	66	18·89	25	3·89
106	41·11	65	18·33	24	4·44
105	40·55	64	17·78	23	5·00
104	40·00	63	17·22	22	5·55
103	39·44	62	16·67	21	6·11
102	38·89	61	16·11	20	6·67
101	38·33	60	15·55		
100	37·78	59	15·00		

TABLE

TABLE FOR THE CONVERSION OF FRENCH WEIGHTS

	1	2	3	4
				1. MEASURES
METRES.				
English yards . .	1·09363	2·18727	3·28090	4·37453
„ feet . .	3·28090	6·56180	9·84270	13·12360
„ inches .	39·37080	78·74158	118·11236	157·48315
DECIMETRES.				
Feet . . .	0·32809	0·65618	0·98427	1·31236
Inches . . .	3·93708	7·87416	11·81124	15·74832
CENTIMETRES.				
Inches . . .	0·39371	0·78742	1·18112	1·57483
MILLIMETRES.				
Inches . . .	0·03937	0·07874	0·11811	0·15748
				2. MEASURES
LITRES.				
English cubic inches	61·02711	122·05422	183·08133	244·10844
„ cubic feet .	0·035317	0·070633	0 105950	0·141266
„ imp. gallons	0·22017	0·44033	0·66050	0·88066
„ „ quarts	0·88066	1·76133	2·64199	3·52266
„ „ pints .	1·76133	2·52266	5·28399	7·04531
CUBIC CENTIMETRES.				
Cubic inches . .	0·06103	0·12205	0·18308	0·24411
				3.
KILOGRAMMES.				
Cwts . . .	0·01970	0·03939	0·05909	0·07879
lbs. (avoirdupois) .	2·20486	4·40971	6·61457	8·81943
KILOGRAMMES.				
lbs. (troy) . .	2·67951	5·35903	8·03854	10·71805
GRAMMES.				
Grains . . .	15·44242	30·88484	46·32726	61·76968
DECIGRAMMES.				
Grains . . .	1·54424	3·08848	4·63273	6·17697
CENTIGRAMMES.				
Grains . . .	0·15442	0·30885	0·46327	0·61770
MILLIGRAMMES.				
Grains . . .	0 01544	0·03089	0·04633	0·06177

V.

AND MEASURES INTO ENGLISH WEIGHTS AND MEASURES.

	5	6	7	8	9
OF LENGTH.					
	5·46816	6·56180	7·65543	8·74906	9·84270
	16·40450	19·68539	22·96629	26·24719	29·52809
	196·85394	236·22473	275·59552	314·96630	354·33709
	1·64045	1·96854	2·29663	2·62472	2·95281
	19·68539	23·62247	27·55955	31·49663	35·43371
	1·96854	2·36225	2·75596	3·14966	3·54337
	0·19685	0·23623	0·27560	0·31497	0·35434
OF CAPACITY.					
	305·13555	366·16266	427·18977	488·21688	549·24399
	0·176583	0·211900	0·247216	0·282532	0·317849
	1·10083	1·32100	1·54116	1·76133	1·98149
	4·40332	5·28398	6·16465	7·04531	7·92598
	8·80664	10·56797	12·32930	14·09062	15 85195
	0·30514	0·36616	0·42719	0·48822	0·54924
WEIGHTS.					
	0·09848	0·11818	0·13788	0·15758	0·17727
	11·02428	13·22914	15·43400	17·63886	19·84371
	13·39757	16·07708	18·75659	21·43610	24·11562
	77·21210	92·65352	108·09694	123·53936	138·98178
	7·72121	9·26535	10·80969	12·35394	13·89818
	0·77212	0·92654	1·08097	1·23539	1·38982
	0·07721	0·09265	0·10810	0·12354	0·13898

TABLE VI.

TABLE FOR THE CONVERSION OF THE MILLIMETRE BAROMETER SCALE INTO THE SCALE OF ENGLISH INCHES.

Millimetres.	Inches.	Millimetres.	Inches.	Millimetres.	Inches.
700	27·560	730	28·741	760	29·922
701	27·590	731	28·780	761	29·961
702	27·638	732	28·819	762	30·000
703	27·678	733	28·859	763	30·040
704	27·717	734	28·898	764	30·079
705	27·756	735	28·938	765	30·119
706	27·795	736	28·977	766	30·158
707	27·835	737	29·016	767	30·197
708	27·876	738	29·056	768	30·237
709	27·914	739	29·059	769	30·276
710	27·953	740	29·134	770	30·315
711	27·992	741	29·174	771	30·355
712	28·032	742	29·213	772	30·384
713	28·071	743	29·252	773	30·434
714	28·111	744	29·292	774	30·473
715	28·150	745	29·331	775	30·512
716	28·189	746	29·371	776	30·552
717	28·229	747	29·410	777	30·591
718	28·268	748	29·449	778	30·631
719	28·308	749	29·489	779	30·670
720	28·347	750	29·528	780	30·709
721	28·386	751	29·567	781	30·749
722	28·426	752	29·607	782	30·788
723	28·465	753	29·646	783	30·827
724	28·504	754	29·685	784	30·867
725	28·543	755	29·725	785	30·906
726	28·583	756	29·764	786	30·945
727	28·622	757	29·804	787	30·985
728	28·661	758	29·843	788	31·024
729	28·701	759	29·882	789	31·063

28 inches = 711·187 millimetres.
29 „ = 736·587 „
30 „ = 761·986 „
31 „ = 787·386 „

1	millimetre	= 0·03937 inch.	1	inch	= 25·39954 millimetres.
0·1	„	= 0·00394 „	0·1	„	= 2·53995 „
0·01	„	= 0·00039 „	0·01	„	= 0·25400 „
			0·001	„	= 0·02540 „

INDEX.

Abscesses, pus in urine from, 259
Acetone, 314
in diabetic urine, ib.
mode of obtaining, ib.
Petter's observation of, 315
properties of, 314
Acid, anisic, 392
anthranilic, 337
benzoglycolic, 337
benzoic, 145, 148
camphoric, 391
carbolic, 339
carbonic, 226
cholalic, 273
cholic, 272
cholinic, 273
choloidinic, 272
cholonic, ib.
cinnamic,
citric, 387
cuminic, 392
damaluric, 343
free, of urine, 192
gallic, 232, 388
glucic, 305
glycocholic, 272
hippuric, 139
lactic, 373
malic, 381
melassic, 305
oxalic, 345
phenylic, 339
phosphoric, 179
salicylic, 390
salicyluric, ib.
succinic, 381
sulphuric, 169
tannic, 388
Acid, tartaric, 382
taurocholic, 273
toluric, 389
toluylic, ib.
uric, 77
Acidity of urine, 9
Addenda, 411
Age, influence of, on reaction of urine, 12
Albumen, 247
characters, ib.
composition, ib.
in urine, diagnosis, 250
pathological indications, 253
quantity, 252
in chylous urine, 240
Albuminuria, 253
Alkaline urine, 9
causes, 9, 211
from ammonia formed after discharge, 9
from decomposition of urea before emission, 10
causes, 12
experiments of Dr. Snow, 11
inflammation of bladder produced by, 13
therapeutic indications, 15
from fixed alkalies, 14
Allantoine, 298
literature, ib.
mode of obtaining, 299
pathological indications, 301

Allantoine, properties, 300
Ammonæmia, 75
Ammonia, 9, 218
analysis, volumetrical, 220
chemical properties, ib.
demonstration of presence in urine, ib.
formed after emission of urine, 9
formed in bladder under diseased conditions, 11
pathological indications, 12, 224
phosphates of, and magnesia. *See* Phosphate.
physiological origin, 223
quantity discharged in health, 223
urate of, 88
Antimony in urine, 405
Reinsch's test for, ib.
diagnosis from arsenic, 406
Arsenic in urine, 405
Reinsch's test for, ib.
diagnosis from antimony, ib.

Benzamide, 145
Bile, 271
acids, 275
colouring matters, 275
composition, 271
in urine, 5, 276
pathological indications, 277
Bilifulvine, 276
Biliverdine, 275
Bladder, cancer of, 265
causing hæmaturia, 262
conditions of, producing alkaline urine, 12
conditions of producing hæmaturia, 232
conditions of, producing purulent urine, 258
inflammation of, by alkaline urine, 13
Blood in urine, 227
casts, 231
chemical diagnosis, 230
coagula, 238
corpuscles, 227
microscopical appearance and reactions, 228
pathological indications, 227, 230
urea in, 43, 75

Calculi, alternating, 114
ammonio-magnesian phosphate, 207
cystine, 295
Calculi, fusible, 209
hæmorrhage from, 231, 232
mixed, 114
mulberry, 370
oxalate of lime, ib.
phosphate of lime, 207
phosphates, earthy, ib.
pisiform, 110
urates, 113
uric acid, 111
uric oxyde, 287
xanthic oxyde, ib.
xanthine, ib.
Cancer of bladder, 265
of kidneys, ib.
Cancerous matter in urine, ib.
Carnine. *See* Sarcine or Sarkine
Casts of uriniferous tubules,
epithelial, 243
fatty, 244
granular, 243
hyaloid, 242
intra-tubular, ib.
large, 244
small, 242
waxy, 242
Chloride of sodium, 154
chemical properties, 155
crystallography, ib.
detection in urine ib.
occurrence, ib.
Chlorine in urine, 153
analysis, 155
quantity discharged in health, 161
quantity discharged in disease, 165
Cholera, urine in, 367
Chylous urine, 238
albumen in, 240
fat in, ib.
fibrine in, 239
microscopical appearances, ib.
pathological indications, 244
Clearness of urine, 1
Collection of urine, 18
Colouring matter of bile, 275
in urine, 5, 276
of urine, normal, 2, 131
abnormal, 4, 234, 276, 321, 326, 338
Composition of urine of twenty-four hours—table, 416
Copper in urine, 408
test for sugar, 306-7

Creatine, 115
chemical properties, 118
composition, 115
decompositions, 118
history, 115
modes of obtaining, 116
occurrence, 115
physical properties, 117
physiology, 119
Creatine, quantity in twenty-four hours, 120, 124
tables of, 130
Creatinine, 121
chemical properties, 124
composition, 121
compounds, 124
crystallization, 123
mode of obtaining from creatine, 126
mode of obtaining from putrid urine, 122
mode of obtaining from urine, 121
occurrence, ib.
quantity in twenty-four hours, 126
tables of, 130
Cyanourine, 326
Cystine, 295
literature, ib.
occurrence, ib.
properties, 296
Cystitis, 13
Cysts of Echinococci, 267

Diabetes insipidus, 41
mellitus, 312
acetone in urine of, 314

Earths, phosphates of. *See* Phosphate.
Echinococcus hominis in urine, 267
cases, 268
cysts, 267
symptoms, 268

Fat in urine, 263
forms of, ib.
in chylous urine, 240
pathological indications, 264
Fermentation, 306
lactic acid, 307
vinous, 306
viscous, 307
Fever, urine in, 74
deposit of uric acid in, 101
Fibrine, 238
from blood, in urine, 228
in chylous urine, 239
Fibrinous casts, 241
Fibrinous casts, pathological indications, 245
Food, influence on reaction of urine, 211
on urea, 73
Free acid of urine, 192
analysis, volumetric, ib.
quantity in health, 193
in disease, 194

Glucose, 303
Glucosides, ib.
Glycocoll, 272
Grape sugar. *See* Sugar, 302
volumetric analysis for, 303
Gravel, uric acid, 109
oxalate of lime, 370
Gravimeter, 34
Guanine, 294

Hæmatine, 234
Hæmato-globuline, 234
distinction from dissolved blood, ib.
observations, 235
pathological indications, 237
Hæmaturia, 235
Hæmorrhoids of bladder, 232
Hæmorrhage from bladder, 232
from kidneys, 230
Halophile, 132
Hempseed calculi, 370
Herbivora, urine of, 140
Hippurate of baryta, 146
iron, 147
lead, ib.
lime, 146.
Hippuric acid, 139
chemical properties, 143
composition, 139
compounds, 145
decompositions, 143
deposits, 147
history and literature, 139
means of procuring, 142
occurrence, 140, 148
pathological, 141, 151
physical properties, 143
physiology, 148
quantity, ib.
salts, 146

Indican, 328
decompositions, 329
identity with uroxanthine, 327
occurrence, ib.
physiology, 337
Indigo blue, history, 326

Indigo blue, identity with uroglaucine, 332
metamorphoses, 336
modes of obtaining, 329
glue, 329
red, history, 326
identity with urrhodine, 332
mode of obtaining, 329
white, 330, 336
Inosite, 313, 318
mode of obtaining, ib.
properties, 319
Iodine in urine, 401
analysis of, volumetrical, 401
Iron, 214
analysis of, 215
physiology of, 216
Isatine, 336

Kidneys, cancer of, 265
diseases of, indicated by albuminous urine, 253
diseases of, indicated by blood in urine, 230
diseases of, indicated by fibrinous casts, 245
diseases of, indicated by pus in urine, 258
tubercle of, 265

Lactates, 377
Lactic acid, 373
analysis, in urine, 375
compounds, 377
mode of obtaining, 373
occurrence, ib.
pathological indications, 378
properties, 376
Lactide, 376
Lead in urine, 406
Leucine, 279
analysis, 285
compounds, 284
history and occurrence, 279
production, 280
from urine, 285
properties, 283
Lime, 198
analysis, 199
carbonate, 213
oxalate. *See* Oxalate of Lime.
physiological quantity, 209
phosphate. *See* Phosphate of Lime.
table of quantity discharged in twenty-four hours, 210

Magnesia, 198
analysis, 199
Magnesia, phosphate. *See* Phosphate of Magnesia.
physiological quantity, 209
table of quantity in twenty-four hours, 210
Mercury in urine, 408
Mucus, 1, 260
characters, 260
excess, 261
pathological indications of, ib.
physiological quantity, ib.
Murexide, 82
Muscle, creatine in, 115
creatinine in, 121
lactic acid in, 374
sarkine in, 291

Odour of urine, 8
Oil in urine, 264
Oxalate of lime, 347
calculi, 370
concretions, ib.
characters of, 371
statistics, 372
crystallization, 348
pathological indications of, in urine, 367
polarisation, 361
preparation of, for microscope, 353
Oxalic acid, 345
analysis, in urine, 362
compounds, 347
decomposition, ib.
history and occurrence, 345
mode of obtaining, 346
pathological indications, 362
properties, 346
Oxaluria, case of so-called, 358
Oxyde, uric, 287
xanthic, ib.

Phosphate of lime, 180, 198
analysis, 199
calculi, 208
deposits, 205
pathological indications, 210
of magnesia, 180, 198
ammonio-, 180
calculi, 207
deposits, 206
pathological indications, 210
of soda, 180
Phosphates, alkaline, 180
earthy, 180, 198

Phosphates, calculi, 207
deposits, 203
pathological indications, 210
physiological quantities, 209
mixed, 180
Phosphoric acid, 179
analysis, volumetrical (Liebig's method), 183
analysis in alkalies and earths separately, 185
chemical properties, 180
physical properties, 179
physiology, 187
quantity in health, 186
in disease, 189
salts, 180
Pigments, abnormal, 6
Pneumonia, urine in, 74
Polarisation of diabetic urine, 309
oxalate of lime, 361
Potash in urine, 195
analysis of, ib.
physiological relations of, 196
Prostate, enlargement of, 12
Purpurine, 320
diagnosis, 322
diseases in which it commonly occurs, 324
history, 320
mode of obtaining, 321
occurrence, ib.
pathology, 323
properties, 322
Pus, 256
casts, 258
globules, 256
pathological indications, 258
Pycnometer, 32

Quinidine, 393
Quinine, ib.
tests for, ib.

Reaction of urine, 8
table of substances causing, 15
Rheumatism, urine in, 324

Saccharimetry, optical, 309
volumetrical, 307
Salts, inorganic, 409
organic, in urine, 15
urophanic, 409
Santonine in urine, 398
Sarcina ventriculi, 413
Sarcine, or sarkine, 291, 411
characters, 292
compounds, ib.
history and occurrence, 291
modes of obtaining, 292, 411
Soda in urine, 195
analysis, ib.
phosphate of, 180
physiological relations, 196
Sodium, chloride of, 153
Solids in urine, 30
calculation from specific gravity, 35
Specific gravity of urine, 30, 32
Spermatozoa in urine, 269
detection of, 270
indications, 269, 270
Stone. See Calculus.
Strychnine in urine, 397
Sugar, grape, 302
analysis, volumetrical, 307
optical, 309
combinations, 304
decompositions, 305
mode of obtaining, 302
occurrence in body, ib.
pathological indications in urine, 312
properties, 304
Sulphur in cystine, 296
in taurine, 275
Sulphuric acid, 169
analysis of, volumetrical, 170
analysis, direct, 171
pathological indications of, 177
physiological origin of, 173
quantity discharged in health, 172
quantity discharged in disease, 176

Tartaric acid, 382
experiments on appearance in urine, ib.
experiments, table of, 386
Tartrates, 383
Taste of urine, 8
Taurine, 274
Test paper, 11
Tobacco, ammonia from, 224
Trimethylamine in urine, 411
Tubercular matter in urine, 265
Tubules, uriniferous, casts of, 241
Turbidity of urine, 1

Tyrosine, 279, 285
history and occurrence, 279, 286
production, 280
properties, 286

Uræmatine, 131
determining groups of urine, 134
modes of obtaining, 132
pathological indications, 138
physiology of, 137
properties, 131
quantity in disease, 138
table, showing amount in urine of different colours, 133
Uræmia, 11
Urate of ammonia, 88
lime, 91
soda, 90
Urates, calculi of, 113
with layers of uric acid, 114
deposits of, 96
after emission, 99
in urinary organs, 101
differential diagnosis of, 91
Urea, 43
analysis quantitative, 52
Bunsen's method, 67
Davy's method, 69
Liebig's method, ib.
modifications in, 61
other methods referred to, 72
artificial preparation, 45
combinations of, 47
with chloride of sodium, 48
nitrate of mercury, 50
nitric acid, 48
oxalic acid, 49
protoxide of mercury, 48
composition, 43
crystallization, 45
decompositions, 46, 69
definition, 43
detection, 51
diminution, 75
excess, 74
history, 44
occurrence in blood and tissues, 43
physical properties, 45
quantity in health, 73
in disease, 74
Urea, retention of in blood, 75
Urerythrine. See Purpurine.
Uric acid, 77
amount of, in health, 93
in disease, 95
analogues of, 82
analysis, 83
volumetrical, 85
calculi of, 111
alternating with urates, 114
composition, 77
concretions, 111
chemical characters of, 112
crystallography, 80
deposits, 96
after emission, 104
in urinary organs, 105
gravel, 109
history, 77
metamorphoses, 81
methods of procuring pure, 78
occurrence, ib.
physical properties, 79
salts, 87
sediments, crystalline, 109
crystallized, 107
Urinal for hospitals, 18
Urine, acetone in, 314
acidity of, 8
albumen in, 250
alkaline, 9
allantoine in, 298
ammonia in, 10, 218
bile in, 5, 276
blood in, 227
cancerous matter in, 265
carbolic acid in, 338
carbonic acid in, 226
changes on cooling, 16
chemical reaction, 8
table of substances causing, 15
chloride of sodium in, 154
chlorine discharged in, 161
chylous, 238
clearness and turbidity of, 1
collection of, 17
colour of, 1, 131, 321, 327
groups of, 134
constituents of, 416
creatine and creatinine in, 120, 126
cystine in, 296
damaluric acid in, 343
echinococci in, 267
fat in, 263

Urine, fibrine in, 338
fibrinous casts in, 241
free acid in, 192
hæmatine in, 5, 234
hippuric acid in, 139
hypoxanthine in, 289
incineration of, 153
indican in, 327
inorganic substances in, 401
iron in, 214
lactic acid in, 373, 378
leucine in, 280
lime in, 198
magnesia in, ib.
mucus in, 1, 260
odour of, 8
organic acids in, 380
bases in, 393
oxalates in, 348, 367
oxalic acid in, 346, 362
phenylic acid in, 338
phosphatic, 180, 198
phosphoric acid in, 179
physical characters of, 1
potash in, 195
purpurine in, 321
pus in, 256
quantity in health, 21
in given times, 20, 24
in diseases, 27
sarkine in, 291
soda in, 195
Urine, solids of, 30
specific gravity, 31
spermatozoa in, 269
sugar in, 302, 312
sulphuric acid in, 169
taste of, 8
tubercular matter in, 265
tyrosine in, 210
uræmatine in, 131
urerythrine in, 321
uroglaucine in, 327
uroxanthine in, 327
urrhodine in, 326
Urogravimeter, 34
Uroglaucine, 5, 331
Urophanic organic acids, 380
bases, 393
inorganic bodies, 401
Urostealith, 414
Uroxanthine, 4, 326
Urrhodine, 5, 326
Vegetable acids, 15

Water of urine, 30
Weight of urine of different densities, 36

Xanthic oxyde, 287
Xanthine, ib.
calculi, ib.
mode of obtaining, ib.
properties, 288

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STAINLESS STEEL

