Intestinal auto-intoxication / by A. Combe. Together with an appendix on the lactic ferments with particular reference to their application in intestinal therapeutics / by Albert Fournier ; only authorized English adaptation by William Gaynor States.

Doctor R. M. G. Binnie

With kind regards from

Mrs. C. J. Stewart

Easter 1911

GASTRO-INTESTINAL
AUTO-INTOXICATION

INTESTINAL AUTO-INTOXICATION

BY

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TOGETHER WITH AN APPENDIX ON THE LACTIC FERMENTS WITH PARTICULAR REFERENCE TO THEIR APPLICATION IN INTESTINAL THERAPEUTICS

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ONLY AUTHORIZED ENGLISH ADAPTATION

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AUTHOR'S PREFACE

The object of this book is to make my methods of treatment known. As clinical professor of children's diseases, I have had occasion many times to occupy myself with the intestinal disorders so frequently met with in children.

Circumstances have also, for several years past, obliged me to see many adults suffering from intestinal affections, and it is the ensemble of these two classes of patients that has occasioned my study of the digestive diseases from a nearer point of view.

As physician to children and specialist in that branch, I had as a matter of fact, not particularly studied the affections of the digestive tract until then; moreover, having but little familiarity with their classical treatment, I was very naturally led to create for myself personal methods and special procedures. Among these disorders there is one, which by its frequency and its importance, has more especially attracted my attention, and that is *Gastro-intestinal auto-intoxication*. It has led me to seek out its pathogeny, to establish its symptomology and diagnostic features and to study its rational treatment.

From different quarters I have been asked to publish the results of my methods of treatment. To this invitation I have very willingly responded and that is the genesis of this work, which is dedicated to the history of digestive auto-intoxication.

I have reserved in it, an important place for the treatment, for that is the practical side, to which all medical study should lead. The regimen in this condition has been the object of my constant preoccupation. I attach so great an importance to it, that I have had organized throughout Switzerland, in many hotels, tables of regimen where, under the direction of special and responsible cooks, my dietetic prescriptions are scrupulously followed.

Patients are assured of finding, besides the lodgings of their choice, the foods that are permitted them without having the temptation of those forbidden. An end which all physicians in watering places should endeavor to attain.

While playing a less important role, medicines and other therapeutic means, have their use in well-determined cases, and I have not omitted giving them the consideration they merit.

Such as it is, this book, it seems to me, brings well to the fore, the so important question of gastro-intestinal auto-intoxication. I have made use of the works that have already appeared upon the subject and particularly the beautiful researches of *Strauss*, *Albu*, *von Jacksch*, etc., in Germany and of *Charrin*, *Gilbert*, *Widal*, etc., in France.

I hope my work may prove useful and that it will be of service to practitioners; if so, I shall be happy to have attained my aim.

TRANSLATOR'S PREFACE

The immediate recognition and more than favorable reception accorded abroad by the medical press and profession to the work of *Professor Combe*, as well as the importance of the subject and its timeliness have led me to undertake its translation and adaptation in the belief that it would prove of service to the English-speaking medical profession.

Digestive auto-intoxication while long recognized and admitted by many, rested until within late years upon almost purely hypothetical grounds, for the known and scientifically proven facts relating to it were but few.

To *Bouchard* belongs the credit of being one of the first to investigate the subject in a scientific manner and the warm discussion excited by his famous experiments upon the toxicity of the urine paved the way for the many researches and investigations which have since taken place.

The great advances made in physiological chemistry and in the various departments of experimental research, have brought to light many new and unquestionable facts pertaining to metabolism, and the origin and action of toxins as well as showing the relation and interdependence of the various glandular organs concerned with the nutrition, their supplemental and complemental action and the effects upon the organism of their insufficiencies.

The subject is of interest not only to the practitioner and internist, but also to the specialist in different branches of medicine, for many obscure and baffling conditions are explained by it.

As may be inferred, the treatment of auto-intoxication demands an alimentation adapted to the particular condition with such adjuvant therapeutic measures as may be indicated. To

this part of the subject as well as to the diagnosis, *Professor Combe* has devoted much space and presents in detail the methods he has adopted after many years experience including the discussion of the relative merits of the various soured milks and lactic ferments now so widely engaging the attention of the medical world.

Craving indulgence for the defects inherent to a translation, I hope that the book will prove useful to the reader.

WILLIAM GAYNOR STATES.

New York.

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GASTRO-INTESTINAL AUTO-INTOXICATION

INTRODUCTION

Auto-intoxication is a toxæmia caused by substances, which are formed through the influence of the vital processes of the organism.

We must, therefore, if we wish to be faithful to this definition of auto-intoxication (as we understand it), eliminate from our study all toxæmias in which the toxic substances have been produced outside of the body and even those in which the toxins have been formed within the body, but under the influence of microbes introduced accidentally from without. Many authors have extended the limits of auto-intoxication much beyond those we assign to it here; for that reason we must examine and discuss the pathogeny of all these conditions, so as to remain within the limits of our subject.

1st. Toxinemias by infection.

2d. Toxinemias by absorption.

3d. Alimentary intoxications.

Let us briefly see why we do not include these conditions in the group of the auto-intoxications.

TOXINEMIAS BY INFECTION

We shall not include within the limits of auto-intoxication (as most German authors do) the toxic phenomena caused by microbes. Undoubtedly in infectious and contagious diseases, the toxins are formed in the organism, but they are not produced under the influence of a vital process, for they are a consequence of microbes which have accidentally penetrated

the body. In order to distinguish them from auto-intoxications, we shall reserve to the symptoms which accompany the infectious diseases (typhoid fever, measles, scarlatina, etc.), the term symptoms of intoxination as we proposed some years ago.

TOXINEMIAS BY ABSORPTION

Neither shall we include within the limits of auto-intoxications those intoxinations caused by absorption, notwithstanding the opinion and high authority of *v. Jacksch*[1]. The toxinemias by absorption are both numerous and frequent. We may, in fact, see quite a series of pyogenic intoxinations; a suppurative inflammation of the posterior urethra, of the prostate, the glands of *Bartholin*, or a pneumococcus infection of the peritoneum or other serous cavity, or else the pus from a bronchiectasis or tubercular cavity; all of these may give rise to toxic products of bacterial origin accompanied by indols, phenols, etc., which absorbed may cause more or less accentuated morbid symptoms.

Anæmia, emaciation, the pyæmic color, dry and shining tongue, profuse sweats, the rheumatic pains (rheumatism of bronchiectasis of *Gerhardt*) they are the most characteristic signs of these pyogenic intoxinations.

When the urine decomposes in the bladder and produces amines and ammonia, it may give rise by reabsorption of these products, to the symptoms known as ammoniæmia. We may at other times, see the development in the bladder, under the influence of the colon bacillus, of sulphureted hydrogen, which, reabsorbed, gives rise to the *hydrothionæmia* of *v. Jacksch* and *Senator*.

Ulcerated carcinomas give rise to numerous products of decomposition of bacterial origin, among which may be cited several aromatic substances such as phenol, skatol, which by reabsorption bring about the cancerous cachexia.

In all these cases of intoxination by reabsorption, the toxins which are of bacterial origin are, it is true, formed within the organism, but they are produced at the expense of bacteria

[1] Von Jacksch Nothnagel's Handbuch.

accidentally penetrating cavities in which they do not normally exist.

They have, therefore, no relation with the vital processes of the organism and hence we cannot consider them as true auto-intoxications.

ALIMENTARY INTOXICATIONS

It is also too comprehensive to consider as auto-intoxications (like *Senator* does), those food toxæmias resulting from tainted meats, sausages, fish, sardines, canned goods, moldy cheese, butter, etc. Undoubtedly, we find in the three classical forms of this condition the stamp of auto-intoxication; be it under the pseudo-typhoid form with its scarlatinal or rubeola-like eruptions (epidemic of *Trogen*) or the botulic form, a true ptomaine toxæmia with insignificant intestinal symptoms, but grave nervous manifestations, such as nuclear paralysis with diplopia, ptosis, strabismus, etc., peripheral paralysis with aphonia, dysphagia, etc. (disease of *Gerlier*), or under its most frequent form, a muco-dysenteric enteritis, with vomiting, bloody mucus stools and varied eruptions, mixed with purpuric elements (epidemic of *La Sarraz*). In all of these we will find the characters of digestive auto-intoxications, but the intoxication is caused by the flesh of diseased animals as *Bollinger* declares, or by pathogenic microbes or their toxins accidentally developing in healthy foods (bacillus of *Gärtner*), even when cooked such foods are noxious and may determine intoxications, the toxins not being destroyed either by cooking or boiling.

There is, therefore, no reason for including these digestive intoxications within the limits of the auto-intoxications; we shall not except even those caused by milk in the infant (milk disease of the English).

Milk, even when boiled or sterilized, may contain the bacillus of *Flügge*, and it may contain toxins as *Marfan* has shown; moreover, *Flügge* and *Lubbert* have proved that the toxins of the proteolytic bacilli of milk are dangerous only to puppies and not to adult dogs. This fact readily explains why, in a family using the same milk, the infants only suffer from its use while the adults do not.

But these infants do not suffer from digestive auto-intoxication as many authors claim, but from an alimentary toxæmia, coming from without; very little is required to bring about digestive intoxication in infants, and we must be on our guard before speaking of true auto-intoxication; for do we not often see slight dietetic indiscretions on the part of the wet nurse, or the change of food in cows from dry to green fodder, or fodder mixed with beets, turnips, etc., bring about in young infants grave symptoms of digestive intoxication, thanks to the peculiar idiosyncrasies of that age?

As a matter of fact, we find idiosyncrasies at all ages. They vary with the individual and kinds of food; with some, game, lobsters, prawns, etc., with others, eggs, strawberries, certain mushrooms, even vinegar, may suffice to produce digestive intoxication, while others partaking of the same foods do not suffer. These cases, nevertheless, like the preceding ones, and, notwithstanding their contrary appearance, belong to the alimentary intoxications and have nothing to do with digestive auto-intoxication. The differential diagnosis between these two forms of intoxication is without question delicate; hence we must never speak of auto-intoxication judged from appearances only; we must critically and carefully examine each individual case, if we do not wish to err in the treatment which will necessarily differ in an alimentary intoxication or a digestive auto-intoxication.

AUTO-INTOXICATIONS

These restrictions made, we can now take up the study of the true auto-intoxications, that is, those conditions the symptoms of which are caused by toxins produced under the influences of the vital processes of the organism.

These toxins may derive from two sources:

From the functions of the tissues and organs of the body or, from the functions of the digestive canal; hence they may be divided into two great groups.

1st. The dycrasic auto-intoxications.

2d. The gastro-intestinal auto-intoxications.

DYCRASIC AUTO-INTOXICATIONS

These we shall briefly review: This group is difficult to delimitate because the toxic substances produced by the functions of the different organs of the body, are not found at their point of origin; they are diffused in the blood or only appear in the secretions or excretions, and it is often difficult to trace their true source.

In the second place, a certain number of these substances are not poisonous in the true sense of the word; they act much less in causing by their presence qualitative changes (toxic) in the blood than in causing quantitative changes affecting its isotonicity. Now, we actually know that very serious symptoms, even death, may result from it, and it has been demonstrated that, when large molecules of albumin, sugar or intermediary products of metabolism increase in the blood, they may determine grave troubles which formerly would certainly have been attributed to true intoxication. The term of intoxication must, therefore, be extended and include not only the qualitative modifications of the blood, but its isotonic quantitative modifications as well.

The accumulation in the blood of normal or abnormal products may be caused by either.

An abnormal function of the tissues, or by an incomplete or insufficient action of the antitoxic glands, whose duty it is to convert the end products into useful or inoffensive substances.

Hence two types of dycrasic auto-intoxications may be described.

1st. *Histogenic dycrasic auto-intoxication* when the tissues produce the poison.

2d. *Organopathic dycrasic auto-intoxication* when the cause is due to the antitoxic glands.

A. HISTOGENIC AUTO-INTOXICATIONS

Histogenic auto-intoxications occur under very varying conditions. When the nucleins are destroyed and decomposed into uric acid, into purin bodies, xanthin, hypoxanthin, oxalic acid

and these substances are formed in excess in the blood, we find present the *uric acid diathesis of arthritism.*

The same state of the blood may be found in leukæmia and pseudo leukæmia, owing to the abundant destruction of the nuclei of the leucocytes. This first group constitutes the *nucleolytic auto-intoxications.*

Whenever the albumin, and especially the fats of the body are destroyed in too great quantities or too rapidly, fatty volatile acids are formed and also large quantities of ammonia, which these acids take from the albumin to saturate themselves with. When the fats are especially attacked, acetone is likewise produced.

This form of intoxication is sometimes called acid intoxication, sometimes acetonæmia. It accompanies and is characteristic of starvation, insufficient food, carcinomatous cachexia, certain grave anæmias, many intestinal affections, but especially grave diabetes; in other words, it may be observed whenever the fats and albumins of the body are destroyed in exaggerated proportions.

This second group constitutes the *proteo* and *lypolyptic auto-intoxications.*

Forced marches, physical overexertion produce an undue quantity of sarcolactic acid, which cannot be eliminated as fast as formed; its accumulation brings on fatigue; should it become chronic there results an intoxication of which physical weariness or exhaustion is the symptomatic picture. The same probably holds good for nervous exhaustion.

Such are the histogenic auto-intoxications; they have nothing to do with our special subject.

B. ORGANOPATHIC AUTO-INTOXICATIONS

The organopathic auto-intoxications are very numerous and vary greatly.

A first group of glands is intended for the elimination of substances noxious to the organism. These are the glands of external secretion.

Whenever one of these glands becomes insufficient, there occurs a retention in the body, of toxic substances which may

bring about grave morbid symptoms, varying with the gland at fault.

Symptoms of uræmia when it is the kidney.

Symptoms of cholæmia when it is the liver.

These constitute the *organopathic auto-intoxications of external secretion.*

A second group is intended to furnish the organism with substances indispensable to its normal life, or else to destroy by their antitoxic power substances noxious to it; whenever one of these glands becomes diseased or insufficient these toxic bodies accumulate in the body and give rise to serious manifestations and symptoms according to the gland affected.

Such are the *organopathic auto-intoxications of internal secretion.*

A most interesting group, for administration to a patient of the analogous gland taken from a healthy animal, will cause the disappearance of the morbid symptoms.

In this manner are developed Tetany from insufficiency of the parathyroid bodies.

Myxœdema from insufficiency of the thyroid:

Acromegaly from insufficiency of the pituitary body.

Addison's disease from insufficiency of the suprarenal capsules.

Having now eliminated all the dycrasic auto-intoxications and defined the limits of our subject; we may now take up with profit the gastro-intestinal auto-intoxications.

II. GASTRO-INTESTINAL AUTO-INTOXICATION

Intestinal auto-intoxication is the toxæmia caused by qualitative or quantitative alterations in a normal digestion, but by normal digestion we do not mean only, that described by physiologists, but the much more complete and complicated digestion which takes place in every normal man, for, besides the digestion by the enzymes of the stomach and intestines, there occurs in every man a digestion brought about by the action of the microbes which live and thrive in the digestive tract. The digestive enzymes convert starches into sugar, emulsify fats, transform nitrogenous bodies into albumin, peptones and crystalline bodies.

The microbes do the same; there are bacilli which convert starches into sugar, others which emulsify fats, still others which know admirably how to transform albumin into albumoses, peptones and crystalline bodies.

The action of the microbes is, however, not limited to that, for, we find in the chyle and fecal matters a gas: sulphureted hydrogen, some acids, lactic, butyric, propionic, etc., which are derived from the fermentation of the carbohydrates; we find besides, aromatic substances and ptomaines derived from the putrefaction of nitrogenous bodies; these are not produced by the enzymes themselves. So we must admit that they are derived from the action of the microbes. Thus, the microbes of the normal digestive tract, digest and bring about putrefaction at the same time, and their action, varying with different individuals, varying in the same individual according to circumstances, enables us readily to understand why clinical digestion can hardly be compared to that of the physiologists, how it is that two digestions each normal cannot be superimposed, one upon the other (*Marfan*), and why, in the same person, the morning digestion often differs from that of the evening without ceasing for that reason to be normal.

This constant intervention of the microbes in digestion permits us to consider it a normal process of the organism; the intoxication which results from it is, therefore, a true auto-intoxication.

These facts now actually admitted, give rise to three questions of high importance, namely:

1st. Is the microbic intervention useful to the organism?
2d. Is the microbic intervention indispensable?
3d. Can the microbic intervention become harmful?

1st. *Is the microbic intervention useful?* It certainly is, because it aids digestion; it digests foods as well as the enzymes —and because it supplements in many cases, the insufficiency of the gastro-intestinal glands.

It is especially useful because it transforms and renders assimilable certain foods (cellulose for example), which the enzymes are incapable of digesting.

2d. *Is microbic intervention indispensable*! Can we conclude that it is so useful, so necessary as to become indispensable? In other words, would the organism suffer, if deprived of it, or would it perish if it were entirely lacking.

Pasteur had so supposed. *Nutall* and *Thierfelder*[1] in the hope of disproving *Pasteur's* contention, succeeded in keeping alive young guinea pigs aseptically taken from the mother's womb, and fed upon sterile food only.

The animals lived, but in a defective manner, for they remained much below the weight and size of the control guinea pigs.

Schottelius[2] in more prolonged experiments seems to have shown that *Pasteur* was justified; for his aseptic chickens aseptically fed, all died while the control birds thrived normally.

Charrin and *Guillemonat* demonstrated that the adult organism deprived of all microbic contact by sterilization of the air, surroundings and food, becomes emaciated, anæmic and less resistant to infection.

Hence (without wishing to conclude from these still none too conclusive experiments), we may say that the microbes intervene actively in all the digestive processes, but that, besides their undeniably useful role, it is also undeniable that their action transforms the digestive canal, even in the normal state into a receptacle and constant laboratory of poisons (*Marfan*).

So that the third question becomes necessary.

3d. *May the microbic intervention become noxious*? Is it possible for the quantity of toxic substances produced, to become so great or the power of the antitoxic glands diminish so much, that these substances may pass into the blood and give rise to intestinal auto-intoxication?

This question is of the greatest importance, in relation to the subject before us, for upon its answer will depend the existence of the theory of intestinal auto-intoxication. It was *Senator*, who, in 1868, first made mention of it, when he then described the intoxications, the cause of which resides in the intestine. Fifteen years later and nearly at the same time *Bouchard* and *von Jacksch* introduced into science the term of gastro-intestinal

[1] Nutall & Thierfelder: Zeits. f. phys. Ch. XXII, p. 71.
[2] Schottelius: Arch. f. Hygiene, XXIV, p. 210.

intoxication; but it must be said that it is especially to *Professor Bouchard* that is due the great merit of having founded the theory of gastro-intestinal intoxication upon a solid basis, to have studied it in all its aspects and to have extended its domain to the farthest limits.

He furnished an experimental proof which, at the time seemed decisive, by demonstrating that the urine of auto-intoxicated individuals, when injected into animals was incomparably more toxic than normal urine. After having been accepted without question, the theory of auto-intoxication and the experiments of *Bouchard* have in the last years been strongly combatted by the German school. The great majority of German physicians speak only of the *hypothesis* of intestinal auto-intoxication. They exact, and with reason, that before admitting its existence, that physiological chemistry should demonstrate the poison and that experimental pathology should reproduce in the animal injected with this poison all the symptoms of auto-intoxication.

They showed through *Posner* that the experiment of *Bouchard* (the injection of urine into animals), may be explained and is explained without needing the supposition of toxic substances; a simple isotonic defect in the injected fluid sufficing to produce the same symptoms.

The question of intestinal auto-intoxication was discussed at the Congress of Wiesbaden in 1895. The great majority of those taking part in the discussion arrived at negative conclusions or else expressed doubts as to its existence.

Even the greatest authorities on intestinal auto-intoxication in Germany: *Senator*, *Ewald*, *Brieger*, *Albu* and *Strauss*, expressly recognized that, the experimental proof of this condition was far from having been given, but at the same time they called attention to the fact that, if properly considered there was nothing astonishing in this, for the difficulties are enormous and the conditions under which the experiments should be made almost impossible to realize, and that as a matter of fact, in the most frequent chronic forms; the quantities of toxins contained in the urine are so slight, that, with our present methods, we cannot think of isolating them.

In the acute forms where there might be sufficient, it is difficult and most frequently impossible to collect enough urine owing to the state of the patient.

Secondly, even if we succeed in isolating from the urine of these patients one or more toxins—and this has been accomplished several times—the quantities recovered are so slight, so infinitesimal that experiments upon animals are absolutely illusory, and even positive results—they have also been obtained several times—are far from being convincing.

Brieger, the distinguished chemist, in conclusion, said: "Our researches in the domain of physiological chemistry are as yet so incomplete, so insufficient, that a negative result proves nothing at all."

These reservations of the great German scientist were well made, for since that time the progress made in physiological chemistry permits the demonstration—either in the fæces or urine—of the existence of numerous and undoubted toxic substances.

Unquestionably, if we should examine each one of the bodies produced by microbic intestinal putrefaction; we would find that they are far from all having the same degree of toxicity, but it must not be forgotten that these same bodies individually but slightly toxic, may by combining their toxic value with that of their fellows, bring about a general and cumulative toxæmia; which can become considerable, if their quantity increases greatly. Secondly, the greater part of these toxic bodies—as is shown by the refraction index of the urine—is constituted by large molecules, capable of causing great variations in the osmotic pressure and superficial blood tension, when they enter the circulation.

That, in itself, is sufficient to bring about grave disorders, even death.

It is, therefore, quite likely, that the morbid symptoms of auto-intoxication are not only of a chemical nature, but of a physical nature also. Contemporaneously with the results achieved in physiological chemistry, the progress made in experimental pathology has enabled *Charrin* and his pupils —thanks to better methods and especially to a remarkable

technic—to reproduce in animals either by the injection of intestinal products or their inoculation, all of the lesions found in auto-intoxicated man. The *hypothesis* of intestinal auto-intoxication being thus demonstrated; we may now take up the consideration of the *theory*, as scientifically verified.

Let us add, that, abstraction made of the experimental point of view (the most important of all). It is equally true that clinical observations also lead us to admit the theory of intestinal auto-intoxication, for better than any other, it explains the symptoms of which our patients complain, better than any other does it indicate the most suitable treatment and most useful therapeutic means to employ.

Finally a glance at the anatomy and physiology of the intestine and its annexes, will demonstrate without difficulty, that the intestinal canal was constructed and adapted in view of the intestinal poisons and for the purpose of combatting them.

If the intestinal microbes and their products were so inoffensive, why should the organism have accumulated such abundant means of defense? of the first, second and third order. Why should the digestive juices possess the power of neutralizing digestive toxins? Why should the intestinal epithelium play the antitoxic role so well demonstrated by the experiments of *Queirolo, Heidenhain, Charrin* and *Tedeschi?* Why should the blood returning from the intestines be obliged to pass through the liver, the epithelium, of which is endowed with mighty toxicolytic power?

Why should we find that third line of defense, the antitoxic glands, thyroid, thymus, suprarenal the zymases of which modify and neutralize certain toxins of intestinal origin which circulate in the blood as we definitely know? Why, finally, should the eliminating organs constantly reject and throw out the products of intestinal putrefaction, if these were harmless? Ammonia and acetone are eliminated through the respiration; the skin throws out with the sweat, indol, phenol and sulphoethers; lastly, the kidneys eliminate through the urine the majority of the intestinal poisons.

The economy is, therefore, powerfully armed against the substances continually formed in the digestive tract. What

does that prove? If not, that these products constantly formed by the enzymes and microbes, contain poisons which may become dangerous to the organism.

We can see that, whether we consider the anatomy or physiology of the digestive tract, whether we examine the symptomatic pictures presented at the clinic or whether we should seek in biological chemistry or experimental physiology for decisive and scientifically demonstrated proofs, we find everywhere evidence of the existence of intestinal auto-intoxication.

This condition presents a particular etiology, a distinct pathogeny, a well-defined clinical picture and symptomology, a very special prognosis and treatment; more than enough to make an entity of it and more than enough to justify the detailed study of gastro-intestinal auto-intoxication which we are about to make.

TOXIC SUBSTANCES

The study of auto-intoxication, which we are about to make, will be confined to the morbid phenomena produced by the toxic substances derived from albumin.

We shall, therefore, leave out all the toxic substances derived from the decomposition of ternary bodies; fats and carbohydrates, because their biological chemistry is too incomplete at the present time. Even when thus limited, the study is still considerable for the researches made during the last years almost exclusively in Germany by *Kossel, Fischer* and their collaborators, have profoundly modified our previous knowledge of the transformation, which the albuminous molecule undergoes in the digestive tract of man.

In order to understand nitrogenous auto-intoxication of microbic origin, it is necessary to have an exact knowledge of the bodies that arise from the disintegration of the albuminous molecule, and to be able to distinguish on the one hand those produced in the digestion by the enzymes, on the other, those produced by microbic putrefaction; for it is only in the latter, that we shall find the toxic bodies capable of causing auto-intoxication. As the French textbooks are not up to date with the contemporaneous work done upon the chemistry of the albumins; we shall be obliged to fill in the gap, and give a short *résumé* of the present status of the question.

We shall consider in their order:

1st. The transformation of the albuminous molecule in the digestive tube caused by the enzymes or the microbes.

2d. The non-toxic products derived from the disintegration of the albuminous molecule.

3d. The toxic products derived from its disintegration.

I. TRANSFORMATION OF ALBUMIN IN THE INTESTINE

The study of the peptic and tryptic digestion of the albuminous molecule, appeared to have been determined in the most exact manner by *Kuhne*[1] and his school. It was believed as *Kuhne* taught that the digestion of the proteids was limited to a simple hydrolysis giving birth, only, to non-crystalline albuminoid bodies—the albumoses and the peptones—but the researches of *Salaskin*[2], of *Larow*[3], of *Zunz*[4], have shown that the transformation of the albumins, was much more complete than was thought and that the action of the digestive ferments (enzymes and microbes) changed the peptones into crystalline bodies which no longer gave the characteristic reaction of the proteids (biuret reaction or reaction of *Rose Piotrowski*).

Let us examine the matter more closely and let us try—basing ourselves upon the modern works—to follow the enormous albuminous molecule, in its course, throughout the intestine; so that we may study its successive transformations into simpler molecules of gradually decreasing molecular weight. *Kossel* looks upon the albuminous molecule as being formed of a basic protamic nucleus (constituted by hexone bases), combined with amino acids of the fatty and aromatic series.[5] It was based upon this hypothesis that *Fischer*, in an experiment that will forever remain celebrated, succeeding in resolving the synthesis of albumin.

Let us see what becomes of this molecule, when it comes in contact with chemical agents outside of the body and with the organic agents (enzymes and microbes), in the digestive tube itself.

A. THE ACTION OF ACIDS UPON THE ALBUMINOUS MOLECULE

Proteids in the presence of boiling mineral acids give rise to the following bodies:

1st. *Diamino acids*, or *hexone bases:* Lysin, arginin, histidin.

[1] Kuhne: Zeits. f. biol. Ch. XXVIII, p. 571.
[2] Salaskin: Zeits. f. phys. Ch. XXXII, p. 592.
[3] Larow: Zeits. f. phys. Ch. XXX, p. 312.
[4] Zunz: Contribution à l'étude de la digestion. Bruxelles. 1902.
[5] Kossel: Zeits. f. phys. Ch. XXV, p. 115.

2d. *Ammonia.*

3d. *Monamino acids.*

Aromatic Series. Phenylaminopropionic acid or phenylalanin, tyrosin, indolaminopropionic acid or tryptophan.

Fatty Series. Leucin, glycocol, aminopropionic acid or alanin, aminovalerianic acid or butylalanin, aspartic acid, glutamic acid. The acids, therefore, bring about the decomposition of the albuminous molecule as far as the amino acids and no further.

B. ACTION OF ALKALIS UPON THE ALBUMINOUS MOLECULE

Proteids in the presence of caustic alkalis give rise to the following bodies:

1st. *Diamino acids*, or *hexone bases:* Lysin, arginin, histidin.

2d. *Ammonia.*

3d. *Monamino acids.*

Fatty Series. Leucin, glycocol, alanin, aspartic acid, aminovalerianic acid.

Aromatic Series. Phenylalanin, tryptophan, tyrosin.

4th. *Fatty Acids.* Acetic, valerianic, butyric, derived from the decomposition of leucin.

5th. *Aromatic bodies* derived from the decomposition of tyrosin and tryptophan.

(*a*) *The aromatic oxyacids;* paraoxyphenylacetic acid and paraoxyphenylpropionic acid.

(*b*) *The phenols.*

(*c*) *The indoxyls and skatoxyls*, as will be noticed—the alkalis carry the decomposition of the albuminous molecule much further than do the acids; they decompose a part of the amino acids into fatty and aromatic bodies.

C. ACTION OF THE PROTEOLYTIC ENZYMES UPON THE ALBUMINOUS MOLECULE

1. GASTRIC DIGESTION (PEPSIN AND PSEUDO PEPSIN).

According to *Kuhne*, gastric digestion gave rise to two distinct bodies—the hemibodies (hemialbumoses and hemipeptones),

and the antibodies (antialbumoses and antipeptones); the latter being fixed bodies underwent no further changes; the hemibodies alone underwent ulterior transformation through the action of the pancreatic trypsin.

Hence *Kuhne* and his school looked upon the hemipeptones and the antipeptones as the end products of peptic digestion.

It has been demonstrated by the researches of *Larow* and *Zeitz*—already cited—and by the more recent investigations of *Langstein*[1] that pepsin and the pseudo-pepsin of *Glæssner*[2] do not stop at the formation of peptones, but that they go to the point of forming crystalline bodies.

Zunz has shown (and Emerson[3] has confirmed it), that as soon as three hours after digestion from 30 to 40 per 100 of the ingested albumin no longer has an albuminoid structure, does not give the biuret reaction and is constituted only by crystalline bodies.

From this we see that the proteolytic enzymes of the gastric juice decompose albumin with the absorption of water; albuminous bodies are first formed (the albumins and peptones), then more than a third of these substances undergo a further decomposition and are changed into crystalline bodies.

These crystalline bodies play an important part in the utilization of the chyme; if we are to believe the researches of *Zunz*, for this author has shown that the gastric absorption, much slower and much less important than the intestinal does not act upon the albumoses and peptones, but solely upon the crystalline albuminous bodies.

ACTION OF PEPSIN UPON THE ALBUMINOUS MOLECULE

1st. *Non-crystalline bodies* albumose, peptones.
2d. *Ammonia.*
3d. *Diamino acids.* Lysin, arginin, histidin.
4th. *Monamino acids.*
Aromatic Series. Tyrosin, tryptophan, phenylalanin.
Fatty Series. Leucin, glycocol, alanin, glutamic acid.

[1] Langstein: Hofmeister's Beiträge, I, p. 507.
[2] Glæssner: Hofmeister's Beiträge, I, p. 27.
[3] Emerson: Deutsch. Arch. f. kl. Med. 1902. p. 415.

Aspartic acid amidovalerianic acid. The gastric enzymes therefore give rise to the same products as the action of the acids.

2. INTESTINAL DIGESTION (EREPSIN AND TRYPSIN)

Intestinal digestion much more powerful than the gastric, disposes of several enzymes.

A. THE SECRETION OF BRUNNER'S GLANDS. Isolated by *Glæssner* contains proteolytic ferments, the importance of which has not yet been determined.

B. EREPSIN. The small intestine secretes a second ferment isolated by *Cohnheim*[1], which he named erepsin; it has no digestive action upon native albumins with the exception, however, of casein[2], but on the contrary, has the faculty of converting albumoses and peptones into crystalline bodies.

The existence of this ferment is doubted by *Schmoll* (of Basle), who gives an excellent view of this difficult question[3], but the investigations of *Kutscher* and *Seemann*[4], of *Salaskin*[5] and *Emden* and *Knoop*[6] have confirmed, not only its existence but its importance.

Erepsin is secreted in small quantities with the intestinal juices, but it is especially found in the cells of the mucosa, and it is during their passage through it, that its action upon the albumoses and peptones becomes preponderating. The action of erepsin is therefore that of an intracellular digestive of the absorbed peptones, but its action does not exceed that of trypsin, nor that of boiling acids, for it only gives rise to basic diamino crystalline bodies and monamino acid crystalline bodies, but not *to their secondary products of fatty and aromatic decomposition*, as shown by *Mochizuki*[7].

C. TRYPSIN. The pancreatic juice is much the more active and the most important of the three. Be it as it may, the pancreatic juice is secreted through the influence exercised by

[1] Cohnheim: Zeits. f. phys. Ch. XXXIII, p. 401.
[2] Cohnheim: Zeits. f. phys. Ch. XXXV, p. 139.
[3] Schmoll: Sem. med. 1902. p. 250.
[4] Kutscher & Seemann: Zeits. f. phys. Ch. XXXV, p. 528.
[5] Salaskin: Zeits. f. phys. Ch. XXXV, p. 419.
[6] Emden & Knoop: Hofmeister's Beiträge, III, p. 120.
[7] Mochizuki: Hofmeister's Beiträge, I, p. 44.

contact of the gastric hydrochloric acid upon the mucosa of the duodenum (*Pawlow*), or as claimed by *Bayliss* and *Starling*[1], through the influence of *secretin*, a substance produced by the action of hydrochloric acid upon the inactive *prosecretin* which is found in the mucosa of the duodenum and small intestine.

The pancreas secretes an inactive enzyme *zymogen*, which, under certain conditions becomes transformed into one of the most active proteolytic enzymes—namely *trypsin*.

These conditions were discovered by *Pawlow* and studied by his pupils, *Schepowelnikoff*, *Sawitsch*[2], *Popielski*[3], etc. These authors discovered and described a special body in the intestinal juices, which does not of itself exercise any digestive functions, but which has the faculty of changing zymogen into trypsin, and to which they gave the name of *enterokinase*.

The secretion of enterokinase is not caused by either chemical or mechanical agency; it only occurs when the pancreatic juice (and it only), comes in contact with the intestinal mucosa.

The bacteria do not produce any, but according to *Delezenne*[4], it is secreted through the influence of the leucocytes of *Peyer's* patches; the pancreatic juice is rendered active by enterokinase and exercises a most powerful proteolytic action.

ACTION OF TRYPSIN UPON THE ALBUMINOUS MOLECULE

Kuhne considered that, as in gastric digestion, the albuminous molecule was divided by the action of trypsin into the two bodies—hemibodies and antibodies—the anti group (anti-albumoses and antipeptones) resisting tryptic digestion and being absorbed as such by the intestinal cells, to undergo retransformation into circulating coagulable albumin, destined to replace that used up by the cells of the organism. The hemibodies (hemialbumoses and hemipeptones), undergoing an ulterior decomposition into crystalline bodies which (still according to *Kuhne*), never entered into the reconstitution of the organs, nor assisted in new tissue formation. A pupil of

[1] Bayliss & Starling, Journ. of Phys., XVI, p. 121.
[2] Schepowelnikoff: Sawitsch Wratch, I, p. 200.
[3] Popielski: Wratch, I, p. 672.
[4] Delezenne: Soc. biol., LIII, p. 1161.

Kossel, F. Kutscher[1], succeeded in demonstrating how far *Kuhne* had been from recognizing the true facts, and showed, that, on the contrary, tryptic digestion disassociated the anti-peptones as well as the hemipeptones into diamino hexone bases (arginin, lysin, histidin), and into monamino acids.

Moreover, *Kutscher* and *Seemann*[2] have shown us that, in a dog after a meal of 500 grammes of meat, there is found, beginning from the middle of the small intestine, a chyle containing only traces of albumoses and peptones, all the rest being constituted solely by hexone bases and monamino acids, that is to say, crystalline bodies. To conclude, both artificial and natural tryptic digestion decompose the albuminous molecule, with extreme facility, and give rise to the following bodies:

1st. *Non-crystalline bodies:* albumoses and peptones.

2d. *Ammonia*[3].

3d. *Diamino acids:* lysin, arginin, histidin.

4th. *Monamino acids:*

Aromatic Series: tyrosin, phenylalanin, tryptophan.

Fatty Series: leucin, glycocol, alanin, aspartic acid, glutamic acid, amidovalerianic acid.

Digestion by trypsin, therefore, gives rise to the same bodies as gastric digestion and the action of boiling acids, the only difference being that trypsin has an action incomparably more powerful and especially more rapid than pepsin.

D. ACTION OF BACTERIA UPON THE ALBUMINOUS MOLECULE

Besides the digestion by the enzymes, there exists, as we know, a microbic digestion.

Let us see what action the microbes exercise upon the proteids.

A. IN THE OPEN AIR. On allowing as *Odermatt* did, a pancreatic digestion of albuminous substances to putrefy in the open air; we shall see indol appear beginning from the second day. After the fourth day, phenols are produced in considerable proportions (weak alkalis increase these proportions; acids

[1] F. Kutscher: Zeits. f. phys. Ch. XXV, p. 195.
[2] Kutscher & Seemann: Zeits. f. phys. Ch. XXXIV, p. 528.
[3] Fischer: Zeits. f. phys. Ch. XXXIX, p. 83.

suppress them). If the putrefaction is allowed to go on for two weeks, the indol volatilizes and the putrid odor diminishes, while that of the phenols increases more and more. The formation of so antiseptic a substance as phenol under the influence of putrefaction is astonishing, but not without analogy in nature.

B. IN THE INTESTINE. In the intestine we see the same substances appear as in the open air, and that under the sole influence of bacteria.

The conditions for their formation appear to be even more favorable in the intestine than in the open air, for these substances are formed with very great rapidity, as *Brieger*[1] was able to show while examining the fæces.

As to the products of this putrefaction, we actually know what they are, thanks to the labors of *Baumann, Brieger, Nencki, Salkowski, Hoppe-Seyler* and their pupils. In nitrogenous putrefaction, there are produced in the first place the same substances that result from digestion by the enzymes; but the microbes do not stop there, for they bring about the decomposition of the crystalline bodies into secondary bodies which we shall enumerate.

C. MICROBIC DECOMPOSITION OF THE ALBUMINOUS MOLECULE

1st. *Non-crystalline bodies:* albumoses, peptones.

2d. *Ammonia:*

3d. *Diamino acids:* lysin, arginin, histidin.

4th. *Monamino acids:*

Aromatic Series: phenylalanin, tyrosin, tryptophan.

Fatty Series: leucin, alanin, glycocol, aspartic acid, glutamic acid, amidovalerianic acid.

5th. *Fatty bodies:*

(*a*) Butyric, caproic, valerianic acids.

(*b*) Ptomaines.

6th. *Bodies of the aromatic series:*

(*a*) *Oxyacid group:* paraoxyphenylacetic acid, paraoxyphenylpropionic acid.

[1] Brieger: Journ. f. prak. Ch. XVII, p. 134.

(*b*) *Phenol group:* phenol and paracresol.

(*c*) *Group of the indoxyls:* indol, skatol.

7th. *Gases:* methane, hydrogen, carbonic acid, sulphureted hydrogen, methylmercaptan.

From this, it will be seen that the microbic digestion gives rise, not only to the amino acids, but also to the products of their secondary decomposition; the aromatic and the fatty bodies.

In what portion of the intestine does this secondary decomposition, of microbic origin and which characterizes putrefaction, take place?

Ernst[1] has been able to demonstrate it. To a dog fasting for several days was given a quantity of meat; four hours later the animal was killed and each portion of the digestive tube was separately examined.

	Stomach	Jejunum	Ileus	Large Intestine
Peptones	abundant	none	none	none
Tyrosin	none	abundant	weak	none
Acetic acid	none	abundant	weak	none
Oxyacids	none	weak	weak	none
Phenol	none	weak	traces	strong
Indol	none	weak	strong	strong
Skatol	none	weak	strong	very strong

This shows that in the carniverous dog, the putrefactive processes are almost *nil* in the upper portions of the small intestine, and that they increase little by little in the lower parts, but they only become intense when in the large intestine and they do not again diminish until its lower portion is reached; the watery parts having been largely reabsorbed and the contents having become formed and hard. *Nencki* and *Sieber*[2] followed up this important investigation in a man suffering from a fistula of the lower portion of the ileus, and they arrived at the following conclusions:

The contents of the small intestine have an acid reaction of

[1] Ernst: Zeits. f. phys. Ch. XVI, p. 216.
[2] Nencki & Sieber: Arch. f. exper. Path., XXVIII.

1 per 1,000. They are inodorous. They contain large proportions of fatty acids; lactic acid, paralactic, acetic and biliary acids, some dextrin, sugar, alcohol, peptones, albumoses, some amino acids, but no aromatic substances or ptomaines.

Hence that the bacteria of the small intestine did not exercise any action upon the albumins, unless in very exceptional cases, but that they caused a considerable fermentation of the carbohydrates with formation of alcohol and fatty acids (lactic and succinic acids). These are the acids which inhibit the action of the proteolytic bacteria, and prevent the putrefaction of nitrogenous bodies.

Jakowski[1] completed these findings by numerous investigations of the large intestine and he concluded that, *albuminous putrefaction occurs normally only in the large intestine in which the reaction is alkaline.* We, therefore, are in position to say that, in the small intestine:

1st. The united action of the enzymes and bacteria give rise to products of the digestion of the carbohydrates mixed with the products of their fermentation.

2d. The action of the proteolytic ferments extends to the formation of dia and monamino crystalline bodies, the proteolytic bacteria being unable to develop in them their putrefactive action. In the large intestine, the reaction becoming more alkaline owing to the liberation of the albuminous bases, the action of the proteolytic bacteria can manifest itself and give rise to the aromatic bodies (phenol, skatol, indol), and ptomaines.

Hence, that normally the fermentation of the carbohydrates takes place in the small intestine and that the putrefaction of the nitrogenous bodies occurs in the large intestine. In extreme cases of putrefaction the action of the proteolytic bacteria begins in the lower portion of the small intestine.

D. COMPARISON OF RESULTS

We have seen that outside of the organism we must distinguish between the action of the acids, which decompose the albumins up to the formation of dia and monamino crystalline

[1] Jakowski: Arch. soc. biol. St. Petersburg. I, p. 4.

bodies, and the much more powerful action of the alkalis which carry their action much further and which, instead of stopping at the amines, attack them also with the formation of derivatives of the fatty and aromatic series.

These two modes of decomposition of albumins, are reproduced within the organism in exactly the same manner.

The digestive enzymes (pepsin, pseudo pepsin, erepsin and trypsin), end (as with the hydrolysis of the acids), with the formation of the mono and diamino crystalline bodies and go no further. Microbic digestion (as with the caustic alkalis), determines the formation of the same amino bodies, but does not end there; for by attacking and secondarily decomposing them it causes the formation of derivatives of the fatty and aromatic series already mentioned; so that the digestion by the enzymes corresponds to the action of the acids; that of the microbes to that of the alkalis.

We may say that microbic digestion is useful in the sense that it aids in the formation of the crystalline bodies, but that on the other hand, it is harmful in that it takes away from the organism a certain number of substances which it at first renders useless and ultimately noxious.

Let us look into the matter more closely and consider the following questions:

1st. What is the ulterior fate of the amino acids?

2d. What is the ulterior fate of the aromatic bodies derived from them?

1st. FATE OF THE AMINO BODIES

Until recently it was thought, according to *Hofmeister*[1], *Shore*[2], and *Neumeister*[3], that the hemialbumoses and the hemipeptones produced by the gastric and intestinal digestion, were retransformed into albumin by the cells of the digestive mucosa, but *Embden* and *Knoop*[4] never found the albuminous synthesis in the mucosa, and *Cohnheim* has shown that, if the peptones disappeared in the cells of the mucosa, it was not

[1] Hofmeister: Zeits. f. phys. Ch. VI, p. 51.
[2] Shore: Journ. of Phys., XI, p. 528.
[3] Neumeister: Zeits. Biol., XXVII, p. 309.
[4] Embden & Knoop: Hofmeister's Beiträge, III, p. 120.

because they were changed into albumin, but because they had been decomposed into amino acids, so that we are able to admit, thanks to the labors of *Kutscher* and *Seemann*[1] and of *Lœwi*[2], that all the albuminous substances utilized by the intestine must undergo crystalline formation, no longer reacting to the biuret test.

It is only under that form that they are absorbed and utilized in the cephalopods[3]. *Lœwi*[4] has confirmed these views which he practically demonstrated by feeding his dog during a period of five weeks with nothing but crystalline bodies derived from a peptic digestion, and without a trace of albuminous substances. The dog, not only maintained an excellent nitrogenous equilibrium, but even increased in weight. The cells of the digestive mucosa have therefore the property as *Glæssner* showed[5] of reconstituting at the expense of the mono and diamino bodies, a new albumin of different constitution from that found in the intestine (the human albumin of *Schmoll*), which, when absorbed in the blood serves to rebuild the organs; while an animal albumin entering the blood without undergoing the preliminary transformation into crystalline body, would act as a foreign body (*Wassermann* and *Schultze*), and be expelled through the urine.

Schotten and *Baumann*[6] have also shown in another manner, the importance of crystalline bodies to the organism. All of them are entirely consumed in the body and are completely oxidized into urea, carbonic acid and water; whether they belong to the aromatic series like tyrosin, phenylalanin, and indolalanin, or whether they belong to the fatty series like glycocol, leucin, aspartic acid, glutamic acid, alanin, etc.

The crystalline bodies derived from albumin are consequently of the greatest importance to our nutrition and it is very probable that they will play a major role in the artificial nutrition of the future, for it was by combining them that *Fischer* was able to solve the synthesis of albumin.

[1] Kutscher & Seemann: Zeits. f. phys. Ch. XXIV, p. 528.
[2] Lœwi: Centrabl. f. Physiol., XV, p. 590.
[3] Cohnheim: Zeits. f. phys. Ch. XXXV, p. 396.
[4] Lœwi: Schmied Arch., 48, p. 504.
[5] Glæssner: Hofmeister's Beiträge, I, p. 328.
[6] Schotten & Baumann: Zeits. f. phys. Ch. X, p. 120.

2d. FATE OF THE AROMATIC BODIES DERIVED FROM THE AMINO ACIDS

Very different is the fate of the aromatic bodies produced by the putrefactive action of bacteria. They cannot be utilized by the organism; they can no longer be burnt up into urea, carbonic acid, and water. They are consequently excrementitious substances, absolutely useless and constitute an irreparable loss to the economy.

The intervention of the microbes in intestinal digestion, while it has its advantages, also brings about a deficit in the utilization of the nitrogenous substances. According to the experiments of *MacFayden, Nencki* and *Sieber*[1], the small intestine assimilates but six-sevenths of the alimentary nitrogen, the rest becomes the prey of the bacteria. *Tappeiner*[2] even estimates the loss at 10 per 100, but this deficit is not the only bad feature of microbic intervention. These substances (*i.e.*, aromatic bodies) but slightly noxious individually, can, when combined, and especially when they increase sufficiently, exercise a *harmful action* upon the organism.

There is no doubt that the body has gradually adapted itself to this order of things and that it has organized means of defense against these poisons; and that owing to the constant presence of bacteria a sort of association exists, in which the two partners receive from their life in common certain advantages at the price of inevitable disadvantages. This adaptation, however, is not unlimited, and it may be destroyed whenever the aromatic products exceed the normal limits or, whenever the defensive means become insufficient. This is the more likely to happen, since the intestinal microbes can give birth to bodies infinitely more toxic and dangerous than the aromatic bodies; namely, the ptomaines of which we shall have to speak further on. Be it as it may—useless or dangerous the aromatic bodies cannot be retained long in the body, and it therefore seeks, by different procedures, to render them less harmful and to rid itself of them through the various excretory channels.

[1] MacFayden, Nencki & Sieber: Arch. f. exper. Path., XXVIII, p. 311.
[2] Tappeiner: Zeits. f. Biol.

II. PRODUCTS OF THE DISINTEGRATION OF THE ALBUMINOUS MOLECULE

It is not our intention to describe these different bodies in detail. Their complete description will be found in the treatises on physiological chemistry. We simply wish to bring out their more important characters; those which may prove useful in our further study.

NON-CRYSTALLINE BODIES

(Albuminoids responding to the biuret test)

ALBUMOSES. The albumoses, propeptones or proteoses, are intermediary products resulting from the peptonization of albumin. According to *Neumeister* they first pass through the stage of *primary albumoses* (the proto and hetero albumoses of *Kühne*), to arrive at that of the *secondary albumoses* (the deutero albumoses of *Kuhne*), which then become changed into peptones. Hence there are numerous intermediary stages differing slightly in character, according to whether they approach more closely the albumin or the peptones. The albumoses are not coagulated by heat, but they are by nitric or acetic acids; the precipitate is redissolved by heat and reprecipitated by cold. The albumoses are also precipitated by the sulphate of ammonium. According to *Schroetter*, the albumoses have a greater molecular weight and a more considerable proportion of nitrogen than the peptones; finally they contain sulphur, something which the peptones never do.

PEPTONES. These are the terminal products of the peptonization of the albumins by the proteolytic enzymes. They, like the albumoses are formed through the influence of hydrolysis by the acids and alkalis and by the action of microbic putrefaction.

They are soluble in water, not coagulated by heat, nor are they precipitated by either sulphuric or acetic acids or the sulphate of ammonia.

AMMONIA

The pancreatic digestion of the proteids produces peptones, amino acids, aromatic substances, etc., but all these substances

reunited contain less nitrogen than the albumin from which they originated. This fact led *Hirschler*[1] to seek for another nitrogenous body and this, he found in ammonia.

Habermann and *Schutzenberger* have confirmed this discovery and these authors came to the conclusion of *Mochizuki*[2] that ammonia forms an important part of the nitrogenous bodies derived from the decomposition of the albuminous molecule, whether this proteolysis is performed by the acids, enzymes or bacteria.

Salaskin[3] pursued these investigations in the living being and came to the following conclusions:

1st. That the cells of the gastric and intestinal mucosa were much richer in ammonia in those animals fed with meat than in those fed on bread or milk.

2d. That the portal vein contained during digestion a variable quantity of ammonia (3 mgr, 5 to 8mgr, 4. per 100), but always a more considerable quantity than the rest of the body.

3d. That in the arteries there is found an almost constant proportion of ammonia.

In the dog, .0014 gm. per 100 with meat diet.
In the dog, .0011 gm. per 100 with milk diet.
In man, .00096 gm. per 100 with mixed diet.

4th. That the *lymph* contains somewhat less and the organs a still lesser proportion.

From this, we may conclude that the cells of the digestive glands (stomach, pancreas) produce ammonia, that the digestion by the proteolytic enzymes and finally the microbic intestinal putrefaction are accompanied by the formation of ammonia. This substance passes into the blood of the portal vein, and by combining with the fatty acids (derived from the fermentation of the carbohydrates), or with the carbonic acid, it prevents the diminution of the blood's alkalinity; a very serious and grave symptom of acid intoxication.

The ammoniacal salts when they reach the liver, are transformed into urea as *Nencki*, *Pawlow* and *Zaleski* have demonstrated.

[1] Hirschler: Zeits. f. phys. Ch· IX, p. 302.
[2] Mochizuki: Hofmeister's Beiträge, I, p. 45.
[3] Salaskin: Zeits. f. phys. Ch. XXV, p. 457.

MONAMINO ACIDS

The study of the amino acids has been particularly difficult, and it is only very lately that we have learned to know them in their pure state. This we owe to *Fischer*[1] whose method has made their study possible.

The number and the proportions of the amino acids varies according to the albuminous bodies from which they are derived.

Generally, we find in all analyses, leucin, glycocol, alanin, aspartic acid, glutamic acid, tyrosin, phenylalanin, tryptophan, pyrrolidinic and carbonic acid.

The monaminated acids are produced by the decomposition of the albuminous molecule, as readily by the action of the acids or caustic alkalis as by the action of the proteolytic enzymes and bacteria.

Kuhne[2] was one of the first to show that their formation was at the expense of the albumins either through the action of acids or alkalis or that of trypsin and the bacteria; but according to this author only a feeble proportion of the peptones and the hemipeptones underwent this transformation in the organism.

We now actually know that this proportion is already considerable in the intestine, and that it becomes still greater when passing through the cells of the mucosa, owing to the influence of the erepsin of *Cohnheim;* so much so that we are led to admit that it is only under the form of crystalline bodies that the peptones are absorbed. Does the albumin of the organism in its nutritive mutations also furnish aminated acids? This is not impossible since enzymes are found even in the muscles; but the proof is still lacking.

What becomes of the amino acids in the organism?

We know from the researches of *Schultzen* and *Nencki* and those of *Salkowski* that leucin and glycocol are changed into urea in the body.

Van Knierem has demonstrated that the same happens with aspartic acid, and it is more than probable that this transformation is common to all the monaminated acids. *Salaskin,*

[1] Fischer: Zeits. f. phys. Ch. XXXIII, p. 151.
[2] Kuhne: Virchow's Arch., XXXIX, p. 133.

by means of artificial circulation showed that the transformation took place in the liver. *Lœwi* and *Ascola* consider that the agent of this transformation is an enzyme, but how it occurs remains to be seen.

Most authors actually admit that it is through the intermediary of carbamic acid. *Dreschel* has in fact shown that the amino acids undergoing oxidation in an alkaline solution outside of the body, gave rise to carbamic acid and that the carbamate of ammonia was transformed into urea by the action of electric currents.

Quite a number of observations have confirmed this theory by demonstrating the presence of carbamate of ammonia in the organism. *Dreschel* has found it in the blood and *Abel, Nencki* and *Hahn* in the urine; but the most striking demonstration seems to have been given by *Nencki* with dogs, in whom a fistula of *Eck*[1] had been established. These all died with the same symptoms of intoxication as non-operated dogs in whose veins carbamate had been injected.

A. FATTY SERIES

We have no intention either of giving the history of all the monamino acids; we shall limit ourselves to a short résumé of the new works which have recently appeared.

LEUCIN. (Aminocaproic acid $C^6\ H^{13}\ NO^2$). Leucin is with tyrosin, one of the first products of the decomposition of the albuminous bodies—whether this proteolysis occurs through the action of the acids, alkalis, or the action of the enzymes and proteolytic bacteria. This decomposition takes place so readily that it is difficult when these two substances are found, to decide whether they are part of the living body or formed after death.

Normally, leucin is found in the pancreas, the spleen, the thyroid, the salivary glands, the liver and the kidneys.

It is also found in the detritus of the skin, between the toes and in sweating feet to the bad odor of which it contributes largely.

[1] Eck fistula. An experimental operation performed on animals, whereby the current of the portal vein, is made to empty into the vena cava, so that, none of the blood returning from the intestines passes through the liver (tr).

Leucin undergoes, through the action of bacteria, a secondary decomposition into fatty volatile acids (butyric, acetic, valerianic, etc.). It is transformed by the hepatic cells into urea, which appears normally in the urine; whenever the hepatic cells are destroyed or become insufficient, leucin appears in the urine while the urea is diminished.

Hence, when leucin appears in abundance in the urine, it is a sign of hepatic insufficiency.

ALANIN. (Aminopropionic acid C^3 H^7 NO^2.) This monaminated acid is produced by the action of the acids, alkalis, the enzymes and the proteolytic bacteria upon animal albumins (fibrin, egg albumin, casein). This substance is related to lactic acid into which it may be easily converted by nitric acid; it was found by *Weyl* in the fibroin of silk and in casein by *Fischer*. It is worthy of attention, because its chemical composition seems to bring about other important derivatives from its decomposition; cerin and cystein, which are easily condensed into cystin. From alanin, moreover, phenylalanin is derived through the addition of a benzenic radical; this is found in germinating plants and constitutes one of the monoaminated aromatics of which we shall speak presently.

ASPARTIC ACID (aminosuccinic acid C^4 H^7 NO^4). This monaminated acid is produced by the action of the acids, alkalis, enzymes and the proteolytic bacteria upon the vegetable albuminoids (legumen and gluten), and the animal albumins (fibrin, egg albumin, casein).

It is widely distributed throughout the vegetable kingdom under the name of *asparagin* and plays an important part in the development of plant life and in the formation of vegetable albumin.

GLUTAMIC ACID (aminoglutaric acid C^5 H^9 NO^4). Like the preceding, this acid is formed by the action of the same bodies upon the animal and vegetable albumins.

BUTYLALANIN (aminovalerianic acid $C^5H^{11}NO^2$). This monaminated acid was found by *Salkowski* in the decomposition of fibrin, animal gum, and by *Fischer* in that of casein.

GLYCOCOL (aminoacetic acid C^2 H^5 NO^2) is a product of the decomposition of certain albuminoid bodies (elastin, animal gum, collagen), but not of true albumins.

B. AROMATIC SERIES

TYROSIN (oxyphenylaminopropionic acid $C^9\ H^{11}\ NO^3$) is formed at the expense of most of the proteids (with the exception of animal gum) and under the same conditions as leucin, which it generally accompanies; it is found in old cheese but does not seem to be present in fresh glands.

Tyrosin apparently constitutes the aromatic nucleus of the albuminous molecule, and is characterized by reaction to Millon's test and by the secondary production of part of the aromatic bodies. (Kossel.) In fact it is decomposed by the alkalis and proteolytic bacteria into phenols and cresols.

TRYPTOPHAN (indolaminopropionic acid $C^{11}\ H^{12}\ NO^2$). The tryptophan of *Neumeister*[1] is a chromogen which treated with chlorine or bromine gives a purple product termed proteinochrome. *Nencki* thought this body was the origin of several of the coloring matters of the organism. *Hopkins* and *Cole*[2] finally showed that tryptophan is formed parallelly with tyrosin by the action of the acids, alkalis and bacteria on the proteids. They proved that it was an indolaminopropionic acid and characterized by the reaction of *Adamkiewicz* (red coloration obtained by heating an albuminoid in the presence of sulphuric acid to which a few drops of glacial acetic acid are added).

This reaction is apparently due to the tryptophan nucleus of the albuminoids, in the same manner that the reaction of *Millon* is due to their tyrosin nucleus.

Finally, to complete its analogy with tyrosin, it decomposes under the action of the bacteria into indol and skatol.

It is thus seen that tyrosin is the mother substance of the phenols and cresols; that, tryptophan is the mother substance of indol and skatol.

PHENYLALANIN (phenylaminopropionic acid $C^9\ H^{10}\ NO^2$). This monaminated aromatic acid was found by *Schultze* and *Bar-*

[1] Neumeister: Zeits. f. phys. Ch. XXVI, p. 329.
[2] Hopkins & Cole: Zeits. f. phys. Ch. XXIII, p. 412.

bieri in the microbic putrefaction of vegetable proteid substances. *Fischer* discovered it in the decomposition of casein by acids; *Abderhalden* in that of the hæmoglobin. This acid can apparently become oxidized in the body into benzoic acid. *Phenylalanin by its combination in the kidneys, and perhaps also in the liver with glycocol may be the mother substance of hippuric acid.*

DIAMINO ACIDS

The diamino acids formed through the hydrolysis of the albumins by the acids, alkalis, enzymes and proteolytic bacteria are lysin, histidin and arginin; they have been termed by *Kossel* the hexone bases.

LYSIN ($C^6 H^{12} N^2 O^2$). Isolated first by *Hedin*[1].

HISTIDIN ($C^6 H^9 N^3 O^2$). Isolated first by *Kossel*, then by *Hedin*.

ARGININ ($C^6 H^{14} N^4 O^2$). Arginin is a constant product of the decomposition of albuminoid bodies by the ferments (such as trypsin and erepsin); its chemical decomposition leads to the consideration of it as the ureogenic group of the albuminous molecule. If arginin is boiled in the presence of barium sulphate, it is decomposed and gives up urea and ornithin (or diaminovalerianic acid). Until the present time it had been impossible to directly observe the formation of urea from arginin.

But *Kossel* and *Dakin*[2] have recently succeeded by demonstrating a diastase in the organism (*arginase*), which disintegrates arginin into urea and ornithin. Arginase is found mixed with the erepsin of *Cohnheim;* also in the liver, the kidneys and the thymus; but it never appears to be present in the pancreas, the spleen or the suprarenal capsules.

This discovery cleared up to a great extent the formation of urea at the expense of the albuminoids, by showing that arginin and perhaps other diaminated acids contain a ureogenic nucleus.

[1] Hedin: Arch. du Bois Raymond. 1891. p. 273.
[2] Kossel & Dakin: Zeits. f. phys. Ch. XLI, p. 321.

III. TOXIC BODIES PRODUCED BY THE DISINTEGRATION OF THE ALBUMINOUS MOLECULE, THROUGH THE INFLUENCE OF MICROBES

We have thus roughly reviewed the products of the disintegration of the albuminous molecule by the enzymes.

As we have already seen, the microbes extend their action further. The products of disintegration, which they furnish, are in the first place the same mono and diamino acids we have just reviewed, and in the second place the products of the more complete decomposition of these acids.

1st. It is thus that the destruction of the aromatic monoaminated acids forms numerous secondary aromatic bodies; the nucleus of tyrosin gives birth to the aromatic oxyacids, to cresol and phenol. The nucleus of tryptophan gives rise to skatol, indol and pyrrol. These bodies possess a very nauseating and characteristic odor.

2d. It is thus that the destruction of the monaminated acids of the fatty series, give rise to fatty acids and to diamines known as ptomaines or putrefactive alkaloids.

3d. Finally it is thus that the putrefaction of the proteids engenders gases: hydrogen, carbonic acid and sulphureted hydrogen.

At the same time, the fluids acted upon by the anærobic microbes become more and more alkaline and charged with ammonia, which indicates that the mono and diamino acids are profoundly attacked.

The greater part of the bodies produced by the anærobic microbes are toxic; they consequently require a most careful study because their presence in the economy is most serious and grave, since they may lead to intestinal auto-intoxication.

We shall successively study:

1st. The fatty volatile acids.
2d. The ptomaines and leucomaines.
3d. The aromatic bodies.
4th. The gases.

A. FATTY VOLATILE ACIDS

Whenever the fatty acids accumulate in the blood, there results an acid intoxication, or *Acidosis*. Acidosis is therefore characterized by a diminution in the alkalinity of the blood.

We know that the greater part of the carbonic acid gas in the blood is chemically bound, so that the ability of the blood to absorb carbonic acid gas depends upon its alkaline reaction.

Likewise, the kidneys have for their mission that of eliminating all excess of acid and that is why they are able to extract from the blood (an alkaline medium) a liquid that is acid—"the urine"—but if the proportion of acids entering the blood becomes excessive, the kidneys no longer suffice for the task of removing it, hence the diminution in the alkalinity of the blood will lead to an intoxication caused by the retention of the carbonic acid, the tissues being no longer able to rid themselves of it through the blood.

This acidosis only occurs when the fatty acids are formed in excess and this rarely happens except under the influence of the breaking up and fermentation of the ternary bodies, the fats in particular.

As to the formation of the fatty volatile acids (formic, acetic, butyric, valerianic, etc.), through the influence of nitrogenous putrefaction—that of leucin particularly—it is extremely slight, so slight that many authorities even doubt its formation. *Rosenfeld*[1] alone takes exception and in a recent paper he attributes the formation of the fatty acids principally, to the putrefaction of the proteids in the intestine; his investigations, however, lack confirmation. At all events, we may, for the present, conclude with the majority (almost unanimous) of observers that the proportion of fatty acids derived from nitrogenous putrefaction is too slight to be able to cause the least intoxication of the organism.

B. PTOMAINES AND LEUCOMAINES

The putrefactive processes which accompany digestion by the enzymes and microbes, give rise to two series of substances to

[1] Rosenfeld: Deutsch. med. Woch., p. 13. 1903.

which toxic properties are attributed. These are the leucomaines and the ptomaines; the first are derived from the cells, the latter from the bacteria.

LEUCOMAINES

The leucomaines are bases formed by the organic cells in the metabolic decomposition of living proteid bodies.

They are therefore normal and physiological products of the nutritive changes in our tissues. They are also formed in the intestine by the decomposition of nitrogenous substances either through the action of the enzymes or that of the bacteria; concerning this point of view, a few words are necessary.

1st. **KREATINIC LEUCOMAINES.** Kreatin ($C^4 H^7 NO^3$) is formed in the kidneys at the expense of the kreatin in the muscles and blood; it appears in the urine at the same time with urea. Its quantity does not depend upon the amount of albumin, but upon the quantity of meat ingested; infants taking nothing but milk do not excrete any, and it is diminished by conditions of starvation and by vegetable diet.

It is but slightly increased by muscular work and only when it is excessive (*Oddi* and *Tarruli*). It has a feeble toxicity and according to *Feltz* and *Ritter*, to bring about any toxic phenomena, it would be necessary to introduce in the economy and at the same time an amount equivalent to thirteen days' elimination.

The normal proportion of kreatin excreted in the urine during twenty-four hours is from one gram (0.60 to 1.30)

2d. **XANTHIC OR PURIN LEUCOMAINES.** These bases termed purin bases, xanthic, alloxuric, are the products as *Kossel* has shown of the decomposition of the neucleins (neucleinic bases) in other words the cell nuclei.

In the microbic putrefaction the nucleins are first decomposed on the one hand into xanthin and guanin, on the other into hypoxanthin and adenin and these soon become converted into xanthin ($C^5 H^4 N^4 O^2$) and hypoxanthin ($C^5 H^4 N^4 O$) only. These two bodies are transformed in the liver into uric acid.

It is only when an abundant destruction of the nucleins is taking place (as for example in leukæmia) or when theobromin or caffein has been ingested, that we find an increased amount in the urine.

The xanthin bodies are but slightly toxic.

The normal amount of xanthin excreted in the urine of twenty-four hours is from (0.015 gm.)

3d. **LECITHINIC LEUCOMAINES.** *Gulewitsch* has demonstrated that through the action of bacteria, lecithin is decomposed into cholin and glycerophosphoric acid. Cholin in its turn, may also through the same agency be decomposed into neurin and muscarin, alkaloids, which, according to *Brieger*, are extremely toxic and capable of causing grave symptoms.

The lecithins are found in many of our foods, the yolks of eggs, brains of animals, and fish roes contain them in appreciable quantities; meat and milk in slight proportions. They are combined in these foods with albuminoids under the form of proteids (lecithalbumin), the constitution of which has long been known; it consists of one molecule of glycerin, two of fatty acid (stearic), one of phosphoric acid and one of cholin.

The intestinal microbic putrefaction in decomposing these foods produces neurin and muscarin, violent poisons; but is their quantity sufficient to exercise any action on the organism or contribute to auto-intestinal intoxication? While possible, it has not yet been demonstrated.

PTOMAINES

Ptomaines are basic bodies produced by the microbic decomposition of the amino acids. They were discovered by *Selmi* in dead bodies, and for that reason, he named them ptomaines. Some are harmless, others extremely toxic.

Most of them do not contain oxygen, and belong to the diamine group and their presence in the intestine can undoubtedly be attributed to the microbic fermentation of the diamino acids, the existence of which in the products of the physiological degradation of the albuminoids has been demonstrated.

Hence it is easy to prove that putrescin is derived from diaminovalerianic acid by simply its loss of carbonic acid. This transformation by reduction is very naturally explained by the action of the anærobic bacteria of the intestine[1]. We possess actual knowledge of several ptomaines belonging to the fatty series.

Ethylendiamin.

Trimethylendiamin ($C^3 H^{10} N^2$).

Tetramethylendiamin or putrescin ($C^4 H^{12} N^2$).

Pentamethylendiamin or cadaverin ($C^5 H^{14} N^2$).

Hexamethylendiamin ($C^6 H^{14} N^2$).

Others among the ptomaines, such as *pyridin, parolin,* and *collidin* are derived from complex nuclei. The constitution of a great number of them is closely allied to that of the alkaloids and is moreover unknown[2].

The first ptomaine analyzed was *collidin,* derived from the putrefaction of animal gum. It was discovered by *Nencki* in 1876.

Brieger, in 1885, discovered in putrefying meat numerous ptomaines, among them he demonstrated the presence of putrescin and cadaverin.

PTOMAINES IN THE STOOLS

Garcia[3] endeavored to show that ptomaines also existed in the organism; here are his conclusions:

1st. The putrefaction of the proteids in intestinal digestion gives rise to the following ptomaines; putrescin, cadaverin, and hexamethylendiamin.

2d. The proportion of ptomaines is diminished by two thirds in the presence of carbohydrates.

3d. These same ptomaines are found in the fæces.

Roos[4] also demonstrated numerous diamines in choleric stools and in patients suffering from malaria.

Baumann and *Van Ildranski*[5] found tetra and pentamethyl-

[1] Lecoq: Biol. medic., III, p. 368.
[2] Lecoq: loc. cit.
[3] Garcia: Zeits. f. phys. Ch. XVII, p. 568.
[4] Roos: Zeits. f. phys. Ch. XVI, p. 192.
[5] Baumann & Van Ildranski: Zeits. f. phys. Ch. XIII, p. 562.

endiamin in the stools of cystinuria, and *Ellinger*[1] has very recently demonstrated the formation of cadaverin at the expense of lysin and putrescin from ornithin, both of which are found in the intestine. So there can be no doubt that ptomaines are formed in the intestine by the action of bacteria.

Bouchard had already, in 1882, tried to prove indirectly the existence of these intestinal poisons. Based upon numerous experiments, he had shown that the extract from seventeen grams of fecal matters was sufficient to kill one kilogram weight of living animal; whereas when the digestive tube had been disinfected, the extract from two hundred grams of fecal matters was required to produce the same result.

It would seem difficult to demonstrate in a better way the influence of putrefaction in the production of toxins in the fæces.

What becomes of these intestinal ptomaines?

What we do actually know, is that they are eliminated (partly at least) by the kidneys.

PTOMAINES IN THE URINE

Dombrowsky[2] asserts that all urines contain ptomaines even when normal, and that with his methods it is possible in all cases to detect cadaverin.

In pathological conditions, ptomaines have been frequently demonstrated in the urine.

Roos discovered cadaverin and putrescin in the urine of two cases of enteritis. *Arslan* has described the ptomaines found in the urine in cases of ankylostoma; *Mossler* and *Piper* those in children suffering from lumbricoids. *Selmi*[3], *Eliacheff*[4], *Bouchard*[5], described the ptomaines found in the urine of diseased human subjects.

Lepine and *Guerin*[6], *Villiers*[7], *Adduco*[8] found in the urine

[1] Ellinger: Zeits. f. phys. Ch. XXXVI, p. 261.
[2] Dombrowsky: Sem. med. 1902. p, 252.
[3] Selmi: Chir. Centralb., 1888, p. 1544.
[4] Eliacheff: Mem. soc. biol., III, p. 71.
[5] Bouchard: Rev. med., II, p. 825.
[6] Lepine & Guerin: Rev. med. 1884. p, 767.
[7] Villiers: C. R. Acad. Sc., 100, p. 1240.
[8] Adduco: Arch. biol., LIX, p. 263.

toxic substances soluble in ether. In 1891, *Kerry* and *Kobler*[1], *Griffiths* in 1892[2], *Albu* in 1894[3], found toxic bases in the urine of many diseased individuals. If these substances are eliminated by the kidneys there can be no doubt that they may have exercised their harmful action upon the organism before their excretion. *Bouchard*, through his researches, believed that he was able to demonstrate the urotoxic coefficient. This author killed a rabbit with 45 c.c. of normal urine per kilogram weight of the animal, and a dog with 60 c.c. per kilogram weight. He calculated that in fifty-two hours a man originated sufficient toxins to kill himself with his own urine.

Bouchard further showed that in disease the urine is still more toxic and that the urotoxic coefficient is the measure of its toxin content.

But while this demonstration is interesting, it is not sufficient, because the urotoxic coefficient is not proportional to the urinary ptomaines; as a matter of fact, it depends three-fourths upon potassium salts and one-fourth only upon extractive matters. (*Charrin.*)

Lepine goes even further and asserts that 85 per 100 of its action is due to salts and only 15 per 100 to organic substances.

Stadthagen[4] also does not admit the urotoxic coefficient as a measure of the ptomaine content of the urine; according to him its toxicity is mixed and due to potassium salts, leucomaines and to the sum total of the toxicity of the aromatic bodies.

Finally *Posner* showed that the urotoxic coefficient can be readily explained without drawing upon the ptomaines. This observer, by simply varying the proportions of salts dissolved in distilled water, produced effects absolutely identical with those obtained by *Bouchard*.

The symptoms of intoxication caused by the injection of urine into animals are therefore not due to toxins, but to a defect in the isotonicity of the injected fluid with that of the blood. The methods employed for the search and determination of the urinary ptomaines are extremely delicate and difficult,

[1] Kerry & Kobler: Deuts. med. Woch. 1891. p. 525.
[2] Griffiths: Chem. News., LXI, p. 87.
[3] Albu: Berl. Bl., XXI, p. 1081.
[4] Stadthagen: Zeits. f. klin. Med., XV, p. 383.

and they can only be carried out in well-equipped laboratories and by experienced chemists. Furthermore, as *Brieger* himself admits, the methods themselves are as yet none too exact and need considerable improvement. The search for ptomaines cannot in consequence be carried out clinically and the knowledge of these toxins has only a theoretical interest at present.

From the summing up of these facts we may conclude:

1st. That intestinal putrefaction produces relatively large quantities of ptomaines in the intestine.

2d. That part of these ptomaines are absorbed, circulate in the blood, and may cause toxic phenomena before being eliminated through the kidneys.

3d. That we do not yet possess any practical method for detecting the ptomaines or ascertaining their dosage.

C. AROMATIC SUBSTANCES

We have seen that under the influence of microbic putrefaction, the aromatic nucleins of the albuminoids were decomposed in the intestine into aromatic bodies, which were largely eliminated through the urine. The question arises:

Are these aromatic bodies formed in the intestine only?

Some authors admit that they may be formed normally in the organic cells through the sole influence of the metabolism of albumin—and without the participation of bacteria.

Since this question is of capital importance to our study, we must examine it very closely and take up successively:

1st. The derivation of the aromatic bodies.

2d. The excretion of the aromatic bodies.

3d. The biological characters of the aromatic bodies.

1. Derivation of the Aromatic Bodies

They are derived *normally* from two sources:

1st. From the putrefaction of nitrogenous foods in the intestine.

2d. From the putrefaction of the nitrogenous secretions of the intestine.

I. THE AROMATIC BODIES ARE DERIVED FROM THE PUTREFACTION OF THE NITROGENOUS FOODS IN THE INTESTINE

In nature all the aromatic bodies (oxyacids, phenol, skatol, indol, brenzacatechin, hydrochinon, alkapton), derive from the preformed aromatic nuclei in the proteids (tyrosin, tryptophan, phenylalanin), or else from vegetable matters containing benzol derivatives. It is not the same in the human organism as *Baumann*[1] has taught us, and in this respect the chemistry of the animal is much inferior to that of the vegetable.

For while the plant easily forms aromatic bodies at the expense of the carbohydrates, fats or bodies of the fatty series, the animal cannot.

In the animal and in man, all the aromatic substances are derived from albumin and the products of its decomposition. The formation of aromatic bodies at the expense of ternary substances must be absolutely excluded. This advantage which the plant has over the animal is not limited to the extraction of the ordinary aromatic bodies (oxyacids, phenol, skatol, indol), but extends to that of the rare bodies (brenzcatechin, hydrochinon, and alkapton), which are products of vegetable decomposition.

These last substances are found in most vegetables, and may be easily extracted by heating them with alkalis. But as *Baumann*[2] has shown the human organism is not capable of extracting them and the small quantities existing in the urine are not derived from the ingested vegetables, but from the microbic putrefaction of the nitrogenous foods.

From this we see that the human organism can extract the aromatic bodies only from the preformed aromatic nuclei in the nitrogenous foods, for even the digestive enzymes of man cannot succeed in decomposing nitrogenous foods into aromatic bodies.

Only the vegetable parasites of man—the anærobic bacteria of the intestine—are capable of producing this decomposition.

[1] Baumann: Zeits. f. phys. Ch. X, p. 123.
[2] Baumann: *Loc. cit.*

The extraction of the aromatic nuclei, therefore devolves upon the vegetables and their zymases, and in man and the animal it is still the microscopic vegetables, the schizomycetes or bacteria that bring about this decomposition.

Hence we can deduce from these experiments, and conclude from the long series of observations of *Baumann* and his pupils:

that, the aromatic substances formed in the intestine of man, are derived solely from the microbic putrefaction of proteid foods of animal origin, and that the carbohydrates and fatty substances do not produce any.

MAY NOT THE ORGANISM FORM AROMATIC BODIES OUTSIDE OF THE INTESTINE?

Is the intestine the only source of aromatic substances or can they originate elsewhere in the organism?

Two orders of facts would seem to demonstrate it.

1st. Experiments on animals.

2d. Clinical observations.

1st. **EXPERIMENTS ON ANIMALS.** In states of inanition, the aromatic substances do not disappear from the intestine, and indol and phenol only diminish in the urine without ever disappearing.

Numerous observations demonstrate it:

Van der Velden[1] and *Salkowski*[2], in famished dogs, found besides the disappearance of phenol only a diminution of indol during a period of five days.

Müller[3], in his observations of the faster *Cetti*, showed that indol diminished rapidly and disappeared on the fourth day of the fast, but that on the contrary, from the fifth day, phenol increased considerably. *Blumenthal*[4] only a few months ago, while seeking to show that in the rabbit, indican was also derived from the cellular disintegration of the body, without the influence of bacteria, called attention to the fact that in this animal,

[1] Van der Velden: Virchow's Arch., LXX, p. 343.
[2] Salkowski: Deuts. Chem. Gesell. 1876. p. 408.
[3] Müller: Berl. klin. Woch. 1887. p, 308.
[4] Blumenthal: Charité Annalen, XXVII, p. 124.

which in the normal state has no phenol, it is produced when it is subjected to starvation or to injections of phlorizin.

Can we not conclude from these experiments upon animals that the using up of the organic cells, the consequence of inanition is not also the cause of the formation of indol and phenol?

To the first series of objections might be opposed the experiments of *Ernst*, which demonstrate that inanition does not deprive the intestine of proteids capable of furnishing aromatic bodies through microbic influence. This author shows, in fact, that the putrefaction of bile and pancreatic juice, both rich in albumin, gives birth to phenol, indol and skatol; that the intestinal mucus, which, according to *Paijkull* is constituted by nucleo albumin, furnishes it also when subjected to microbic action.

Hence we can easily account for the presence of aromatic substances in the urine of animals or man, when in a state of prolonged inanition.

If to this we add that *Müller* has demonstrated that a state of starvation increases the putrefactive power of the bacteria, by diminishing the formation of the antitoxic organic acids and by causing intestinal hemorrhages, which are themselves a source of production for the aromatic bodies, we shall have replied to the last objection of *Blumenthal*.

2d. Clinical Observations. Numerous clinical facts seem to be in favor of this theory and appear to show that man in a state of inanition, nevertheless produces phenol and indol even when the intestine is empty and contains no food.

It is thus that in man in certain cases of profound inanition caused by carcinoma of the stomach or pylorus, we find an increase in phenol and indol, which seemingly proves that the disintegration of the organic albumin is the cause.

Senator[1] found augmentation of indol in the inanition caused by carcinoma of the pylorus. *Professor Bourget* of Lausanne found the same in several cases of carcinoma of the esophagus.

Salkowski[2] also, so that these observers conclude from these

[1] Senator: Centralbl. f. med. Wiss., LXXVII, p. 70.
[2] Salkowski: Zeits. f. phys. Ch. X, p. 266.

facts that the aromatic substances may—at least in part—derive from the fixed albumins of the body.

To the second series of objections we shall oppose the fact that the presence of aromatic derivatives has never been demonstrated in the blood, nor in the lymph, muscles or organs, not even in animals in a profound state of inanition.

Furthermore, thanks to a long line of investigations, it appears actually certain, *that it is only in the presence of bacteria that the albumin of the body is decomposed into aromatic bodies.*

It is therefore not surprising that carcinomas of the pylorus esophagus and uterus, when ulcerated and gorged with bacteria, should augment considerably the amount of aromatic substances in the urine, in the same manner that it occurs in advanced phthisis or in any case of suppuration or microbic inflammation. So falls the second series of objections.

But that is not all. We are actually acquainted with several facts which absolutely and directly demonstrate that if we succeed in suppressing intestinal nitrogenous putrefaction, the aromatic bodies are no longer found in the urine.

Baumann[1], while observing for several weeks a patient suffering from a fistula of the lower portion of the small intestine, and who was rapidly emaciating, discovered an important diminution in the sulphoethers and an almost complete disappearance of indol, phenol and aromatic oxyacids, while the intestinal contents were issuing through the fistula. As soon as this was closed and the normal course was re-established, the excretion of the sulphoethers took place again, and phenol, indol and the oxyacids reappeared in the urine.

Ewald[2] saw the same conditions reproduced in an analogous case of fistula of the small intestine; extreme emaciation with no trace of indol or phenol before operation; reappearance after a radical cure had been obtained. Hence we may say:

1st. That the aromatic substances are produced only through the influence of intestinal putrefaction, acting upon the nitrogenous foods and upon the nucleo albumins contained in the bile, the juices and mucus secreted in the intestine.

[1] Baumann: Zeits. f. phys. Ch. X, p. 120.
[2] Ewald: Arch. f. path. Anat., LXXV, p. 409.

2d. That even the rapid destruction of the organic albumin, as produced in the two cases of fistula, did not in any way augment the proportion of the urinary sulphoethers. A second series of still more convincing facts. *Baumann*[1], after bringing a dog to a famished state and noting the diminution of aromatic substances, disinfected the intestine by means of one gram of calomel (the best intestinal disinfectant according to *Wassilieff*[2]). He was then able to show that the urine no longer contained any trace of indol or phenol, and that only the oxyacids were present, but in very slight proportions.

From this *Baumann* deduced that the indols and phenols were derived only from the putrefaction of the nitrogenous foods in the intestine, but that the oxyacids can—at least in part—derive from the tissues of the body. *Salkowski*, at first bitterly opposed to this view, declared himself convinced by this experiment.

He even thinks that *Baumann's* restriction of the oxyacids is not absolute, for these bodies are very resisting; their elimination is very slow, and they are very sensitive in their reaction to *Millon's* test; all of which readily explains why they may still be found a few days after indol and phenol have disappeared. Experiments prove that they are more resistant, but not that they are formed in the body.

The beautiful experiments of *Nutall* and *Thierfelder*[3] gave the final solution of the problem. In animals with absolutely sterile intestine and receiving only a mixed diet also sterile (that is to say, animals in whose intestine bacteria could not develop), the urine did not contain the slightest traces of phenol, cresol, indol, skatol and brenzcatechin, whereas the oxyacids were present, but only in small quantities.

All these facts go to show that the aromatic bodies with the exception of a feeble proportion of oxyacids, are formed only in the intestine and only by the influence of microbic putrefaction.

We can now understand why the stools of the newborn—the meconium—contain no aromatic substances, whereas the

[1] Baumann: Zeits. f. phys. Ch. XVI, p. 221.
[2] Wassilieff: Zeits. f. phys. Ch. VI, p. 112.
[3] Nutall & Thierfelder: Zeits. f. phys. Ch. XXII, p. 71.

urine does, they having been furnished to it by the blood of the mother. We can also understand why the urine of an infant brought up on the breast contains but few aromatic substances, whereas it contains large amounts when artificially fed, because in the first case the intestine contains many less bacteria than in the second.

Lewandowski[1], in seeking which of the bacteria of the intestine produced aromatic substances, found that out of twenty-three species, nine produced phenols and indols and six indols only.

THE AROMATIC BODIES ARE DERIVED FROM PUTREFIED INTESTINAL JUICES

It is necessary to insist on this second source of aromatic bodies, for they are also produced by the action of the proteolytic bacteria of the intestine.

Bile. The coloring matters of the bile are decomposed by the intestinal bacteria; it is thus that bilirubin is transformed into urobilin in the large intestine (*Nencki* and *Sieber*); that taurocholic acid is entirely decomposed while glycocholic acid remains intact, and is found in the stools. In the fetus, in which there is no intestinal putrefaction, the biliary acids and coloring matters are found unchanged in the stools.

Secretions. The bile, the pancreatic juice, the intestinal juices all rich in albumin and nucleo-albumins, are subjected like nitrogenous foods, to the action of the putrefactive microbes. It is especially the pancreatic juice which undergoes the phenomena of putrefaction. (*Pisenti*[2] demonstrated that the elimination of indol and phenol diminished considerably when the duct of *Wirsung* was ligated.) That is the reason why the elimination of the aromatic bodies continues even during inanition. (*Ernst.*)

To recapitulate: The aromatic substances are derived solely from the intestinal putrefaction of the proteids existing in the food and intestinal juices, hence their proportion augments with the intensity of intestinal putrefaction.

There are two exceptions to this rule:

[1] Lewandowski: Deuts. med. Wiss. LI. p. 1186.
[2] Pisenti: Maly's, XVII, p. 277.

1st. The ingestion of medicines containing aromatic substances (phenol creosote, etc.), is sufficient of itself to cause the appearance of these bodies in the urine.

2d. The existence in the body of a microbic suppurative lesion furnishing phenol and indol, which appear in the urine.

II. THE EXCRETION OF AROMATIC BODIES

A small proportion of these bodies is expelled with the stools without having been absorbed, but it is especially the skatol derivatives that are expelled through that channel.

All the other aromatic bodies are reabsorbed by the intestinal mucosa, and enter the liver through the portal circulation. It is in that gland as we shall see that most of these bodies undergo transformations (oxidations and combinations) destined to render them less harmful. Under these different forms they enter the general circulation through the vena cava, and are eliminated through the various emunctories. Some like the oxyacids are eliminated as such. Others combine with sulphuric acid or glycuronic acid and are found in the excretions under the form of sulpho-conjugated acid or glycuro-conjugated acid; it is the phenols and cresols that give rise to phenolsulphuric and phenolglycuronic acids. Lastly, others undergo preliminary oxidation before conjugating with sulphuric or glycuronic acids. They are indol and skatol which appear in the urine as indoxylsulphuric and glycuronic acids, and skatoxylsulphuric, glycuronic acids.

III. BIOLOGICAL CHARACTERS OF THE AROMATIC BODIES

1. Aromatic oxyacids.
2. Phenols.
3. Indoxyls.

I. AROMATIC OXYACIDS

Aromatic Oxyacids. We have seen that the digestion and putrefaction of the proteids gave rise to tyrosin or oxyphenylamidopropionic acid.

This substance is itself changed, especially through the action of bacteria, into aromatic oxyacids, of which a certain number are known, but only two are constant: paraoxyphenylacetic and paraoxyphenylpropionic acids.

PARAOXYPHENYLACETIC ACID ($C^8 H^8 O^3$) is soluble in water and ether and melts at 148° C.; exposed to putrefaction it is split into paracresol and carbonic acid. It is therefore an intermediary product of tyrosin and the cresols.

PARAOXYPHENYLPROPIONIC ACID ($C^9 H^{10} O^3$) soluble in water and ether, melts at 125° C.; exposed to putrefaction it splits into paracresol (40 per 100) and phenol (60 per 100).

It is therefore an intermediary product of tyrosin and phenol. *Baumann* found these two products of the putrefaction of tyrosin in the inferior part of the small intestine, and in the large intestine. *Brieger* noted them in putrid pus which did not yet contain phenol. Hence the oxyacids are intermediary products of albuminous decomposition of microbic origin.

They are also formed independently of bacteria but in extremely feeble proportions. The oxyacids are undoubtedly intermediary products, but nevertheless we must not infer that when the urine contains large quantities of phenols we should also expect a diminution of the oxyacids, for it is the contrary that happens.

The proportions of the oxyacids augment with the intensity of the phenomena of intestinal putrefaction.

Other oxyacids are found as the result of the putrefaction of tyrosin.

PARAOXYBENZOIC ACID. Not stable, splits up rapidly into phenol and carbonic acid as shown by *Baumann*[1]. It is split up so quickly that it has never been found in the urine in the free state.

HOMOGENTESINIC ACID ($C^8 H^8 O^4$) was discovered by *Wolkow* and *Baumann*[2] in a case of alkaptonuria and noted in the same affection by other authors, *Emden*, *Voirin*, *Ogden*. These observers showed that homogentesinic acid results from

[1] Baumann: Deuts. Chem. Gesell, XIII, p. 381.
[2] Wolkow & Baumann: Zeits. f. phys. Ch. XV, p. 145.

abnormal phenomena of the putrefaction of tyrosin, in the upper portions of the intestine.

To recapitulate. The putrefaction of tyrosin produces aromatic oxyacids which in turn may split up into phenols and cresols. Tyrosin never splits into indol and skatol. Only the first two of these oxyacids are found free or as salts in the urine, and only a small part of them combine with sulphuric acid to form sulphoethers.

AROMATIC ACIDS. A few words remain to be said about three other aromatic acids, for they present some peculiarities; they are phenylacetic, phenylpropionic, and hippuric acids, which are also produced by the putrefaction of albumin.

PHENYLACETIC ACID ($C^8\ H^8\ O^2$) is a secondary product of putrefaction; it is not oxidized in the body but combines with glycocol to form phenaceturic acid.

PHENYLPROPIONIC ACID ($C^9\ H^{10}\ O^2$) is formed at the expense of phenylaminopropionic acid, which we have already described when speaking of the amino acids. This amino acid which, according to some, is formed only at the expense of vegetable albumin, decomposes through microbic putrefaction into phenylpropionic acid.

The investigations of *Baumann, Schotten, Boas*[1], seem to demonstrate that this last acid—at least—is never of animal origin; in any case the putrefaction of tyrosin never produces any.

Phenylpropionic acid oxidizes in the body into benzoic acid and is eliminated in combination with glycocol as hippuric acid.

HIPPURIC ACID ($C^9\ H^9\ O^3$) or **benzoylaminoacetic acid.** It is by reason of the above stated combination that hippuric acid augments with the intensity of the intestinal putrefaction, diminishing after energetic disinfection (*Baumann*) and disappearing when the intestinal contents are sterile. (*Nutall* and *Thierfelder*.)

But hippuric acid is not an index of intestinal putrefaction, because too many vegetables contain substances which give rise to benzoic acid.

[1] Baumann, Schotten, Boas: Zeits. f. phys. Ch. XI, p. 131.

It is thus that many vegetables and fruits contain chinic acid (*chinasäure*) which is reduced into benzoic acid; this in turn combines in the kidneys with glycocol to form hippuric acid.

Therefore hippuric acid is considerably augmented by the intestinal putrefaction, but cannot serve to measure its degree, because its presence depends too much on the character of the ingested food.

The normal amount of hippuric acid excreted in the urine of twenty-four hours is 0.75.

II. PHENOLS

PHENOL. We have seen that the phenols (phenol and paracresol) are products of the intestinal putrefaction of tyrosin with paroxyphenylacetic and paraoxyphenylpropionic acids as intermediary products.

The phenols were discovered in the urine by *Stædeler*[1]. *Baumann*[2] recognized that they were found in it as sulphoethers. In a second paper[3] this author showed that phenol was not a preformed substance in aliments, as had been believed until then, but that it was a result of the putrefaction of the proteids. This was soon confirmed by *Brieger*[4], who noted its presence in the fæces and intestinal contents.

To conclude from this that the urinary phenol must be derived from the intestinal phenol caused by intestinal putrefaction was but a short step, and it was demonstrated by *Brieger*[5] in the following year.

1st. **FORMATION OF PHENOL IN THE INTESTINES.** *Baumann's*[6] conception of the formation of phenol is as follows:

The microbic putrefaction of the tyrosin contained in either the proteids or intestinal juices, produces paraoxyphenylpropionic and paraoxyphenylacetic acids; these are changed into paracresol ($C^7 H^7 OH$), the latter into phenol ($C^6 H^5 OH$). If

[1] Stœdeler: Ann. d. Chem., LXXVII, p. 17.
[2] Baumann: Arch. f. Phys., XII, p. 69.
[3] Baumann: Zeits. f. Phys., Ch. I, p. 63.
[4] Brieger: Journ. f. prak. Ch. XVII, p. 134.
[5] Brieger: Zeits. f. phys. Ch. II, p. 241.
[6] Baumann: Zeits. f. phys. Ch. IV, p. 804.

there is sufficient oxygen, the oxyacid undergoes direct transformation into phenol.

According to *Brieger*[1] the body most frequently formed is paracresol, phenol appearing in it in very slight quantity. Hence the generic denomination of phenols is applied to the mixture of the two bodies. There is no marked parallelism between the formation of the phenols and indoxyl.

We have seen that in intestinal putrefaction, phenol appears long after indol. So that we may at times find considerable quantities of phenol and only feeble amounts of indol, and *vice versa*. Although, as a rule, the increase and diminution of these bodies run a parallel course.

SITE OF PRODUCTION OF PHENOL IN THE INTESTINE. Most authorities admit that the putrefaction of tyrosin never occurs in the small intestine, but only in the large intestine.

When therefore in disease, there is stasis of the small intestine, but small quantities of phenols are found, the tyrosin not having entered the colon or only in an incomplete manner.

Per contra: in all affections in which stasis of the large intestine is increased, we find phenols in considerable quantities.

These are the apparent results of the experiments of *Jaffé* on dogs. In man, this localization exists, but it is certainly less marked and unless there existed a considerable quantity of phenols, such as is found in intestinal obstruction, it would be imprudent to base a diagnosis of situation upon this one sign.

FORMATION OF PHENOL OUTSIDE OF THE INTESTINE. We must also add that the action of the proteolytic bacteria upon the organic albumins gives rise to the production of phenols; thus, empyæmias, putrid bronchitis, tubercular cavities, ulcerating carcinomas, etc., are accompanied by a notable formation of phenols.

EXCRETION OF PHENOLS THROUGH THE URINE. The phenols by combining in the liver with the sulphur derived from the disassociation of the albumins, form sulphoether acids: the phenolsulphuric and cresolsulphuric acids.

If the phenols are in excess of the sulphur, the surplus of

[1] Brieger: Zeits. f. phys. Ch. IV, p. 240.

these bodies combines with glycuronic acid, to form phenol-glycuronic and cresolglycuronic acids.

All of these acids are eliminated by the urine under the form of alkaline salts; a form much less toxic than their previous state.

A great distinction exists between the formation of phenol in the intestine and its excretion by the urine, because a small part of it is eliminated with the stools, a second part is oxidized in the organism (*Salkowski*), and cannot be detected by analysis; and it is only the third part, which, exceeding the oxidizing power of the body, is excreted through the urine. If the quantity of phenols formed is within the oxidizing ability of the organism, only traces will be found in the urine.

This explains the experiments of *Jonge*[1], who, after administering 0.010 of phenols, did not find any in the urine, their excretion only appeared when 0.040 had been ingested.

The important fact relating to auto-intoxication is not the quantity of phenols that is formed, but the amount that is excreted, for that only circulates in the blood and can react on the organism.

Normally there is found in the urine of twenty-four hours:

According to *Munch* 0.016 of phenol.

According to *Brieger* 0.015 of phenol.

Normal average of phenol 0.010 to 0.015 gm.

VARIATIONS OF PHENOLURIA

Phenol diminishes: in inanition, cachexia, anæmia, first stage of phthisis, heart diseases, etc., in other words, in all the affections in which the nutrition from the proteid point of view is insufficient.

But this is not absolute, for we frequently see anæmias and phthisical cases in which very strong proportions of phenols are found; according to *See*[2] this would be a very bad prognostic sign as indicating a deeper lesion.

PHENOL AUGMENTS: 1st. *In all the suppurations of the organism:* empyæmia, putrid bronchitis, pulmonary gangrene, cancerous ulcerations, in pyæmia and puerperal fever, etc.

[1] DeJonge: Centralbl. f. med. Wiss. 1880. p. 42.
[2] *See* Wien. med. Wiss. 1888. p. 1706.

2d. *In all conditions of stasis of the large intestine:* in constipation; simple and tuberculous peritonitis; in perityphilitis, when as much as 0.410 may be found; in intestinal obstruction during which the phenols may go as high as 0.630. We have even found as much as 0.720 in a case of chronic invagination of the cæcum.

3d. *In all exaggerated intestinal putrefactions of nitrogenous foods.*

III. INDOXYLS

INDOL ($C^8 H^7 N$) was discovered in the urine by *Hill-Cassel*[1] under the form of indigo. *Schmunck* showed that indigo is found in the urine only in a combination, which he termed *indican.*

Jaffe[2] succeeded in proving that urinary indican was derived from the intestinal indol, by making subcutaneous injections of indol. These were always followed by indicanuria, occurring a few hours later.

FORMATION OF INDOL IN THE INTESTINE. *Penrosch*[3] showed that indol is formed at the expense of meats and that it disappears with a farinaceous and sugar diet.

Hufner and *Kuhne* demonstrated that indol is formed in the body by the action of bacteria only, and that it must be looked upon as a product of the microbic putrefaction of the proteids. *Baumann* and *Brieger*[4] confirmed these findings and they also showed that indol is a result of the microbic intestinal putrefaction of the proteids. Indol is formed before phenol, and in the lowest portions of the small intestine, whereas phenol is formed only in the large intestine. *Hopkins* and *Cole*[5] finally showed that indol and skatol are formed at the expense of tryptophan, a body homologous with tyrosin and formed by a combination of aminoskatolpropionic and aminoindolpropionic acids; under the action of putrefaction, tryptophan is split up into indol and skatol.

[1] Hill-Cassell Phil. Mag. 1853. p. 9.
[2] Jaffé: Centralbl. f. med. Wiss. 1872. p. 1.
[3] Penrosch: Diss. inaug. Koenigsberg. 1877.
[4] Baumann & Brieger: Zeits. f. phys. Ch. III, p. 254.
[5] Hopkins & Cole: Loc. cit.

The formation of indol in artificial digestion is quite considerable. In the intestine it is slight; this is partly due to the fact that normally the peptones and crystalline bodies are formed in the stomach and upper portions of the small intestine, where they are at once absorbed and before they can give rise to indol, and partly to the fact that the absorption of indol is slight, for an important part of it is eliminated with the fæces; the characteristic odor of which is due to indol and skatol. As with phenol, *Ernst* proved that a part of the indol is due to the putrefaction of the bile, the intestinal and pancreatic secretions and mucus; this explains why it is found in famished man and animals.

Indol is not found in the meconium of newborn animals or infants. (*Senator.*)

The character of the food exercises a great influence on the production of indol in the intestine. Its quantity is proportional to the amount of albumin ingested; it is increased with a meat diet and decreased with a vegetable one. It is augmented by fibrin and diminished with the collagens[1]. If the quantity of meat taken is in excess of the digestive power, if the assimilation of the crystalline bodies is diminished, if there is stagnation of the contents of the small intestine, putrefaction increases and indol is formed in larger quantities in the intestine.

Hirschler[2] finally showed that by adding farinaceous articles to a meat diet indol and skatol were both diminished.

SITE OF PRODUCTION OF INDOL IN THE INTESTINE. The solution of this problem has been attempted by experiments on animals and by clinical observations.

EXPERIMENTS UPON ANIMALS. *Jaffé*[3] sought for indol in dogs, the intestines of which he had ligated; he found that ligature of the small intestine produced a constant increase of indol, whereas ligature of the large intestine exercised no influence upon the indicanuria.

Ellinger and *Prutz*[4] sought by a number of experiments to

[1] Salkowski. Zeits. f. phys. Ch. VIII, p. 417.
[2] Hirschler: Zeits. f. phys. Ch. X, p. 306.
[3] Jaffé: Arch. Virch., LXX.
[4] Ellinger & Prutz: Zeits. f. phys. Ch. XXXVIII, p. 399.

verify the so important assertion of *Jaffé*. Here are their conclusions:

1st. Stasis in the small intestine considerably increases the indicanuria; stasis of the large intestine has no effect upon it.

2d. That if indicanuria occurs with stasis of the large intestine, we may be sure that it is complicated by stasis of the small intestine. This secondary insufficiency of the ileocæcal valve can be diagnosticated only in this manner.

3d. Stasis of the duodenum and the superior portion of the small intestine is not accompanied by indicanuria.

4th. The symptoms of intestinal occlusion frequently come on suddenly, and yet on operating, we often recognize that the cause must have existed for some time; progressive indicanuria enables us to make a diagnosis at a period devoid of clinical indications.

The experiments of *Ellinger* reveal that in fact only a moderate degree of stasis is necessary to produce indicanuria.

2d. Clinical Observations. Have they confirmed these theoretical views? In a very interesting paper, "The Urine in Intestinal Affections," *Nothnagel* took up this question and considered it in all its aspects.[1]

In chronic constipation of even severe type, indicanuria is not observed.

The same fact was verified by *Brieger* and *Ortweiler* in experimental constipation induced by opium; unless there is stasis of the small intestine, indicanuria does not occur.

Carter, *Jaffé*, *de Kiess*, *Henninger*, *Senator*, *Leube*, *von Jacksch*, *Ortweiler*, and *Nothnagel*, have studied this question at the bedside and this is the *résumé* of their investigations.

Every stasis and especially all occlusions of the small intestine bring about indicanuria frequently considerable.

Jaffé has noted in some cases from 100 mg. to 150 mg. (ten to fifteen times the normal amount). It is only after twenty-four hours' duration of stasis, that indicanuria is manifested; so

[1] Nothnagel: Nothnagel's Handbuch, XVII, p. 673.

that *Nothnagel* was able to observe some cases of intestinal obstruction which, being quickly relieved (like hernias), gave no signs of it.

But as soon as stasis outlasts twenty-four hours, indicanuria rapidly appears and progresses to the maximum.

Stasis or even occlusion of the large intestine does not produce indicanuria.

It is only after several days when the stasis reaches the small intestine by forcing through the Bauhinian valve, that indican augments in the urine.

In diffuse peritonitis. Indicanuria "frequently extreme" is observed as *Jaffé, Senator, Brieger, Henninger, Ortweiler* and *Nothnagel* have shown, especially in the purulent form, sometimes even in the chronic type.

In this disease stasis of the small intestine naturally occurs, and this accounts for the exaggerated formation of indican.

Lastly in certain affections of the small intestine accompanied by diarrheas, indicanuria is observed.

It is thus that in *typhoid fever, cholera nostras, and Asiatic cholera, intestinal tuberculosis, catarrhal affections of the small intestine,* indicanuria may become important.

It is never observed in dysentery or muco entero colitis, both of which are accompanied by exaggerated peristalsis and increased intestinal putrefaction, with diminished absorption owing to the lesions of the intestinal mucosa.

TO RECAPITULATE. INDOL ALREADY BEGINS TO FORM IN THE INFERIOR PORTION OF THE SMALL INTESTINE.

What is the explanation of this phenomena? *Jaffé* submitted the hypothesis that in the normal state, but little indol is formed because nitrogenous putrefaction takes place only in the large intestine and that the substances from which it derives "tryptophan" are absorbed before they reach it; furthermore, the lack of water in the large intestine hinders the decomposition of tryptophan. Whereas, if the inferior portion of the small intestine is obstructed or should stasis be produced, then nitrogenous decomposition may take place and indol increase.

Ellinger thinks that in the normal small intestine, the proteid digestion is performed solely by the enzymes, the bacteria taking no part; *per contra*, when stasis or obstruction occur, the microbic digestion predominates and indicanuria results.

As to knowing why nitrogenous digestion in the upper part of the small intestine is aseptic and why indol is not formed, is a question very difficult to decide affirmatively.

We know, as *Landsberger*[1] has demonstrated, that the intestinal juices are bactericidal; we know that the products of the fermentation of the carbohydrates (lactic and succinic acids), prevent nitrogenous putrefaction, but their action is of short duration and it suffices to have stagnation of the intestinal contents (already charged with bacteria) to make them insufficient, when the inferior portion of the small intestine is reached. Whereas their much greater and predominating action in the duodenum and upper portions of the small intestine, combined with that of the gastric juice, prevents indicanuria when stasis takes place in those portions.

FORMATION OF INDOL OUTSIDE OF THE INTESTINE. As with phenol it must be said that the intestine is not the only microbic source of indol.

Senator has shown that while the destruction of albumin, such as happens under the influence of fever, does not augment indol, *per contra*, all purulent collections in the organism (empyæmia, peritonitis), all tubercular or cancerous ulcerations are accompanied by a more or less abundant formation of indol and skatol. But is that the only source of production?

MAY NOT INDOL BE PRODUCED BY THE ASEPTIC DESTRUCTION OF THE NITROGEN OF THE ORGANISM? This is admitted by *Jaffe*[2], *Salkowski*[3], and *Hoppe-Seyler*[4] has apparently demonstrated it experimentally when he produced indol from fibrin seemingly aseptic.

Kuhne, it is true, succeeded in proving that the experiments of *Hoppe-Seyler* were not aseptic, hence were valueless.

On the other hand, a number of investigators sought to

[1] Landsberger: Diss. inaug. Kœnigsberg.
[2] Jaffé: Centralbl. f. med. Wiss. 1872. p. 31.
[3] Salkowski: Ibid. 1876. p. 46.
[4] Hoppe-Seyler: Arch. de physiol. 1816. p. 12.

prove the production of indol from the destruction of the organic cells, by demonstrating its presence in famished conditions. *Müller*[1] first, *Krauss*[2] next, found it, but in very diminished quantity in famished dogs; *Luciani* demonstrated it in the faster Succi; *Müller* in the professional fasters Cetti and Breithaupt.

But in all these cases, only traces of indol were discovered, and as we have already seen, it is produced by the microbic putrefaction of the intestinal juices, and from the hemorrhages so frequent in starvation.

More recently yet, *Blumenthal*[3] has tried to take up this theory again by basing himself on clinical facts.

Senator[4] noted indicanuria, especially in wasting diseases; the indicanuria coinciding with the anæmia and emaciation. Consequently this author attributed it to the influence of the general inanition and cachexia bringing about destruction of the organic nitrogen. Among these diseases we shall mention carcinoma of the esophagus and stomach, and especially pulmonary phthisis, which is accompanied by a high degree of indicanuria as shown by *Brieger*[5] and *Henninger*[6]. *Senator* first, *Blumenthal*[7] next even attributed great importance to indicanuria in the prognosis of phthisis as it coincides in appearance with it.

The pediatrists took up this view and the labors of *Hoschinger*[8] and *Kahane* seemed at first favorable to it; but the profound researches of *Cattaneo*[9] and *Concetti* demonstrated that indicanuria was only important in phthisis, in case of intestinal complications and pulmonary ulcerations.

Indicanuria appears to play an important role in diabetes. *Schmunk* and *Otto*[10] in Germany; *Gilbert* and *Castaigne*[11], *Gilbert* and *Weil*[12] in France attribute to it considerable prognostic

[1] Müller: Maly's. 1886.
[2] Krauss: Zeits. f. phys. Ch. XVIII, p. 380.
[3] Blumenthal: Festsch. v. Leyden.
[4] Senator: Centralbl. f. med. Wiss. 1877.
[5] Brieger. Zeits. f. phys. Ch. II.
[6] Henninger: Arch. f. klin. Med., 23
[7] Blumenthal: Berl. klin. Woch. 1899.
[8] Hochsinger: Maly's. 1890.
[9] Cattaneo: Maly's. 1898.
[10] Schmunk & Otto: Arch. de physiol., XXX.
[11] Gilbert & Castaigne: Maly's. 1899.
[12] Gilbert & Weil: Maly's. 1892.

importance. It is very difficult to draw any conclusions from all these facts upon the origin of indol; because these observers did not concern themselves with the state of the digestive canal of their patients, nor of their alimentation. These observations therefore cannot help in deciding this very important question Hence, the aid of experimentation was finally invoked.

Harnack[1] showed that man and animals poisoned by oxalic acid presented considerable indicanuria, which, according to him can be explained only by the destruction of the organic nitrogen. *Hildebrandt*[2] confirmed this by a series of experiments.

Lewin[3], in order to demonstrate this theory, caused intoxication by means of phloridzin which greatly increases the nitrogenous destruction. He was able to note both in man and animals a greatly increased indicanuria and phenoluria.

To this the objection may be made that poisonous substances cause intestinal hemorrhages and that these by themselves suffice to explain the increase of the aromatic bodies.

Scholz[4] repeated these experiments and arrived at opposite conclusions; he demonstrated that neither oxalic acid nor phloridzin produced indicanuria.

We thus see that the modern investigations completely confirm the old opinion,

that indol was a bacterial product and that it is formed in the organism only in the presence of bacteria; normally in the intestine or else pathologically in systemic suppurations (abscesses, empyæmia, cancerous and tuberculous ulcers, etc).

THE EXCRETION OF INDOL BY THE URINE. Indol is oxidized in the body into indoxyl; this combines in the liver with sulphuric acid to form indoxylsulphuric acid. This sulphoether appears in the urine in the form of alkaline salts produced by the indoxylsulphate of potassium. In the presence of oxidizers (chlorine) this body splits into sulphuric acid and indoxyl, the latter into indigo, which is characterized by its

[1] Harnack: Zeits. f. phys. Ch. XXIX.
[2] Hildebrandt: Zeits. f. phys. Ch. XXXV.
[3] Lewin: Hofmeister's Beiträge, I.
[4] Scholtz: Zeits. f. phys. Ch. XXXVIII, p. 530.

beautiful red color if there is no oxygen (*red indigo*) or *blue indigo* if the oxidizing substances are in sufficient quantity.

According to *Schmideberg*[1], when sulphur is lacking the indoxyl combines with glycuronic acid under the form of indoxylglycuronic acid.

The excretion of indol is not constant for, like the phenols, it depends

1st. On the composition of the food, which may vary from day to day in its quality and quantity.

2d. On the vigor of peristalsis.

3d. On the power of absorption.

4th. Lastly, on the putrefactive intensity.

Hence, when considering the many factors, it is not surprising to note, that, as with phenol, the normal quantity of indol varies with individuals, and even in the same individual from day to day.

Consequently we should pay more attention to the variation of its curves than to the absolute quantity, unless this should greatly exceed the normal; therefore the normal average should be sufficiently elastic in its range.

The normal daily excretion of indol varies from 0.005 to 0.015.

VARIATIONS IN INDOLURIA

At times the amount of indol becomes enormous.

Prout, Bennecke, Litten[2] have seen all the urine become blue; in other cases a bluish sediment would be slowly deposited[3]; in still other cases true indigo calculi are found. In all those suffering from indicanuria, a thin pellicle with bluish reflections may be observed floating on the still urine; this appears to be due to indoxyl.

Indol lessens : In all affections which diminish the appetite, it gives but few indications in affections of the large intestine, the stomach and in constipation.

Indol increases : 1st. *In all the suppurative processes of the body.* It is not only large abscesses that are capable of provoking

[1] Schmideberg: Zeits. f. phys. Ch. IV, p. 414.
[2] Prout, Bennecke, Litten: Virchow's Arch., VI, p. 260.
[3] Henninger: Virchow's Arch., VIII, p. 350.

indicanuria, but even slight subcutaneous collections of pus can do so.

2d. *In all stagnations of the contents of the small intestine*[1], dilatation, paralysis, lead colic, obstruction and ileus[2], simple and tubercular peritonitis[3], tubercular enteritis[4].

3d. *With all the causes that augment intestinal putrefaction.*

SKATOL

Skatol was discovered by *Brieger*[5] in the fæces and isolated from the urine by *Otto* and *Brieger* under the form of skatoxyl-sulphate of potassium.

Formation of skatol in the intestine. Skatol and indol are near bodies, for they may be transformed one into the other, skatol being a methylindol. Like indol, skatol is derived from tryptophan, a combination of aminoskatolpropionic and amino-indolpropionic acids produced by microbic putrefaction.

Investigations recently carried on by *Weyl* and *Kitasato* on the putrefaction of the proteids, with pure instead of mixed cultures, show that certain bacteria have a predilection for forming certain aromatic bodies to the exclusion of others. This leads to the inquiry whether the predominating bacteria might not be the cause, at least one of the causes, of the variation in the proportions of the different aromatic bodies.

Skatol appears under the same conditions as indol; it increases and diminishes parallelly with indoxyl.

The normal daily average of skatol is 0.005 to 0.010.

There are still other aromatic substances formed in the intestine by the putrefaction of proteids, but they are not constant.

BRENZCATECHIN

Brenzcatechin ($C^6\,H^6\,O^2$) is a dioxybenzol; this substance was discovered by *Ebstein* and *Müller*[6] in the urine of an infant.

FORMATION OF BRENZCATECHIN. It is a frequent compound of the urine but not constant; it gives to it a brownish

[1] De Wriess: Diss. Kiel. 1879.
[2] Salkowski: Centralbl. f. med. Wiss. XIV, p. 818.
[3] Senator: Centralbl. f. med. Wiss. XX, p. 187.
[4] Hoppe-Seyler: Zeits. f. phys. Ch. XII, p. 1.
[5] Brieger: Journ. f. prakt. Ch. XVII, p. 124.
[6] Ebstein & Müller: Virchow's Arch., LXII.

color; should the urine stagnate and become alkaline the color becomes deeper and blackish.

This substance may be extracted from most of the vegetables, fruits, cider and beer.

In the organism, however, the vegetable brenzcatechin does not become free and the liberal ingestion of fruits and vegetables does not cause it to appear in the urine.

Baumann[1] has demonstrated that in man, brenzcatechin is formed in the intestine as an abnormal and exceptional product of the oxidation of phenol.

It therefore is derived from the aromatic nucleus of the proteids.

EXCRETION OF BRENZCATECHIN BY THE URINE. It combines in the liver with sulphuric acid, and forms as with indol and phenol a sulphoether and is eliminated under that form in the urine.

HYDROCHINON

Hydrochinon is a paradioxybenzol. It is, as Hoppe-Seyler shows, a product of the oxidation of phenol[2]. This substance does not appear in normal urine, but it is present in abundance, when phenol has been taken medicinally or as a poison.

EXCRETION OF HYDROCHINON BY THE URINE. Like brenzcatechin, hydrochinon is eliminated as a sulphoether; after its combination in the liver with sulphuric acid. Urine containing this substance becomes black in the open air.

ALKAPTON

Alkapton ($C^6H^6O^4$) was first found in the urine by *Bœdeker*[3]. *Wolkow* and *Baumann*[4] identified it with homogentesinic acid, an oxyacid derived from the putrefaction of tyrosin and phenylalanin as *Langstein*[5] demonstrated.

This substance, when in an alkaline or ammoniacal solution, turns brown then black, so that in those suffering from alkaptonuria, the urine, while presenting a normal color when passed,

[1] Baumann: Zeits. f. phys. Ch. X, p. 523.
[2] Hoppe-Seyler: Zeits. f. phys. Ch. XII, p. 4.
[3] Bœdeker: Zeits. f. klin. Med., III, p. 138.
[4] Wolkow & Baumann: Zeits. f. phys. Ch .XV, p. 228.
[5] Langstein: Zeits. f. phys. Ch. XXXVII, p. 513.

soon becomes brownish, later blackish; a fact which impresses the patient very deeply.

Abderhalden[1] was able to demonstrate the presence of homogentisinic acid in the blood serum of alkaptonurics, this according to him would prove that the faulty nitrogenous metabolism should not be sought for (as *Baumann* thought) in the intestine, but as with cystinuria in the nitrogenous organic transformation. This question is still under investigation.

D. INTESTINAL GASES

Hydrogen is produced in considerable quantities with a milk diet, in butyric fermentation and that of the carbohydrates.

CARBONIC ACID is as much a product of nitrogenous putrefaction as of the butyric and lactic fermentation of the carbohydrates.

METHANE is the consequence of nitrogenous putrefaction.

Ruge found 26 per 100 in a meat diet and still more with a vegetable one, for this gas is also derived from the fermentation of cellulose.

SULPHURETED HYDROGEN is much the most important of the intestinal gases, from the toxic point of view.

It is formed in small quantities in all the nitrogenous putrefactions, but in this dosage does not appear to have any deleterious effects.

When it is formed in large quantities, there may result an intoxication (the hydrothionæmia of *Senator*), which is manifested by nervous symptoms and in which sulphureted hydrogen is found, not only in the intestinal flatus and gastric eructations, but in the urine as well. Since its description *Strauss*[1] has observed six cases of hydrothionæmia, all of gastric origin; abstraction made of ulcerated carcinomas in which this complication is frequently seen.

In all these cases, the conditions were those of dilatation of the stomach with motor insufficiency and normal secretion.

Strauss was able to show in all of them that the poverty in carbohydrated substances (maltose and dextrine) was the impor-

[1] Abderhalden: Zeits. f. phys. Ch. XXXIX, p. 145.
[2] Strauss: Festschrift, p. 2.

tant factor in the formation of sulphureted hydrogen. Whereas in the cases of motor insufficiency with hypochlorhydria, sulphureted hydrogen is not formed, because the stomach contains a strong proportion of carbohydrates and lactic fermentations.

The bacterial cause of sulphureted hydrogen is nearly always the colon bacillus. In hydrothionæmia, there is always found a considerable increase of ammonia in the stomach, which enables us to infer that the formation of sulphureted hydrogen in this organ is at the expense of the proteids it contains.

Strauss[1] did not, in any of his cases of hydrothionæmia, find sulphureted hydrogen in the urine. Hence we must admit that intoxication by this gastric gas is not constant, and that it occurs only in certain conditions but little known at present.

INFLUENCE OF THE INTESTINAL GASES ON THE ORGANISM

The intestinal gases have a double action.

In the first place it is a mechanical action, the distention of the digestive canal bringing about by various reflexes quite a series of disorders, interesting particularly the circulation. Next the action is of a toxic order and from this point of view, the effects of the intestinal gases become joined with those of other noxious substances of intestinal origin.

We know actually through the researches of *Kukala*[2] that the intestinal gases possess toxic properties which appear to be due (as *Senator*[3] and *Strauss*[4] had supposed) almost solely to sulphureted hydrogen. But in sum total, the intestinal gases do not seem to play an important part in the pathogeny of digestive auto-intoxication.

[1] F. Müller: Berl. kl. Woch. 1887. p 23.
[2] Kukala: Arch. f. klin., Ch. LXIII, p. 4.
[3] Senator: Berl. klin. Woch. 1868. p. 24.
[4] Strauss: Berl. klin. Woch. 1896. p. 18.

ANTITOXIC FUNCTIONS OF THE ORGANISM

The digestion by the enzymes and the bacteria of the digestive tract, and the normal and physiological digestion of the proteids, produce as we have already seen, numerous useful and assimilable substances; the albumoses, the peptones, ammonia, mono- and diaminated acids; besides this, it causes the pouring into the intestine of numerous and various digestive juices the saliva, gastric juice, the intestinal juices, the bile, the pancreatic juice, etc.

Already in the first products of a normal digestion, we find substances which when directly introduced into the blood may cause symptoms of intoxication, such as the peptones, ammonia, tyrosin, potassium, the bile and pancreatic juice.

And at the side of these useful and assimilable substances, we find that microbic digestion, while pursuing its work of molecular disintegration, decomposes also (as we have seen) the amino acids into substances inapt to the needs of the organism, non-utilizable, true scoriæ only fit to be promptly thrown out.

Consequently it is necessary and for that reason, that the action of the bacteria should not go beyond certain limits if we wish to avert the damage to the entire organism, which would otherwise ensue.

Furthermore, this microbic putrefaction gives birth to numerous derivatives, endowed with more or less toxic power; these are the fatty acids, aromatic bodies, leucomaines and ptomaines.

The digestive tract is therefore and for all of these reasons, a permanent source of infection, and we are led to ask, how it is, that health can be maintained in the face of all these dangers, and by what means the organism defends itself against the ever-menacing causes of disease. (Marfan.)

This is possible only, thanks to the antitoxic functions of the body which are destined to

1st. Maintain the proportions of the digestive poisons within their proper limits.

2d. To transform these digestive poisons into less harmful bodies.

3d. To expel them without danger to the organism.

In effect there exists in the human body an antitoxic system with the special function of defending it against the intestinal poisons. This antitoxic system comprises:

1st. **In the intestine:** A number of factors with the power of diminishing and limiting the phenomena of intestinal putrefaction.

2d. **Surrounding the intestine:** A triple defensive barrier, destined to change the intestinal poisons into inoffensive or less dangerous substances. This barrier is formed by:

(*a*) The intestinal mucous membrane.

(*b*) The liver.

(*c*) The antitoxic glands.

3d. **OUTSIDE OF THE INTESTINE:** A series of eliminating organs, true emunctories, charged with the duty of evacuating and throwing out the unusable residues of the intestinal poisons, no longer but feebly toxic.

I. FACTORS LIMITING INTESTINAL PUTREFACTION

THE DIET

It is certain that a too nitrogenized diet, too rich in meats and eggs, greatly increases the intensity of the putrefaction. This is all the more true if the meats, fish, eggs, are not fresh, or if the game is too high, the cheese too ripe, etc.

The senses of smell and taste preserve us somewhat from the ingestion of these tainted foods. Vomiting and diarrhea eliminate them, when we do not perceive them in time. But this protection is very incomplete, and the adoption of a mixed diet is a more efficacious safeguard.

In fact the diminution of the quantity of meat eaten, the addition to the diet of a strong proportion of milk, fresh cheese,

and farinaceous foods will greatly decrease the phenomena of putrefaction induced by a diet too rich in nitrogen[1].

The same is true of the diminution in the liquids taken while eating, for dry meals favor the decrease of the phenomena of microbic putrefaction.

ABSORPTION

Absorption is an important antitoxic factor, because it removes the digested matters as they become formed, and before they can become the prey of the intestinal bacteria.

Among the causes which favor absorption, there is but one that we can influence, and that is the diminution of liquids taken with the meals. Water is not absorbed in the stomach as *von Mehring*[2] demonstrated.

Moreover, the absorptive power differs according to the degree of concentration of the dissolved matters. In the stomach the greater the concentration (the less liquids present) the greater the absorption.

Brandt[3], in fact, showed that the maximum absorbing power of the stomach was obtained with a concentration of 20 per 100, and that it ceased completely, when the concentration of the chyme fell below 5 per 100.

Hence a solid and dry meal, strongly favors absorption and assimilation and lessens by so much the phenomena of putrefaction.

Inflammatory or atrophic changes in the gastric or intestinal mucosa greatly lessen the power of absorption, and *per contra*, favor intestinal putrefaction.

The same can be said of all conditions of stasis in the intestinal tract whether paralytic, spasmodic, cicatricial or organic.

THE ACIDITY OF THE GASTRIC JUICE

If the acid of the stomach does not destroy all the bacteria or act upon their spores, it nevertheless diminishes their number; it attenuates their virulence and inhibits their growth.

[1] Hirschler, Biernacki: Zeits. f. phys. Ch. X, p. 306. Winternitz and Schmitz, Ibid., XVII, p. 401.
[2] von Mehring: Centralbl. f. Phys., VII, p. 533.
[3] Brandt: Zeits. f. Biol., XXIX, p. 263.

The insufficiency of the gastric juice, and its abnormalities are therefore of importance in the causation of putrefaction.[1] Lastly, as *Nencki* and *Sieber* have shown, the normal gastric juice is capable of destroying certain toxins.

Hence the stomach plays a considerable role in the genesis of auto-intoxication. But it is due, not so much to the retention and putrefaction of its contents as *Bouchard* believed, as to the insufficiency of its antitoxic power in the production of intestinal putrefaction. Many, we might say the great majority, of gastro auto-intoxicated cases, have no trace of dilatation of the stomach. This, however, does not mean that gastro auto-intoxication from stasis does not exist, but it is rare and exceptional.

THE BILE

The biliary acids and particularly taurocholic acid exercise an important antitoxic action; this has been most completely shown by *Schiff* in the first place then by *Maly* and *Emich*[2], lastly by *Lindenberger*, etc. It is for this reason that icterus is frequently accompanied by evidences of considerable putrefaction.

THE PANCREATIC JUICE

According to *Charrin* and *Levaditi* this secretion neutralizes a rather large number of toxins.

In consequence, pancreatic insufficiency so frequently found in diabetes, plays an important part in the toxic symptoms which accompany acid intoxication.

THE ACID REACTION OF THE SMALL INTESTINE

The contents of the small intestine have an acid but not putrid odor. They contain the products of the microbic fermentation of sugar, young cellulose, fats and carbohydrates, that is to say, methylic alcohol, and the fatty acids (lactic, acetic, butyric and succinic). These are the substances that give the intestinal contents their acid reaction and this in spite of the alkalinity of the secretions poured into them. This acid reaction which is above question and has been clearly explained by

[1] Kast, Stadelmann, Wasbutki, Schmitz: Zeits. f. phys. Ch. XXI, p. 401.
[2] Maly & Emich: Monatshefte f. Ch. IV.

MacFayden, Sieber and *Nencki*, etc., is the most important factor among those which protect the albumin derivatives against the invasion of the proteolytic anaerobic bacteria.

How can this acid reaction be maintained, in spite of the alkalinity of the intestinal juices?

The normal flora of the small intestine is composed principally of aerobic and anaerobic facultative bacteria, of which the *Bacillus coli commune* and the *Bacillus lactis aerogenes* form an important percentage.

Bienstock[1] has established that these two organisms oppose the putrefaction of albumin: "The phenomena of the arrest of putrefaction," this author says, "appears very distinctly in milk. It has been known for a long time that raw milk hinders putrefaction and the reason had been attributed to lactose." He furthermore states: "In my experiments, I have seen that the inoculation of sterilized milk with the *Bacillus putrificus* (a proteolytic bacillus) instead of hindering putrefaction, favored it. On the contrary, when inoculated with the bacillus coli, the sterilized milk behaved like raw milk; the albumin no longer putrified, which made me conclude *that the antiputrefactive agent of milk was not lactose, but the Bacillus coli and lactis aerogenes.*"

The mechanism of this action was discovered by *Tissier* and *Martelly*[2]. They demonstrated that the prevention of the putrefaction of albumin by the proteolytic bacilli, was due to the acid products (lactic and succinic acids) elaborated from the distintegration of lactose, by the *Bacterium coli* and the *Bacillus lactis aerogenes.*

It is owing to the predominance of these bacteria, and thanks to the acid reaction which they maintain in the small intestine, that the proteolytic anaerobic bacilli which cannot exist except in clearly alkaline media, are kept in a state of marked inferiority.

It is for the same reason that in the normal state anaerobic albuminous putrefaction cannot take place in the small intestine, and is very limited in the large intestine.

Therefore it can be easily understood, how in prolonged

[1] Bienstock: Zeits. f. kl. Med., VIII, p. 123.
[2] Tissier & Martelly: Ann. Inst. Pasteur. 1902. p. 12.

inflammations of the small intestine, which modify and may diminish, even abolish the acid reaction of the intestinal contents; serious disturbances of intestinal putrefaction may take place.

THE FLORA OF THE LARGE INTESTINE

The flora of the large intestine in the normal state is varied. But the outcome of the bacteriological analyses of the contents of the large intestine reveals a major fact. That is, the great difference which exists between the microbic flora of the normal intestine and that of the pathological intestine, be it in enteritis as we have shown[1] or in appendicitis as *Grigoroff*[2], pupil of *Massol* has so well elucidated.

In the normal colon or in the healthy appendix, we find especially aerobic bacteria or facultative anaerobies, but we do not meet with any strict anaerobies unless in very small quantities.

Bienstock[3] confirmed these findings in his very interesting work and he further shows that the accidentally ingested anaerobic bacteria are destroyed in the intestine by the aerobic bacilli (*coli* and *lactis*) so much so, that none are detected in the stools.

In the intestine of enteritis or in the pathological appendix the anaerobies (very varied and variable), preponderate and the aerobies disappear.

What characterizes the flora of auto-intoxication and that of appendicitis, is the diminution of the aerobies (coli and lactis) the inhibiting bacteria of putrefaction and the multiplication of the proteolytic anaerobies (proteus putrificans, mesentericus, etc.), which are the bacteria of putrefaction.

Consequently all the causes bringing about modifications in the flora of the large intestine will likewise favor the conditions of intestinal putrefaction.

1st. **The alimentary regimen** has a preponderating influence. Farinaceous diet, milk diet, curdled milk, etc., increase the proportion of aerobies.

[1] Combe: Traitement de l'entérite. Paris. 1906.
[2] Grigoroff: Thèse de Genève. 1905. p. 85.
[3] Bienstock: loc. cit.

A nitrogenous diet bespeaks a strong proportion of meats, eggs, game (and particularly when *high*); all of these augment the proportional quantities of the anaerobies of putrefaction.

2d. The dryness of the fecal matters, such as occurs in the lower portion of the large intestine, considerably diminishes the virulence of the proteolytic microbes, hence the phenomena of putrefaction.

Constipation of the lower bowel therefore, does not materially add to the phenomena of auto-intoxication, notwithstanding prevailing notions.

3d. *The acute and chronic inflammatory affections of the large intestine.* The abundant semi-liquid muco secretions, which accompany these conditions, dilute the fecal matters into thickened soup-like material, offering a splendid culture medium for the bacteria. In consequence, these diseases are accompanied by an excessively fetid odor of the stools which increase the phenomena of putridity to the maximum and strongly favor the development of digestive auto-intoxication.

II. TRIPLE LINE OF DEFENSES SURROUNDING THE INTESTINAL CANAL

This triple line of defense is formed by:

(*a*) The mucous membrane of the intestine.

(*b*) The liver.

(*c*) The antitoxic glands.

FIRST LINE OF DEFENSE

The intestinal mucosa protects the organism against the invasion of the intestinal poisons:

(*a*) by its secretions;

(*b*) by the action of its cells.

A. THE SECRETIONS OF THE INTESTINAL MUCOSA

A first category of defenses functionates within the lumen of the alimentary canal

These are in the first place divers substances that are precipitated and are no longer absorbed; others are antagonistic

to those surrounding them. Besides this, *Charrin* with *Lefevre* have revealed the attenuating role of the diastases. Apt at adulterating the microbic secretions, the diastases also show themselves capable of altering the microbes; at all events of acting on their protoplasm. These important findings show how in certain cases, the diastasic principles may render service and lessen intestinal putrefaction.

Lastly, the vital concurrence, the lack of oxygen, etc., have a great bearing upon the vitality of the intestinal bacteria; certain of their excretions like phenol, ammonia, the acids, etc., restrain their multiplication.

All of these circumstances are very favorable to the diminution of intestinal putrefaction.

The functions of the second category of defenses take place at the surface of the intestinal wall. The mucus acts both mechanically and chemically; the leucocytes exercise their usual function on the soluble and figured elements of the intestinal contents. Nevertheless *Charrin*, with *W. Japha*, has remarked that in sucklings leucocytosis is more pronounced at the moment of digestion; although a very favorable time for the passage of the soluble or figured toxic elements into the capillaries.

Moreover, *M. Delamarre* noted that at that age, a relative insufficiency of the mucins, diastasic compounds and of muscular fibers in the ileus existed. From this it may be understood why the digestive apparatus is predisposed to disease during the first period of life.

B. THE CELLS OF THE INTESTINAL MUCOSA

The recent researches of *Kutscher* and *Seemann*[1] have demonstrated the great importance of the work done by the cells of the intestinal mucosa; they absorb the hexone bases and the amino acids to transform them into living and useful albumin by a veritable organic synthesis.

This function already robs the bacteria of part of their prey. But the importance of the intestinal cells is far greater when

[1] Kutscher & Seemann: Zeits f. phys. Ch. XXXIV, p. 528.

we consider them from the point of view of defending the organism, against the poisons formed in the intestine.

The digestive mucosa is the natural point of entrance for numberless poisons; the extent of the epithelial surface is considerable, and peristalsis carries these toxins into successive zones of the mucosa, so that from these considerations we can easily conceive the importance of its defensive properties when truly demonstrated.

Already in 1887, *Charrin* and *Cassin* showed that a series of toxins lost their toxicity completely or in part when they were introduced into the body through the digestive tract.

Whereas a dose of bacterial cultures (filtered) equivalent to five is fatal, when injected into the circulation; fifty times the same amount does not provoke any appreciable disorder when administered by the mouth.

The same identical results are obtained, when preliminary alkalinization of the stomach is made or when these substances are deposited directly into the ileus thus avoiding passage through the stomach. Under these circumstances the gastric juice could not be the reason, nor could it be attributed to the intestinal juices, since the effects remain the same if we take the precaution of removing them first.

Whereas, if the superficial layer of the intestinal mucosa is denuded by curettage, or altered by heat (dry or moist), iodine, etc., and care is taken to clean the surface immediately after; it will be found that the same quantity of toxins is rapidly fatal. (*Charrin.*) Unquestionably *Stich, Ribbert, Denys, Repin, Queirolo* and *Tedeschi* had already recognized the antitoxic role of the intestinal epithelium, but never until *Charrin* and *Cassin's* conclusive and decisive experiments had the evident antitoxic power of the cells been brought so prominently to light; their conclusions are as follows:

1st. The microbic secretions are more toxic when they penetrate through the veins, the portal vein and the skin, than when they are introduced into the intestine, even with allowance made for the quantities and slowness of penetration.

2d. The hepatic protection is not sufficient to explain these facts.

3d. The effects are more rapid and the lesions differ, when the toxins arrive at the liver from an intestine denuded of its epithelium, nor is this simply due to easier passage by reason of a diminution in the thickness of the mucosa.

4th. Inoculation is easily performed by injecting the bacillary products under the skin, or in the portal vein or by injecting the serum of subjects, who have been inoculated shortly before through the same channels.

Whereas, by utilizing the serum of those in whom the bacillary products had been deposited in the intestine; the inoculation is accomplished with difficulty, sometimes not at all. Consequently we are led to suppose that these products are physiologically modified by contact with the intestinal epithelium.

Phisalix and *Bertrand* demonstrate exactly the same influence of the intestinal epithelium on venoms. As with the toxins, inoculation through the digestive tract is not successful, which shows that the venoms are physiologically changed by the epithelial cells. These cells are therefore absolutely analogous with the glandular cells; those of the liver for example. As *Charrin* has established, they act partly as dialysers by retaining the colloid principles; on the other hand, they exercise upon the bacterial albumins, an action identical with that produced upon the alimentary albumins.

The intestinal cells attenuate the proteids and the toxins, while they permit the passage without metamorphosis of the salts and ammoniacal products.

Hence, the intestinal mucosa exercises, with regard to the microbic poisons, and outside of its passive role of filtrating membrane, a truly antitoxic and protective function.

If therefore the intestine becomes deeply inflamed, as in enteritis and if the cells degenerate or necrose, or should the mucosa atrophy as in athrepsia and the cells disappear; the insufficiency of the antitoxic function will permit a greater number of toxins to enter the general circulation and the grave consequences of auto-intoxication will result.

SECOND LINE OF DEFENSE

THE LIVER

The second line of defense is constituted by the liver. The function of the liver cells is to withdraw from the portal vein the toxic substances which have escaped the first line of defense, so as to prepare and deliver to the blood circulating throughout the organism, substances that are but slightly toxic, eliminated more easily and without danger to the economy.

In the total amount of nitrogen escaping through the kidneys, we find on analysis:

Nitrogen in the form of urea	83.0 per 100
Nitrogen in the form of uric acid	1.8 per 100
Nitrogen in the form of ammonia	5.0 per 100
Nitrogen in the form of extractives:	
Kreatin	2.0 per 100
Hippuric acid	0.5 per 100
Aromatic bodies, etc.	10.0 per 100

CHEMICAL ACTION OF THE LIVER

Urea is formed especially in the liver at the expense of the amino acids and ammonia. The amino acids are partly toxic (tyrosin tryptophan), but their toxicity is limited.

Ammonia is extremely toxic; 0.15 gram sufficing to kill one kilogram weight of animal.

Urea, on the contrary, is one of the least toxic bodies, for six grams per kilogram are required to kill an animal. By transforming the amino acids and ammonia into urea the liver considerably diminishes the toxicity of the excrementitious materials. *That constitutes its uropoietic function.*

Uric acid. Uric acid is also principally formed in the liver but not exclusively; it is formed at the expense of the nucleins and xanthic bases and through the influence of two ferments; *the hydrolytic ferment* which transforms guanin and adenin into xanthin and hypoxanthin and *xanthinoxydase*, which transforms hypoxanthin into xanthin and the latter into uric acid.

The xanthin or purin bases which are products of the decomposition of the nucleins, belong to the leucomaines of *Gautier;*

without being toxic they are far from being inoffensive. Uric acid is barely toxic. By transforming the nucleins and purin bases into uric acid the liver still further diminishes the toxicity of the excrementitious materials; that constitutes its *uricopoietic action*. The liver, considering only the two functions (uro and uricopoietic) already reduces to one-fourth the toxicity of the materials to be eliminated by the kidneys (*Bouchard*), but that is not all.

Aromatic bodies. The aromatic bodies most of which are toxic, are changed in the body into almost inoffensive substances by their combination with sulphuric and glycuronic acids. These acids and their alkaline salts are, in fact, infinitely less toxic than the aromatic substances themselves. The experiments of *Pflüger*, *Embden*, and *Glæssner*, have demonstrated in the most evident manner, that the combination of the aromatic radicals with sulphuric and glycuronic acids, takes place in the parenchyma of the liver.

The presence in the bile of the sulphoconjugated acids was noted by *Munck;* that of the glycuroconjugated acids by *Leersum.*

Besides, *Embden* has experimentally realized the formation of the sulpho- and glycuro-conjugated acids, by means of artificial circulation of the liver.

Moreover, the hepatic cell itself has a strong affinity for the aromatic bodies. It is for that reason that the fresh pulp of the liver retains phenol and cresol with such tenacity that they can no longer be separated from it by distillation (*Herter* and *Wakeman*). It is thus that in the physiological state the liver appears to have the same properties of fixation and retention of the aromatic substances (particularly indol), as its cells isolated from the body have. It appears therefore that the liver not only transforms the aromatic bodies into less offensive matters, but that it retains a certain portion of them. Under the same head still, the liver considerably diminishes the toxicity of the substances brought to it by the portal vein.

Its power sensibly lessens under the influence of intoxications or disease. *Herter* and *Wakeman* have in effect shown that the absorbent power of the liver for the aromatic bodies is

notably diminished by the action of ether, chloroform or toxins. Consequently we see in diseases of the liver, in simple insufficiency, in cirrhosis, the aromatic bodies—indican among others—increase considerably in the urine.

TOXICOLYTIC ACTION OF THE LIVER

Last but not least, there remains for us to speak of the most important antitoxic action of the liver.

The organic poisons and the intestinal ptomaines or entero toxins are subject to the powerful toxicolytic action of the hepatic cells.

Alkaloids. Our venerated master, *Schiff* first, then quite a number of investigators have sought to demonstrate experimentally the action of the liver upon the poisons and have insisted upon the great importance of this function.

Schupper[1] has very recently taken up again the study of this question, and he has shown that the liver, owing to the biochemic activity of its cells, diminishes from 50 to 75 per 100, the toxicity of the alkaloids particularly, atropine, pilocarpine, cocaine and apomorphine.

Enterotoxins. The most interesting question above all would be to know exactly how the zymases secreted by the hepatic cells act upon the enterotoxins. Unfortunately, the paucity of precise notions we possess regarding the ptomaines, has prevented the direct study of this question. The indirect study of their action has been made by *Bellatti*[2], *Colasanti*[3], and *Stadthagen*[4]. These observers found a hypertoxic urine in all cases in which the liver, by reason of functional or anatomical lesions, was unable to arrest or neutralize the organic poisons.

Whereas the urotoxic coefficient became lower as soon as the hepatic functions were re-established.

The protective function of the liver and the connection of the urinary toxicity with the integrity of its cells can be demonstrated by studying the toxicity of the urine in dogs, before and

[1] Schupper: Boll. d. Acc. Roma. XIX, p. 5.
[2] Bellatti: Boll. d. Acc. Med. Roma. XIX, p. 30.
[3] Colasanti: Boll. d. Acc. Med. Roma. XXII, p. 59.
[4] Stadthagen: Zeits. f. klin. Med., XV, p. 389.

after ligating the portal vein by following the method of *Bisso*[1].

By ligating this vein, we can measure the part taken by the liver in the toxicolysis of the blood brought to it from the intestine. With this avenue closed, the enterotoxins being no longer attenuated or destroyed by the hepatic cells, enter the general circulation from which they are eliminated by the kidneys, giving thus a high degree of toxicity to the urine. Whereas the normal urotoxic coefficient of the dog is 0.344; it nearly triples, 0.902, after ligation of the portal vein.

Consequently the liver destroys two-thirds of the poisons of digestive origin; thus protecting the organism against the constant menace of gastrointestinal auto-intoxication.

The urotoxic coefficient varies with the foods administered:

	Before ligation	After
With meat diet the urotoxic coefficient is . .	0.432	0.958
With milk diet the urotoxic coefficient is. . .	0.275	0.822
With mixed diet the urotoxic coefficient is .	0.290	0.878

The urinary toxicity is therefore proportional with the degree of hepatic insufficiency; it increases and diminishes with it. Yet this toxicity is not parallel with any known and dosable substances of the urine. It seems then, that we may and must attribute it to the enterotoxins; the more so as the alimentation exercises an unquestionable action on their production.

Masini (of Genoa) has recently demonstrated in a novel and original manner the toxicolytic action of the liver upon the toxalbumins of intestinal fermentation. After having destroyed in animals two-thirds of their liver, he saw them rapidly succumb, but he succeeded in prolonging the life of these animals by injecting them with extract or infusions of liver.

We may then conclude from these facts *that the liver is, next to the intestinal mucosa, the principal protecting organ against the intestinal poisons.* According to *Charrin* the intestine intervenes particularly to modify the colloids, the albumoses and the toxins, but it permits the alkaloids, and the ammoniacal compounds to filter through without changing them.

[1] Bisso: Archiv. ital. biol., XXV, p. 492.

The liver intervenes especially to destroy substances soluble in alcohol (more or less alkaloidal in character) and the ammoniacal compounds.

Evidently a selective and not merely a supplemental action, for in reality, nature disposes of two lines of defense, the second acting upon the toxins spared by the first; the one and the other bringing about a reciprocal completion.

From all this, it appears that hepatic insufficiency plays a considerable role in the genesis of auto-intoxication, and explains why intoxication may exist when insufficiency is present, even with a normal state of intestinal putrefaction. In such cases all the causes of hepatic insufficiency become causes of auto-intoxications. We shall therefore be obliged to examine them more closely in the chapter devoted to the causes of digestive auto-intoxications.

THIRD LINE OF DEFENSE

THE ANTITOXIC GLANDS

The liver and the intestinal mucosa do not arrest all the poisons, or do so only incompletely. Those that escape wander throughout the organism until they come to the third line of defense, the glands of internal secretion. Biological chemistry has lately made considerable progress in the study of these glands; and it has demonstrated that their secretions caused the penetration into the circulation of oxidizing ferments or reducing agents the antitoxic action of which becomes each day more apparent.

These studies are merely begun, and it is impossible to actually give a *résumé* of them, for too much is unknown and there are too many contradictory results as yet. We shall therefore limit ourselves to a general summary. The antitoxic glands of internal secretion are the suprarenal capsules, the pituitary body, the thyroid and in the fetus the thymus, probably intended to destroy the enterotoxins traversing the placenta and derived from the mother's blood.

THE THYROID

In my work upon myxœdema[1],

I had already advanced the hypothesis, that the enterotoxins and leucomaines of intestinal origin, derived from microbic nitrogenous putrefaction, were transformed into harmless substances by the thyroid and parathyroids in the infant and by the thymus in the fetus.

This hypothesis was based upon the following facts:

That *Schiff*, then *Horsely* had already demonstrated that the carnivora suffered rapidly and greatly from thyroidectomy, while the herbivora suffered but slowly and little.

Later, dating from 1890, came the experiments of *Breisacher*. This investigator, by feeding dogs upon whom thyrodectomy had been performed, with milk, at times with raw or roasted meats, sometimes with beef tea and boiled meats, noticed that the morbid symptoms and death were less rapid when fed with milk and boiled meat, whereas strong convulsions and a rapid death ensued from feeding with beef tea and roast meats. The salts of the beef tea, when added to the milk, did not exercise any influence, which led to the inference that it was particularly the meat extractives, the kreatinic leucomaines and others that exercised the influence on the intoxication.

Since then *Quervain*, *Rosenblatt* and *Loenz*, have verified these facts experimentally. Clinically *Nothnagel*, *Ziemssen*, *Blum*, *Ewald*, and *Combe* have shown the favorable effects of withdrawing meats from those affected with myxœdema, *Basedow's* disease and goitre.

Still later the experiments of *Coronedi* and *Marchetti*[1], *Luzatto*[2] have shown that dogs from whom the thyroid was removed, survive well, if fed with bromated fats instead of meat.

The consideration of all these facts has led two modern investigators, *Blum* and *Kishi*, to formulate an hypothesis very similar to mine upon the functions (antitoxic) of the thyroid.

[1] Combe, Le Myxœdême (Rev. Méd. Suisse, 1892).
[2] Coronedi & Marchetti: Acad. Med. Florent. 1902. t. VI.
[3] Luzatto: Riv. Venat. d. Sc. med. 1904. p. 25.

According to *Blum*[1] the thyroid neutralizes the toxins coming from the digestive canal and probably those produced by the putrefaction of the albumins. According to *Kishi*[2] the thyroid is a secretory organ charged with the destruction of a substance dangerous to the economy.

This dangerous substance is *prothyreotoxin*, a nucleoproteid derived (*Kishi*) from a meat diet.

It is formed in the organism in variable quantity, according to the species of animal (carnivorous or herbivorous) and according to the kind of food (milk, bread, meat) if the animal is omnivorous. From the cells of the thyroid is secreted an *iodized globulin* (*thyroidin*) which has a special affinity for this dangerous nucleoproteid.

These two substances, when combined and bound together in the follicles, form thyreotoxin which normally splits into two absolutely harmless substances, and constitute the internal secretion of the thyroid, and in that state they enter the blood to be excreted through the kidneys. When, on the contrary, the thyro-parathyroid glands are insufficient (congenital or acquired, surgical or experimental), the *prothyreotoxin* accumulates in the body, and there results an auto-intoxication of the nervous system and of the entire organism.

If the insufficiency is in the parathyroids, *tetany* results. If the thyroid is insufficient, *myxœdema* results. If the thyroid is only partially insufficient, we have *myxœdematous infantilism*.

THE PITUITARY BODY

This gland has been recently studied histologically by *Pirone*[3], who distinguishes two parts: one posterior, nervous; the other anterior, in which is found a colloid secretion absolutely analogous to that of the thyroid. *Guarrini*[4], who studied its physiology, demonstrates that it is far from correct to affirm that the pituitary body is an organ without function, for, on the contrary, it is an important antitoxic organ complementary to the thyroid, as *Lusana*, *Rogerditz*, and *Marenghi* had shown;

[1] Blum: Centralbl., t. XXI, p. 695.
[2] Kishi: Virchow's Arch., t. CLXXVI.
[3] Pirone: Archiv. de Fisiol., II, p. 60.
[4] Guerrini: Archiv. Ital. de Biol., XLIII, p. 1.

in fact, lesions of the thyroparathyroid glands, bring about modifications in the pituitary body.

Moreover, *Golgi*, following the researches of *Marenghi*, contends that the effects of the ablation of the suprarenals speak in favor of their being supplemented by the pituitary body.

From all this, it appears that the pituitary body is complemental to the thyroid and suprarenals in the protective antitoxic functions of the body.

THE SUPRARENAL CAPSULES

The labors of *Gley, Abelous* and *Langlois*[1], *Oliver* and *Schæffer*[2], *Szcymonovicz* and *Czybulski*, have established, that the suprarenals possess a very important internal secretion, which is poured into the suprarenal veins and that it is a constant product of their cell activity.

The functions attributed to this secretion appear to be at the same time nutritive, vasomotor and antitoxic.

Nutritive : *Gourfein*[3] was able to show that animals deprived of the suprarenals died rapidly; that those in whom a tenth part of one capsule remained, lived for several weeks, but showing the signs of a profound and progressive depression of the nutrition; the animal becoming emaciated and gradually weaker, although normally fed.

Vasomotor, muscular ; The suprarenal secretion elevates the blood pressure by a vasomotor constriction of the muscular fibers of the peripheral arterioles, as shown by *Biedl* and *Velich*[4], and at the same time by a remarkable tonic action upon the cardiac muscle, as shown by *Gottlieb*[5].

Antitoxic : *Charrin* and *Langlois*[6] demonstrate that, as with the liver, the suprarenal secretion weakens the activity of the alkaloids; that of nicotine in particular.

Gourfein[7] established that besides, the suprarenals acted

[1] Gley, Abelous and Langlois: Arch. de phys. 1892. p. 269.
[2] Oliver & Schæffer: Brit. Med. Journ. 1895. p. 635.
[3] Gourfein: Revue. med. de la Suisse rom. 1896. p. 113.
[4] Biedl & Velich: Wien. med. Pr., No. 86, p. 13.
[5] Gottlieb: Arch. f. exp. Path. 1896. p. 2.
[6] Charrin & Langlois: Sem. med. 1896. p. 28.
[7] Gourfein: Loc. cit.

chemically by neutralizing in the body several toxic substances of unknown nature.

Dubois[1] finds, that the secretion plays an important part in the struggle against the bacterial toxins circulating in the organism, and he affirms that besides, its antitoxic function appears to be exercised against the products of muscular metabolism. Lastly, *Mühlman*[2] saw the destruction by the suprarenals of a toxic body derivative of the intestine (brenzocatechin), which favors the pigmentation of the skin and mucous membrane.

Whatever the outcome of these hypotheses may be, the antitoxic action of the suprarenals has been actually demonstrated, but what the toxic bodies are that they modify through their intervention, remains to be seen.

III. ELIMINATION OF THE INTESTINAL POISONS

The channels of elimination constituted by the natural emunctories of the body, have for office, that of evacuating and casting out, all of the poisons escaping the other means of defense, and also all the useless waste products circulating in the blood.

These emunctories are the respiratory tract, the salivary glands, and particularly the skin and kidneys.

Respiratory Tract

It is through this channel that the volatile products are eliminated, carbonic acid in its totality, ammonia in small proportions, acetone in varying quantities according to the days.

With regard to acetone, the respiration exercises a true supplemental action to that of the urine[3]. As to the bodies but slightly volatile, they are scarcely eliminated through this channel.

THE SALIVARY GLANDS

The saliva serves for the elimination of certain substances, the salts of potassium, bromine, and iodine. Sometimes urea, leucin, and xanthin bodies may be found. In some individuals, crises of auto-intoxication are at times accompanied by frightful

[1] Dubois: Arch. de phys. 1896. p. 412.
[2] Mühlman: Deutsch. med. Woch. 1896. p. 7.
[3] Schumann: Wien med. Woch. 1892. p. 17.

salivation amounting to perhaps several liters in the day. Is it an elimination of enterotoxins? A question impossible to answer in our present state of knowledge.

SUDORIFEROUS GLANDS

Perspiration eliminates water particularly, and the skin is, after the kidneys, the most important organ of elimination; so much so that they may supplement each other. Urea is found in the sweat. According to *Argutinsky*[1], an average of 1.2 per 1,000 exists. Ammonia is also found. In certain cases these substances may be increased, and *Cramer*[2] estimates that about 12 per 100 of the total nitrogen may be eliminated through this channel. In uræmia, crystals of urea may even form on the skin.

Besides these, the sweat may contain fatty volatile acids, cholesterin, and kreatinin, as *Capranica*[3] showed.

Are the products of intestinal putrefaction also cast out by the skin?

We know that children suffering from intestinal auto-intoxication perspire greatly, especially at night during sleep.

We know that auto-intoxication is very frequently accompanied by pruriginous or acneiform eruptions.

Whether the enterotoxins are eliminated in this fashion, is hard to say.

Kast[4] has demonstrated the presence in the sweat of the sulphoethers, phenols, skatol and the aromatic oxyacids, and he found that the coefficient of *Baumann* for the sweat was 12, almost exactly the same as that of the urine in the same individual. *Kizio* and *Amann* found indols in sweat; it should be said, however, that the aromatic bodies are never noted in considerable quantities.

The ingestion of aromatic substances notably increases their excretion through the skin as it does with the urine, but not in the same measure, for their excretion is much greater by the urine.

[1] Argutinsky: Pflüger's Archiv., XLVI.
[2] Cramer: Arch. f. Hygiene, X.
[3] Capranica: Maly's, XII, p. 190.
[4] Kast: Zeits. f. phys. Ch. XI, p. 501.

We can arrive at the conclusion, that, like the urine, the skin eliminates aromatic substances, but in an infinitely lesser degree.

It is therefore not impossible for the enterotoxins to follow the same route, and that the cutaneous eruptions are the consequence. In certain cases, probably due to some special idiosyncrasy, the sweat appears able to supplement the urine; this refers to *indicanhydrosis*.

We had occasion to observe two cases of this curious affection in which the patients had a blue perspiration, which stained their shirts under the arms with the characteristic color.

The chemical analysis, made by *Amann*, demonstrated the presence of indigo in the sweat, and a strong excess of aromatic substances in the urine.

Phenols	0.065	Skatols	0.020
Indols	0.060	Oxyacids	0.070

figures indicating three times the normal.

Amann has, besides, published a paper on three other cases of indicanhydrosis[1], one of which we observed together.

THE KIDNEYS

The kidneys, as we have mentioned, are the principal emunctories for the aromatic bodies.

It is through the urine that almost all of the substances, derived from intestinal putrefaction and *circulating in the blood*, are eliminated, for they alone can have reacted on the organism. They are: 1st. *The aromatic bodies;* indoxyls, skatoxyls, phenols, combined with sulphuric acid, and in smaller proportions, with glycuronic acid. These are excreted as sulpho- and glycuro-conjugated acids.

2d. *The aromatic oxyacids*, the greater part of which are excreted as such, the lesser part as sulphoethers.

3d. *The leucomaines and enterotoxins.*

Hence any insufficiency of the kidneys may lead to a retention of the different products of albuminous putrefaction, and consequently auto-intoxication.

[1] Amann: Journ. Suisse de Chimie. 1902. p. 22.

THE STOOLS

The stools contain the alimentary residues that have not been digested, and all of which have been more or less attacked by microbic fermentation.

They consist of muscular fibers, collections of casein, starch cells, fat droplets, also cellulose, and horny matters, which resist digestion.

We find besides, mucus, glairs, epithelial cells, and products of the secretions of the intestinal glands. Most of these, being of nitrogenous nature, have been subjected to the action of the proteolytic bacteria, and are in full putrefaction.

Lastly, we find the products of the nitrogenous putrefaction, the volatile fatty acids, aromatic bodies (indols, skatols, phenols, oxyacids), leucomaines and ptomaines.

These substances are often found in the stools, frequently in considerable proportions much greater than in the urine. This is due on the one hand, to their excretion by the stools, on the other, to the transformations they undergo in the digestive mucosa, the liver and the antitoxic glands, and to fixation of part of them in the liver.

There is therefore no relation—and it is well to insist on this point—*between the proportion of the aromatic bodies in the intestine and the proportion of the same bodies in the urine.*

Because at times, we may find putrid and fetid stools containing large amounts of putrefactive products and yet the urine excretes but few. On the other hand, it is not exceptional to find apparently normal stools give rise to auto-intoxication owing to insufficiency of the antitoxic glands.

Hence we can state that there is no relation between the degree of putrefaction in the stools and the degree of auto-intoxication, and, that it is impossible to conclude from one or the other. For we must remember that it is not the entero-toxins in the stools that react on the organism, but those only that have circulated in the blood and they are eliminated through the urine.

IV. SUMMARY

The putrefaction of the proteids in the intestine depends

1st. On the food. *The abundance of the meals, their frequency.* Too abundant and too frequent, they leave undigested residues which become the prey of the saprophytic microbes.

Their composition. Too many nitrogenous substances (meats, eggs), increase putrefaction, whereas much farinaceous food diminishes it.

The quantity of liquid influences putrefaction.

2d. The intestinal flora. Parasites and a strong proportion of anærobic proteolytic bacteria increase putrefaction.

3d. The absorptive power of the mucosa. When this power is diminished by stasis, putrefaction increases. When it is diminished by inflammation or atrophy of the mucosa, putrefaction increases.

When it is diminished by the quantity of liquid ingested, putrefaction increases.

4th. The frequency and nature of the stools. The greatest part of the toxic matters is eliminated by the stools in the form of diarrheas.

INTESTINAL AUTO-INTOXICATION DEPENDS:

1st. On the degree of intestinal putrefaction.

2d. Upon the integrity or insufficiency of the antitoxic organs.

EXPERIMENTAL PATHOLOGY

The progress made in experimental pathology and the new methods of experimentation, have, in recent years, made it possible to include the hypothesis of intestinal auto-intoxication in the field of experimental pathology.

Thanks to the modern researches, which we have reviewed in the preceding chapter, we know that even in the normal state, the digestive tract contains numberless poisons, the presence of which is absolutely constant. Thanks to the experiments pursued during several consecutive years, with the aid of these intestinal poisons; several investigators have succeeded, not only in reproducing functional troubles completely resembling those we shall describe in our patients, but in determining the anatomical lesions, which are also absolutely identical with those found in the organs of the auto-intoxicated.

Thus, is the theory of intestinal auto-intoxication actually demonstrated; it issues forth from the domain of hypotheses, to enter the domain of facts, demonstrated and proven by the most exacting scientific experiments.

The number and variety of the observations have greatly extended the limits of intestinal auto-intoxications and have conferred upon the poisons of digestive origin an increasing importance. It is particularly to *Professor Charrin* (of Paris) and his pupils, that we owe these experimental studies.

Hence it is especially to his work that we shall refer and which we will summarize, also drawing largely from a paper[1] from the pen of *Professor Charrin* himself and his pupil, *Doctor Le Play*, and which we should like to cite in full.

Charrin, in the first place, called attention to the fact that the precision of the results, which he obtained, as well as their

[1] Charrin: Le rôle pathologique des poisons de l'intestin. Semaine Medicale, 23 Novembre, 1904.

striking analogy with clinical facts, were due in great part to the method he employed and the technic followed; these differing entirely from those of his predecessors.

Most of the experimental investigators, in fact, in isolating the intestinal poisons, have made use of either heat or filtration, methods which destroy or retain a goodly number of the toxic bodies under examination; or else employed extracts made with water, alcohol, ether, chloroform or carbon sulphide; these separate the soluble poisons, but leave behind the most important, the insoluble.

These investigations therefore were wrong at the start, and the results obtained could only be incomplete. *Charrin* on the contrary, collects the intestinal contents from the newborn (healthy or not) with due respect for the mucosa. He sterilizes the collected material (diluted with three to four times its volume of normal salt solution) by painstaking and patient tyndalizations, at relatively low temperatures.

He obtains in this manner, in a sterile state, all of the pathogenic chemical substances in the intestine, without any molecular modifications and ready for experimental purposes. *Charrin* injects these substances, at times, in strong, sometimes in massive doses into the veins or under the skin, and in this manner provokes acute or subacute conditions. Sometimes seeking to imitate what transpires in the organism, he introduces these liquid substances in fractional doses every four or five days.

Lastly, instead of introducing these toxic matters under the skin or into the blood, he creates total occlusions of the intestine or strictures of the cæcum, thus realizing in the animal certain acute or chronic manifestations observed clinically, and due to the same conditions. The alterations so caused, offer variations depending upon the length of time the animal survives, and this ranges from a few instants to several weeks. These variations in the degree of the lesion *Charrin* states: "have completed the undeniable analogy of our results with the facts observed in human pathology." The following is a résumé of the researches of *Charrin* and his pupils:

"Whether of external or internal, cellular or microbic origin,

the poisons contained in the alimentary tract present many forms. We know that it contains an infinite number of active substances; mucus, diastases, albumoses, alkaloids, toxins, aromatic bodies, biliary, sulphur and ammoniacal compounds, amides, amines, putrid matters, acids, bases, salts, pigments, sulphureted hydrogen, gases, etc.

"Among these substances some are stable, some soluble in alcohol, others are volatile or insoluble; the insoluble elements being the most noxious.

"An important fact is that, at the intestinal outlet, we find relatively as many toxic matters in healthy subjects as in those suffering from chronic gastro enteritis."

Although, and particularly if the process is an acute one, *Charrin* admits with *Hawthorne*, the possibility of an increase of this toxicity in the diseased intestine; we might add, it is true, that the erosions of the mucous membrane by favoring their passage into the blood cause a diminution in the morbid principles escaping by the rectum.

Thus, there exist in the midst of the digestive tube, whether in a physiological or pathological state, poisons capable of determining many lesions and functional disorders, which we shall be called upon to examine.

I. LESIONS AND FUNCTIONAL DISORDERS

We shall now examine the modifications and the lesions produced by the intestinal poisons in the fluids, tissues, and organs of the animal.

THE BLOOD

Exceptionally, analysis reveals lipæmia, acetonæmia, lacticæmia, oxalæmia, etc.

Moreover, its alkalinity sometimes diminishes and at times augments. These variations, which are but slight, are due in the first place to the tendency of the acids to dominate; in the second place their effort results in the transformation of certain insoluble tribasic phosphates into monobasic and bibasic elements, soluble in the organic fluids. But the principal modifications occur in the hemoglobin and iron (these are dimin-

ished), and in the nucleated red cells, the number of which rapidly decreases.

No one ignores the undeniable clinical relations existing between certain anæmias and intestinal processes. Even in *chlorosis*, which has besides a complex pathogeny, the intervention of the retained products of obstinate constipation has been invoked.

Finally, *Einhorn*, *Block* and *Faber* find a connection between one of the forms of pernicious anæmia and gastric achylia as well as atrophy of the mucosa of the ileus, both lesions equally favorable to the elaboration of the putrid fermentations of the digestive canal.

There are, besides, among the intestinal poisons, certain definite bodies, specially the ammonia compounds and sulphureted hydrogen, which are capable of bringing about deterioration of the blood. On the other hand, *Charleton* and *Benedetti* were able to produce *purpura hæmorrhagica* by means of the coli bacilli.

THE LIVER

In the realization of morbid phenomena (*Charrin* adds), simplicity is a rare quality. When we recognize the changes brought about in the liver, through the intestinal toxins, we can perhaps, in order to clear up the genesis of the hematic alterations already mentioned, accuse the liver of participating also.

Physiological pathology, in fact, teaches us that outside of its functions of active hematopoiesis in fetal life; the hepatic gland facilitates besides, exudations from the capillaries by acting upon the *fibrin*, the *iron*, the *mineral constituents* and *coagulation*.

Besides this, and owing to the bile, the liver modifies the red blood cells, and the rapidity and the pressure of the vascular flow.

It thus appears that the diseased liver acts in several manners on the composition of the blood.

As the result of partial intestinal obstructions or in subjects in whom have been introduced substances taken from the alimentary canal, we note lesions in the liver, hemorrhages and

various other modifications. In some portions the trabeculæ are distorted, the cells are degenerated and the reduction of the chromatin into dust, appears undeniable. *Per contra*, sclerosis is scarcely perceived, perhaps on account of the relatively short duration of the process. At all events, whether obtained from the production of occlusion of the ileus, or from injections into animals, the results—analogous with those of *Lewin*—prove that with regard to the hepatic gland, the pathogenic attributes of the intestinal products are markedly accentuated.

Unfortunate is the hepatic gland, deprived of the salutary protection of an intact digestive mucosa! For in its midst—as *Charrin* and *Cooffi* have recognized—accumulate poisons capable of notably increasing the toxicity of its parenchyma and of deteriorating it.

THE SPLEEN

In injected animals the spleen presents a number of abnormalities; the Malpighian corpuscles are altered; the chromatophilia is diminished, the evolution of the lymphocytes appears incomplete and from the reduced number of the macrophages, we may infer a lack of activity on the part of the organic means of defense. Here again in these multiple findings, the complexity of morbid actions is manifest. For while in fact, the noxious compounds derived from the gastro-intestinal tract, react upon the blood, the hepatic parenchyma and the splenic tissue; the latter by "*counteraction*" react upon each other reciprocally.

Some experiments of *Charrin*, pursued with *Moussu*, have brought to light the reaction of the splenic tissue upon the hepatic parenchyma. After having practiced a biliary fistula, ligating the choledocus duct and measured the pigment content of the bile, it is sufficient to remove the spleen to note in the majority of cases a rapid lowering in the proportion of these pigments. Besides this, other findings permit the elucidation of the mechanism of this modification.

When, by means of known poisons—as done by *Jaweinn*—or by the introduction of blood into the peritoneum, we liberate a certain quantity of hemoglobin, we perceive an increase in

the coloring matters of the bile. Also with *Portier*, *Petrone*, *Korschum* and *Morgenroth*, we may recognize that in the midst of the splenic substance, the phenomena of hemolysis is rather active; if it becomes exaggerated, hemosiderin may then accumulate in the hepatic gland.

Hence it seems possible to maintain (as *Bleichröder* and *Meunier* do), that the globular, ferric or chromogenic débris engender cirrhosis of the liver.

CIRCULATORY APPARATUS

The lesions of the circulatory apparatus attributable to the action of the digestive poisons, are not limited to the blood. At times the vessels become indurated and their internal lining membrane is altered. *Bittorf* has noted deteriorations in the aortic valves.

Less rarely the myocardium becomes thickened; this thickening, which may involve both sides of the heart, preferably localizes itself in the left ventricle. Most commonly the muscular fibers maintain their striations in part, but usually their size exceeds the normal; the sarcoplasma appears in abundance; the nucleus is reduced and cariokinesis is sensibly nil.

Degeneration is less exceptionally met with than true inflammation, and blood extravasations appear in the interfascicular tissue. The bearing of these experimental researches assumes greater importance by reason of their concordance with clinical findings.

In fact, in athrepsics, offspring of infected or auto-intoxicated mothers, it is not unheard of, to find hypertrophies of the myocardium. These appear to be independent of the kidneys or of circulatory conditions.

Charrin, with *Courtade* and *Guyon*, noted that if intestinal compounds, in a diluted state, were injected into the veins of a crurarized dog, the variations in pressure were insignificant.

These results eliminate, as a cause, any mechanical pathogeny, and the duration of the process excludes reflex influence as well; hence we are led to invoke the action of the toxic principles themselves.

Be it as it may, in offspring suffering from gastroenteritis,

these lesions occur with a degree of frequency unknown in the cardiac history of the adult.

If, in spite of the gastroenteritis, these new-born survive, they are susceptible of presenting at some time hemovascular disorders, due to these abnormalities, that have remained absolutely latent.

RESPIRATORY APPARATUS

The notions we possess enable us to understand that directly or indirectly the lesser or pulmonary circulation must also feel the influence of the intestinal products. In man or in the newborn, as the result of intestinal occlusion, excessive digestive fermentations or simply of stubborn constipation, we may observe pulmonary congestions, broncho-pneumonias, the germ of which originates at times in the intestine.

In animals, the introduction of these digestive poisons determines modifications in the pulmonary parenchyma usually limited to a more or less pronounced hyperæmia.

To explain these disorders and lured by the recent findings in auto-intoxication, some authors have attributed as sole cause, stable or volatile substances derived from the digestive canal.

Unquestionably, from the contents of the ileus substances may be extracted capable of influencing the vasomotor system. *Grossman*, from the liquid exudate pent up in a hernial sac, was able to extract a base related to muscarin, which, when injected into the veins, provoked rapid blood stases in the lungs.

Undeniable as the toxic mechanism may be, the old pathogeny based upon nervous intervention exists none the less.

If, in conformity with the experiments of *Arloing*, *Morel*, *François Franck*, we irritate the gastric mucosa of an animal, elevations in the pressure of the pulmonary circulation will be noted, and successive sections of the pneumogastric and sympathetic nerves will bring into evidence the centripetal and centrifugal paths followed by this reflex. It is these elevations of pressure that provoke the functional tricuspid insufficiencies, pointed out by *Potain* and *Teissier* in the course of a series of abdominal affections.

NERVOUS SYSTEM

Although the seat of auto-toxic and ptomaine neuritis and studied by *Kouchev*[1] in their paralytic consequences, the peripheral nerves are not the only part of the nervous system to feel the action of the intestinal poisons.

The nerve centers are, by no means exempt; of course the relatively short duration of the conditions in animals has not been sufficient to permit the evolution of medullary or systematic degenerations.

But *Charrin* has discovered meningeo spinal congestions and especially frequent meningeal or cephalic hemorrhages.

These same lesions are met with in children of tuberculous, alcoholic, anæmic mothers, themselves suffering from gastro-enteritis.

Furthermore, the relations between the affections of the central nerve axis and fermentations of the alimentary tract have been established for a long time past. *Féré* has noted the depressing effects of certain digestions and *Soelber*, *Prou* and *Mendel* connect some vertigoes and psychic disorders with them; these opinions have some bearing on the practice of neurologists, who, by administering purgatives, obtain transient ameliorations.

GLANDS OF INTERNAL SECRETION

The influence of auto-intoxication upon the glands of internal secretion is no less considerable.

Bone marrow. Because of its influence upon the solids and liquids of the economy; it is advisable to examine the *bone marrow* of animals poisoned by substances taken from the intestine.

It is the seat of hemorrhages and shows a diminution in the proportions of fat, nucleated red blood cells, etc. Naturally the blood state and the secretions suffer from this condition.

It is the same with the bony frame, which also feels the effects of the direct or indirect action of the digestive poisons. Thus

[1] Kouchev: Sem. Med. 1904. p. 327.

Charrin with *Hauser* and *Spillman* noted various malformations. Radiographic examination reveals greater transparency of the diaphyses and chemical analysis shows diminished amount of inorganic principles.

The completion of this process explains the frequent fragility of these bones.

Glands of internal secretion. The products of the digestive tract injected into animals also act on the other glands of internal secretion; the *genital organs*, the *thyroid*, *parathyroids and suprarenal capsules*.

The histological study of the ovaries, thyroid and suprarenals has brought to light different deteriorations.

The most curious peculiarity offered by the examination of the utero-ovarian organs, relates to the absence of evolution in the Graffian follicles; this abnormality compromises fecundation.

The other glands show signs of karyolysis, degenerative changes, sometimes vacuolar, exceptionally fatty.

While on this subject, it is interesting to recall that in athrepsics in whom the plasma contains poisons, which have escaped the diligence of the altered digestive mucosa, analogous changes are noted.

In more than one case the *capsular extracts* of these athrepsics, the offspring of toxic mothers, does not provoke any appreciable rise in pressure, and their *thyroid principles*, almost devoid of iodine, are powerless to bring about any sensible emaciation, showing that both their constitution and function are impaired.

METABOLISM

All these facts concur to teach us that the organs most apt at governing the intimate cellular mutations, are subject to the action of the intestinal contents.

Hence it is not difficult to foresee that in animals intoxicated by these matters, the secretions, which are what these cellular mutations make them, must present defects.

Development. In a first series of experiments, *Charrin* administered matters taken from the ileus to young rabbits four to six weeks old; these animals lived under conditions

identical with those of the control rabbits taken from the same litter. At the end of from five to seven months, the weight of the control animals exceeded 1,400 grams, while that of the treated subjects ranged in the neighborhood of 420 grams. The introduction of intestinal compounds is therefore accompanied by lack of development.

Dwarfism. *Definite arrest of development, true dwarfism* has been noted.

It is interesting to recall that *Charrin* and *Gley*, by inoculating males and particularly females with intestinal toxins, obtained analogous taints in the offspring. Experimentation can thus reproduce insufficiency of evolution, and the realization of this condition coincides with clinical observations.

We know, as *Variot*[1] recently pointed out, that among the affections of the newborn, those which permit the contents of the ileus to pass easily into the tissues—gastroenteritis, for example—are often accompanied by pronounced atrophies.

Animals injected with intestinal products present, as we have seen, alterations in the thyroid, the genital organs, the suprarenals, and the bone marrow, all of which exercise an influence in the maintenance of the metabolic equilibrium, or of the circulation, and which also act upon the development, although this is not their exclusive function. If, in fact, certain anatomical elements take a more direct part in development, we are none the less justified in considering the progressive evolution of the economy as resulting from the united functions of the cells.

The poisons extracted from the digestive tube appear to make an impression on nearly all of the organic cells, so that these poisoned cells no longer elaborate but languidly and feebly in the same manner that workmen weakened by alcohol or other toxins, perform their allotted task with less activity.

FEVER

Frequently in injected animals the temperature falls. And yet *Cardamatis* found that in the contents of the ileus pyretogenic elements existed.

[1] Variot: Sem. Med. 1904. p. 333.

But it is true that variations in the doses or the avenue of entrance are apt to bring about contrary thermic fluctuations. A small quantity of toxins excites the cells and provokes in the metabolism an excessive generation of heat; the contrary takes place with a large quantity, which, by depressing cell activity, restrains their elaboration.

When the same quantities of toxins are introduced, first, under the skin, next, in the peritoneum, or in the blood, the thermometric rise is frequently followed in the last two cases by thermometric fall. This explains quite well the great variations in temperature observed in the auto-intoxicated.

II. SECONDARY ALTERATIONS

We can see what a series of abnormalities the intestinal poisons may give rise to, yet the evil effects are not limited to their direct action. We must take into account the return shock, the secondary reaction of the existing lesions and the resulting functional disorders.

ANTITOXIC GLANDS

In its struggle with the intestinal poisons, the organism naturally brings into play all the means of defense that we have mentioned; defenses which themselves must suffer from excess of work. The defensive system attenuates and neutralizes the deleterious matters, and it is without doubt due to these successive operations, pursued when in contact with these poisons, that we owe the well-defined alterations described when speaking of the liver, the thyroid, parathyroids, suprarenals, pituitary body, etc.

EMUNCTORIES

To further protect itself, the economy does not neglect its channels of elimination.

Kidneys. In acute intestinal intoxications, an increase in the urinary toxicity signifies that the harmful substances are escaping through the renal emunctory.

Irritated by their passage, the kidneys become flabby and pale; the Malpighian capsules desquamate; the tubular epithelium

becomes irregular and granular. The gland and its filter are involved and nephritis is created.

Urine. *Charrin* was able to observe indicanuria, albuminuria, and cylindruria; it may also contain hemoglobin.

The extractive matters are relatively abundant; the proportion of ureic nitrogen to the total nitrogen is defective, and the cyroscopic point tends away from 0.

These findings, which easily explain the relation existing between digestive defects and the retardation of nutrition, also enable us to foretell an increase in the urinary toxicity, which examination verifies. As to the chlorides, their proportion is lessened; besides, according to their retention or elimination, these substances at times play the part of an aspirating pump, at others a compressing one. But while exact from some points of view, this comparison is nevertheless a lame one, for far from being inert dialysers, the membranes traversed by these osmotic fluxes intervene through their own vitality; the water carried along by these mineral salts, holds in solution numerous principles, which are eliminated under the influence of the current which they provoke.

The skin. Some of the substances of digestive origin, the fatty acids, the salts and urea are excreted by the skin, which in *Charrin's* experimental animals was dry, and covered with lusterless and ill-kempt hair.

The outbreaks of erythema, urticaria and eczema during the course of botulismus, are evidence of the functional relations between the skin and the intestinal mucosa. In traversing the derma and the glands, the abnormal principles create spots of less resistance, which are promptly invaded by the micro-organisms of the skin. According to *Calsé*, the impression of these principles upon the cutaneous nerves is the cause of the vasomotor œdemas (angio neurotic œdemas, etc.).

Respiratory mucosa. The volatile products of the digestive canal are partly eliminated by the broncho-pulmonary channels.

Some physiologists contend that in the normal state no toxic element is eliminated through these channels. Such was not the opinion of *Brown Sequard* or *d'Arsonval*, nor of *Schiff*, who demonstrated the excretion of ammonia and acetone in normal

respiration. At all events in the field of pathology, certain substances are eliminated through the respiratory tract as observed in diabetic coma, and *Charrin* moreover proved that the water of condensation from the expirations of tubercular individuals contained pyretogenic elements.

Intestinal mucosa. A law which, according to *Charrin*, might be termed the law of auto-function exacts that the matters derived from the action of a determined organ, should themselves activate its functions. Thus urine is diuretic; thyroid extract activates its exchanges, the saliva, gastric juice, and intestinal secretions give analogous results.

Consequently, in animals *injected subcutaneously* with intestinal contents, it is not surprising to find a manifest hyperæmia in the digestive mucosa as well as the inception of nuclear kariolysis, and an exaggerated secretion. The intestine, therefore, in its struggle against the morbid materials which it contains, is both an eliminating and antitoxic apparatus.

This explains to us the gastric and intestinal crises so frequently observed in the gastrointestinal auto-intoxication of man.

Such is the *résumé* of the beautiful researches of *Charrin* and his pupils in the field of experimental auto-intoxication, an admirable work, which has elucidated many obscure points in the symptomology of auto-intoxication.

CAUSES OF INTESTINAL AUTO-INTOXICATION

For *Bouchard* the sole cause of intestinal auto-intoxication —at least in the majority of cases—was dilatation of the stomach.

We now know how variable the significance of this syndrome is, and of how little importance this cause is, in the etiology of intestinal auto-intoxication. There exists not one, but very numerous causes and these may be divided into two groups.

A. Causes which lead to excessive formation of intestinal poisons or enterotoxins.

B. Causes which produce a diminution in the destruction of the enterotoxins.

CAUSES LEADING TO EXCESSIVE FORMATION OF ENTEROTOXINS

This first group comprises a series of hygienic faults, functional disorders, lesions, abnormalities, and diseases, all of which augment and favor by varying means, the putrefaction of nitrogenous matters in the large intestine. All these causes —so numerous and varied—develop the vitality of the intestinal micro-organisms increase their toxic products and favor auto-intoxication.

This form is therefore of microbic origin and may be termed the **microbic gastrointestinal auto-intoxication.**

CAUSES PRODUCING DIMINUTION IN THE DESTRUCTION OF THE ENTEROTOXINS

In the second group we shall include all the functional troubles, all the lesions and diseases localized in the organs which protect the economy against the intestine.

All these causes, which may be grouped under the denomination of *organic antitoxic insufficiency* diminish, attenuate or prevent the modification or destruction of the poisons formed in the intestine.

This form is therefore of organic origin and may be termed the **organic gastrointestinal auto-intoxication.**

I. CAUSES AUGMENTING THE PRODUCTION OF INTESTINAL POISONS

DYSPEPSIA

Among the numerous causes belonging to this category, one of the most important is dyspepsia, which is an affection brought about by a disproportion between the aliments and the digestive juices.

If the aliments are given in too great quantity or badly selected, there will remain even with normal digestive ability, an alimentary residue which will become the prey of the bacteria, and will give rise to an exaggerated proportion of enterotoxins.

To this division belong the alimentary dyspepsias.

But even when the diet is rationally measured and selected, dyspepsia and auto-intoxication may exist if the digestive juices are deficient.

To this division belong the organic dyspepsias.

Finally we may have at the same time both an insufficiency of the digestive juices and a deleterious alimentation.

To this division belong the mixed dyspepsias, which more than the other two forms, easily and rapidly lead to digestive auto-intoxication.

A. Alimentary Dyspepsia

The foods may be well selected, that is, proportioned to the digestive juices of the individual, but they may be taken in too large quantities; this results in *quantitative alimentary dyspepsia.*

Or else the quantity may be normal, but badly selected and not correspond to the digestive capacity; this *results in qualitative alimentary dyspepsia.*

Quantitative alimentary dyspepsia. This condition, like the others, may occur as well in the intestine as in the stomach. For many authors, at least half of all cases of dyspepsia are of intestinal origin; this proportion in our opinion is not exaggerated and an attentive observation of dyspeptics easily demonstrates it.

Besides, in many cases and particularly in children it is very difficult to separate clinically gastric from intestinal dyspepsia.

Too frequent and too copious meals. We at times see infants fed at the breast or solely with sterilized milk, present symptoms of auto-intoxication, pallor and loss of weight preceding the digestive troubles by several days, and which, in consequence, can only be explained by the auto-intoxication.

A little closer investigation will show that the child is overfed, either because he takes too much at each feeding or else because he is fed too frequently.

Too frequent meals or too copious meals have the same result; that of provoking dyspepsia. A part of the milk is not digested or only imperfectly and becomes pabulum for bacteria. It is the same with older children, who are overfed with a varied, but much too abundant diet.

Too rich food. All individuals, whether children or adults, who for one reason or another, take nitrogenous foods in excess (meats, eggs, etc.), will end by suffering from dyspepsia with auto-intoxication.

We can include in this category many cases of feeble and anæmic children, complaining adolescents, and convalescent adults to whom raw and underdone meats have been given in the hope of strengthening them and the use of which was soon interrupted by evidences of intestinal auto-intoxication.

We may also include, much too large, a number of phthisical subjects, who, in various sanatoria, have been subjected to overalimentation (twelve to fifteen eggs per day, with large excess of meats, etc.), a diet not compatible with the organic dyspepsia inherent to their tubercular condition, and which they are compelled to stop because of the undeniable symptoms of auto-intoxication. The abuse of meats and eggs observed among certain peoples, and in certain cities, especially when it is not

tempered by the use of farinaceous articles, leads to a disproportion between the quantity of nitrogen ingested and that digested and assimilated.

In consequence, a residue of undigested proteids remains in the intestine, and forms there an alkaline culture bouillon extremely favorable to the growth of the anaerobies of putrefaction. Hence quantitative nitrogenous dyspepsia powerfully favors intestinal putrefaction, and leads in the first place to digestive auto-intoxication and should the resistance of the mucosa of the colon be at fault (arthritism) to mucoid and membranous enteritis and appendicitis, which, as we will see, still further increase and multiply the causes of auto-intoxication.

Too copious and too frequent meals, meals too rich in proteids, all lead to digestive auto-intoxication.

Qualitative Alimentary Dyspepsia

The food may be:

(*a*) Of a quality badly adapted to the digestive ability.

(*b*) Of inferior quality and capable of modifying the digestive ability.

Food badly adapted to the digestive ability. To introduce in the digestive tract nourishment which is not suited to it and which can only be partly digested, necessarily leads to qualitative dyspepsia and digestive auto-intoxication. If the newborn is suckled by a nurse with old milk, or if an infant be given farinaceous food during the first weeks of its life, or a child takes bouillon, meat juice, etc.; if an adult indulges in heavy and irritating food; we shall have aliments ill-proportioned to the digestive power; hence dyspepsia and auto-intoxication. In the first two cases, it is true, there are produced fermentations of ternary substances ending in acid products.

In the last case, it is rather a nitrogenous putrefaction which results, but it is none the less true that in all there will be digestive auto-intoxication.

Aliments of bad quality. In the first place the ingested food, without being bad, may contain, owing to its chemical nature, toxins, volatile or fixed essences, irritating matters, which, instead of favoring the normal secretion of the digestive juices

as normal food does, check it, at the same time paralyzing the protection of the intestinal mucosa.

In the second place, the aliments, while not decomposed, may not be absolutely fresh and wholesome, they may be slightly fermented or susceptible of fermenting too easily; the products of this fermentation will at the same time hinder the secretions and the intestinal defenses.

In both cases we shall have an undigested residue accompanied by an exaggerated putrefaction, exceeding the normal antitoxic power of the digestive canal, and which will lead to auto-intoxication.

Thus, milk coming from a nurse whose psychic state is abnormal (irritable, nervous over sexual indulgence), whose physical condition is bad (drink, poverty, menstruation or pregnancy), presents a chemical composition which renders it less digestible and more easily fermentable.

Milk coming from cows fed with green fodder, vine leaves, oil cake, distillery grains, etc., contains toxins, acids, and has deleterious properties.

What we have said of milk applies to all other foods, which, while not sufficiently altered to be alimentary poisons, are still sufficiently modified to be easily fermented, and irritating and to cause digestive auto-intoxication.

The strong heat of summer, which can create this condition in food, may also increase the fermentation in the digestive canal itself, and thus be an indirect cause of intoxication.

B. ORGANIC DYSPEPSIA

Even with normal alimentation, and with regular meals, not too rich; even with foods hygienically selected as to quality and source, dyspepsia may occur if the secretion of the digestive juices is insufficient. *In such cases we have to deal with organic dyspepsia.*

The *insufficiency of the digestive juices may be congenital.* It is observed in premature births, in certain children whose parents have themselves suffered from digestive troubles; in children of mothers suffering from auto-intoxication or toxæmia during pregnancy, etc.

The insufficiency of the digestive juices may be acquired. It is observed in acute toxæmia, in all the febrile and infectious diseases, but in these conditions it is transient.

It is especially observed in the chronic toxæmias, syphilis, chronic malaria and particularly in tuberculosis.

It occurs in all the cachexias, whether these result from chronic toxæmia or from slow demineralization (the anæmias, rhachitis, myxœdema, diabetes, etc.).

It is observed in certain nervous diseases, cerebral tumors, meningitis, tabes, etc., and in the diseases of the digestive canal itself, chronic gastric catarrh, spasmodic or organic strictures of the pylorus with gastric dilatation, etc.; finally it is observed in the chronic catarrhs of the intestine in muco membranous enteritis, colitis, etc., diseases, which we will have occasion to speak of later on, for they also lead directly to auto-intoxication. In all of these cases, even with normal alimentation, there remains an undigested residue, attacked by bacteria and resulting in auto-intoxication.

STASIS OF THE CONTENTS OF THE DIGESTIVE CANAL

Among the secondary causes, this is certainly the most important. It is a well-known fact found throughout the entire organism, that wherever fermentable stagnant matters and microbes exist, fermentation takes place. It is observed in bronchial dilatation, in the kidneys, in the bladder, but particularly in the alimentary tract for in it, all the causes of putrefaction are reunited.

We find in it extremely putrefactive matters, especially in the large intestine, proteolytic anaerobies, an alkaline reaction, temperature and humidity favorable to their growth; in other words, all the conditions necessary to exaggerated putrefaction and increased microbic virulency.

When stasis still further exaggerates these conditions, particularly when it contributes to paralyze the organic defenses; then auto-intoxication is realized and established. It must be said, however, that stasis *per se* is not sufficient, as the atonic

constipation of the lower bowel proves; for here the dryness of the contents comes into play and prevents microbic action.

Whenever, on the contrary, the atonic constipation occurs in the upper portions of the intestine, in which dryness of the contents does not take place, the conditions favorable to infection are created and auto-intoxication is produced.

A. GASTRIC STASIS

Every stomach that does not empty itself, favors the abnormal fermentation of its chyme.

What is most serious in dilatation of the stomach is not its size, as *Bouchard* taught, for that is a mere symptom; what is important, is the cause of the dilatation, that is, the impermeability of the pylorus. As soon as the pylorus becomes less permeable the circulation of the chyme becomes difficult; it stagnates, ferments, putrefies, and its products mixing with the chyle infect the intestine. In consequence, pyloric stenosis is very frequently accompanied by digestive intoxication.

Tripier, *Soupault*, *Foucaud* and particularly *Jouaust*, in his excellent thesis, insist upon these facts and with reason; we, ourselves, could adduce many examples.

Stenosis of the pylorus. Whether produced by cicatrization of a round ulcer, by cancerous growth involving the pylorus or the prepyloric portion or by a plastic exudate as I observed in one case, is accompanied by an auto-intoxication with chronic enteritis—glairy or muco membranous—which frequently engages all the attention of the attending physician, to the detriment of the primary cause which remains ignored.

Spasmodic contraction of the pylorus frequently accompanies prepyloric ulcerations (*Soupault*); pyloric spasm of nervous origin when it has lasted sufficiently long to produce secondary hypertrophy of its muscle, hence narrowing; the pyloric spasm of hyperchlorhydria, the pyloric spasm so often observed in gastric ptosis.

All of these bring about gastric retrodilatation with hypersecretion of acid, and through stasis fermentation of the chyme; when the latter has existed long enough, it provokes in the

large intestine the phenomena of putrefaction that cause auto-intoxication.

With *Soupault*[1] and others, we have seen many cases in which treatment of the stomach—in grave cases, gastro enterostomy—by relieving the stasis sufficed to cure the chronic enteritis and auto-intoxication produced by it.

B. INTESTINAL STASIS

Intestinal stasis produces the same effects and through the same causes, only in a more frequent and more intense manner.

Enteroptosis or Glenard's disease. This condition plays a most important part.

Is the eminent physician of Vichy right in considering enteroptosis primary and putrefaction as secondary to it, or must we, like *Lyon*, *Langenhagen*, etc., look upon it as a consequence of enteritis?

We cannot follow here the different authors who have discussed the question, nor cite all the reasons which *Glenard* in his works, or *Monteuuis*[2] in his interesting book have advanced to defend their position. For our part we are persuaded that *Glenard* is right, and that enteroptosis is primary and may cause auto-intoxication, owing to the increased intestinal putrefaction which it brings about; but we think he has generalized too much, by looking upon it, if not as the sole cause, at least as the principal factor in auto-intoxication.

Enteroptosis is primary, for it very frequently exists in the child even in the suckling; the big relaxed bellies of *Marfan* are eventrated, over-distended, and flabby with complete disappearance of muscular support. In older children, we can easily follow these cases step by step, both in the clinic and at autopsies and note the descent of the stomach, the intestine, and sometimes even that of the kidney, and yet the intestinal mucosa remains absolutely normal. Without doubt, many children escape the consequences of this loss of abdominal equilibrium, because—and here we differ with *Glenard—they are stout and*

[1] Soupault, Hartmann, Linossier: Traité des maladies de l'estomac. Paris. 1906.

[2] Monteuuis: Les déséquilibrés du ventre. Paris.

fat, and the layer of fat with which they are provided, prevents by its support the full effects of the ptosis.

But should these children become emaciated later on, either through accidental causes or through the influence of tuberculosis la grippe, or other disease, or in adults, because of pregnancy which still further increases abdominal relaxation, then the dislocations of the viscera will manifest their influence, and the conditions of auto-intoxication will be created.

The vicious position of the intestine, its arrangement into *transverse festoons*, its flexures, notably those of the colon, predispose to coprostasis and this, by realizing all the conditions necessary to increased intestinal putrefaction, easily determines not only intestinal auto-intoxication, but infection of the mucosa and the consecutive enterocolitis. May not primary enteritis owing to the emaciation and relaxation of the organs bring about a secondary enteroptosis with the ensuing intoxication? This is very probable, but we have never observed it.

Constipation is the most typical example of intestinal stasis, and suffices to produce the phenomena of putrefaction; but these are not severe when the rectum alone is involved, because of the dryness of the matters, nor in spasmodic constipation, because of the diminution in the number of bacteria.

But whenever stasis is produced in the higher portions of the bowel, the phenomena of putrefaction increase and auto-intoxication manifests itself.

This explains why, in those cases of constipation occurring in adults, even in children, with periods of ten, fifteen or more days between stools, the phenomena of putrefaction are almost nil; whereas partial stasis in the cæcum or ascending colon is sufficient to bring about an intense auto-intoxication.

Intestinal motor insufficiency. Motor insufficiency, such as we find in anæmics, and cachectics; in the paralyses with dilatation of athrepsics and atrophics; in the lengthening of the intestine described by *Marfan* in chronic catarrh; in the spasms of enteritis or the dragging of an adherent intestine; all these causes of intestinal stasis lead to auto-intoxication.

Dilatations of the colon. Spasm or stricture of the colon with the consecutive dilatation accompanying it, plays an important

part in the causation of intestinal stasis and the consequent auto-intoxication. I have, for a long time, both in my lectures and publications, called attention to, and described the dilatations occurring in the cæcum and ascending colon as the most frequent, and that of the transverse colon as the rarest.

What should be remembered, is that, from the pathogenic standpoint the dilatation of the colon by itself, is not important; **only the cause of it is of real importance,** and this may be spasmodic, or due to stricture or an acute flexure of that part of the colon situated below the dilatation. Spasm of the colon, as we have seen, is most frequently symptomatic of acute or subacute inflammation, but it is also at times a sign of irritation from shock (nephroptosis) or of malposition (gastroptosis with festooned colon), or of dragging by uterine deviations, etc., adhesions, bridles.

All of these causes: spasm of the colon as well as bridles (*Quénu*), localized strictures as well as acute flexures (*Terrier*), bring about dilatation above the point of obstruction.

The stagnation of matters occurring in the dilated part or pocket is accompanied by pronounced putrefactive phenomena and symptoms of intoxication, all the more grave, because of the destruction of the first line of defense by the inflammation of the dilated walls.

My description of the symptoms of dilatation of the colon before the pædiatric society of Paris in 1900, is as follows: The complexion becomes pale, then yellowish and cachectic, the skin is dry, the hands cold and moist.

Rapid emaciation gives the sufferer a cancerous aspect. He complains of dizziness, headaches, neuralgias, and rheumatic pains in the extremities. He is in a state of nervous depression and neurasthenia. The breath becomes fetid and attacks of migraine with vomiting supervene; obstinate constipation alternating with foul ill-smelling fecal discharges occur and these relieve the sufferer temporarily.

Finally he complains of attacks of pain on the right side, and there upon examination we find the cæcum thickened, movable, greatly distended, and with perceptible splashing sounds. In many cases it is sufficient to recognize the cause and remedy it,

in order to see the symptoms become modified with surprising rapidity and without having recourse to (cæcoplicature) as *Delbet*[1] proposed.

Since then certain authors have taken up this question. *Terrier*[2], upon dilatation of the transverse colon from exaggerated flexure; *Alglave*[3], upon dilatation of the cæcum from spasm of the ascending colon following nephroptosis; *Robin*[4], dilatations of the colon from spasm, etc. The following is the excellent description of this condition given by *Delbet*:

A description which corresponds exactly with symptoms that I have very frequently observed. This eminent surgeon gives to this condition the denomination of *ptosic typhilitis*, which does not appear very exact since we may see cæcal dilatations without typhilitis, but with ptosis, others without ptosis, but with typhilitis; finally some (but very rarely), without either ptosis or typhilitis. The denomination *dilatation of the cæcum*, it seems to us, corresponds to all cases and providing that it is remembered that this name only designates (as for the stomach) a symptom resulting from very different causes, it will mislead no one.

"There exists," says *Delbet*, "a numerous category of patients, who complain of feeling painful sensations in the region of the cæcum.

"The pains are sometimes frankly intermittent; ordinarily they are dull and constant, but are subject to exacerbations by crises, which may recur two or three times a day after meals, in the more severe cases; one or two times a month in the less severe; in women these crises often precede menstruation. The pains are not accompanied by any general symptoms; the pulse and temperature remain constantly normal.

"Vomiting may exist, but it is purely reflex and caused by the painful attacks, in the same manner that vomiting takes place in hepatic or nephritic colic. The vomiting occurs all the more easily, as these patients are generally dyspeptics.

"Constipation is the rule. The bad digestion and pains end

[1] Pierre Delbet: Sem. med. 1905. p. 553.
[2] Terrier: Sem. Med. 1902. p. 142.
[3] Alglave: Revue de chir. Dec., 1904.
[4] Robin: Gazette des Hôpitaux, 1901. p. 995.

by causing emaciation, with physical and mental debility, also creating a state of nervous depression, of neurasthenia, which often causes these subjects to be looked upon as neuropathic.

"Locally, there is found a certain amount of bulging of the abdominal wall over the region of the cæcum. In some cases percussion enables us to recognize that the bulging corresponds exactly to the limits of the cæcum. In all this region the skin is hyperæsthetic; stroking or slight pinching is acutely felt, whereas the pricking of the skin is sometimes not perceived.

"The analgesia and tactile hyperæsthesia are due to the same cause, the chronic inflammation of the abdominal wall, which provokes congestion of the nerve trunks and a certain amount of œdema or infiltration at the level of the tactile terminations. On palpation we can feel the cæcum distended by its contents, or else by gas, if a preliminary catharsis or irrigation has evacuated the intestine. Superficial palpation by displacing the gas produces a sort of crepitation like that of crunching snow; while on deep palpation a sort of cord or rather pad about one centimeter in thickness and eight to ten centimeters in length, may be felt.

"This last sensation, to be appreciated, must be sought. To that end the surgeon should stand at the right side of the patient and apply next to and a little to the outside of the umbilicus, the four fingers of each hand placed side by side, then, by slightly flexing the finger tips, slowly depress the abdominal wall so as to bring it in contact with the more resistant plane of the iliac fossa; this maneuver is rendered easy by the relaxed condition of the abdominal parietes in this class of cases.

"If then the fingers are slowly carried outward, without bending them and kept in contact with the deeper plane, we shall soon feel this pad-like body; its appreciation begins at the union of the middle third, and the third, external to the spino-umbilical line, a little above and to the outside of *MacBurney's* point. The pressure exercised by the examining fingers upon this pad is painful.

"What the surgeon feels in this exploration is the paralyzed wall of the distended cæcum rolling upon itself under the fingers, and not the appendix as so many believe."

Chronic intestinal obstructions. The chronic intestinal obstructions, no matter what their cause may be, *whether due to a diminution* of the intestinal caliber by cicatrices, stricture, tumors of its wall, or else *to compression of the canal* by ganglions, tumors, cysts, adhesions, bridles, etc., finally to chronic invagination, are all accompanied by intense auto-intoxication. These causes realize to an even greater degree the dangers of intestinal stasis in the upper parts, and they paralyze the intestinal means of defense as well.

Hence the phenomena of intestinal putrefaction are constant in these cases, and the symptoms of auto-intoxication predominate, frequently so much so as to mask the primary cause of the disease. Its recognition is therefore important, if we wish to avoid error in diagnosis and the prolongation to the patient of sufferings most prejudicial to his health.

Diseases of the Intestinal Walls

In all the diseases of the digestive tract we observe on the one hand, an increase in the phenomena of putrefaction, on the other, a diminution in the defenses of the organism; both of which contribute to produce and augment intestinal auto-intoxication.

It is therefore not surprising to see acute and chronic intestinal catarrh, and particularly the acute glairy and dysenteric forms accompanied by a high degree of putrefactive phenomena. The same may be said of the glandular and mucosa atrophy which characterizes athrepsia. These affections, it is true, often eliminate by diarrhea the greater portion of the putrefactive materials, and in that manner greatly lessen the symptoms of auto-intoxication. But whenever constipation predominates, as it does in the chronic forms, the symptoms become accentuated.

Among the chronic forms, two deserve particular mention namely chronic glairy and muco-membranous enteritis and chronic appendicitis.

Chronic Appendicitis

The infectious nature of chronic appendicitis is universally admitted, and there is no difficulty in understanding why this

condition is accompanied by symptoms of digestive auto-intoxication.

Chronic Glairy and Muco-membranous Enteritis

We have demonstrated[1] that, contrary to common opinion, these affections are also infectious and this we have proved clinically, by pathological anatomy, by the etiology and finally by the undeniable contagiousness of the disease.

This infection of the intestinal mucosa is accompanied and sometimes preceded by a frequently enormous increase of the nitrogenous putrefaction in the colon, and by a very evident diminution in the defenses of the first line; this explains the very marked symptoms of auto-intoxication from which these cases suffer; symptoms which many authors declare to be of nervous origin. Only lately *van Embden* supported this idea, basing himself on a very interesting study of the eosinophiles, that are ordinarily found in the stools of muco-membranous enteritis.

After showing that eosinophilic cells are met with in variable abundance in the intestinal contents of *subjects suffering from the most diverse affections* (*helminthiasis, acute and subacute intestinal catarrh, chronic constipation after administration of senna, etc.*), hence taking away any diagnostic value their presence may have had (*Combe*), *van Embden* observes that they are also frequently found in *mucus colitis* and *pseudo membranous colitis;* basing himself upon these facts, he establishes between this variety of colitis and nervous asthma an interesting connection worthy of mention.

"In nervous asthma we also find eosinophilic leucocytes which are really mononuclears.

"There exists," *van Embden* adds, "other points of relation between these two affections; both begin with crises, and are accompanied by painful spasmodic phenomena. They attack nervous subjects; they are brought on by the influence of emotions or by slight irritating causes and end with the expulsion of special secretory products; we may presume," he concludes, "that these two affections originate from some nervous trouble yet unknown."

[1] Combe: Traitement de l'entérite muco membraneuse. 1906.

This reasoning does not alter our view.

We have, it is true, like *van Embden*, often found eosinophiles in the stools of chronic enteritis.

But we also find them, and in much greater abundance, in glairy and blennorrhagic enteritis, but no one will conclude from that, that these affections are of nervous origin.

The inference is that the presence of eosinophiles is far from being a criterion of the nervous character of the affections of the mucosa.

While, on the contrary, the great putrefaction present with chronic enteritis, and which is characterized by the large increase in the sulphoethers and aromatic substances of the urine, readily explains the nervous symptoms as well as the digestive auto-intoxication.

DISEASES OF THE NOSE AND THROAT

We cannot finish this chapter without mentioning certain *diseases of the nose and throat* that augment the production of intestinal putrefaction. Among the diseases of the nose, chronic nasal catarrh, ozœna, and specially unrecognized sinusitis.

In the throat adenoids, and hypertrophy of the tonsilar crypts.

In all these diseases, there occurs during sleep, when the stomach is empty and contains no hydrochloric acid, a constant deglutition of purulent matters filled with more or less virulent bacteria.

This continual source of infection, and particularly of intoxication, is certainly worthy of being appreciated and recognized for it is frequently the key to many therapeutic failures, and furnishes a valuable indication for treatment preliminary to that of the intestine.

INTESTINAL PARASITES

We know how frequently the parasitic nematodes are found in the intestinal canal of children.

The lumbricoids, oxyuris, and the tricocephalus introduced into the body through impure water, unwashed vegetables, and fruits.

The tænias and the bothriocephalus are less frequent, but in no wise unexceptional.

The nematodes have an intestinal content gorged with more or less virulent microbes, all secreting toxic substances; many of these parasites can injure the intestinal walls, even imbed themselves in it, like the trichocephalus which is the most common denizen of the cæcum and appendix.

They may bring about congestions, secretory modifications and exalt the microbic virulence, thus increasing intestinal putrefaction.

When dead, they may become the seat of intense putrefaction. The parasitical symbiosis may cause therefore (exceptionally, it is true), marked auto-intoxication which will most frequently pass unperceived.

It is largely a question of degree and of idiosyncrasy, for these bodies while inoffensive to most may be gravely felt by others. Again, given the frequency of these parasites (48 per 100 in Switzerland, according to the investigations of one of my pupils[1], and the relative rarity of symptoms of parasitical auto-intoxication, we should not exaggerate their importance in the genesis of intoxication.

II. CAUSES DIMINISHING THE DESTRUCTION OF ENTEROTOXINS

We may here distinguish general and local causes.

The first act upon the general defenses (phagocytosis and the formation of alexins).

The second are due to the insufficiency of the local means of defense; that is to say, the antitoxic organs disposed in quadruple line of defense around the intestine.

A. Causes Diminishing the Defenses of the Organism

We have long known that certain diseases, such as measles, grippe, etc., provoke secondary infections; they, in fact, determine rheumatic pains and favor tubercular tendencies; they augment intestinal decomposition and thus predispose to enteritis and appendicitis.

[1] Golosmanoff: Thèse de Lausanne. 1904.

Marvel[1], *Faisans*, and *Lucas-Championnière* insist upon the great influence the epidemics of influenza have had upon the increase of intestinal infections, noted in recent years and characterized by the various forms of enteritis and appendicitis.

We have been able to demonstrate from previous studies of the blood[2] that these two diseases are accompanied during the febrile period by *a considerable degree of polynuclear hypoleucocytosis*. In consequence, in measles and influenza, there exists a short period (three to eight days, during which the principal defense of the organism by phagocytosis is extremely reduced. Therefore the bacteria present in the body (rheumatism, tuberculosis), in the exterior cavities (nose, ears, etc.), or in the intestine, may multiply without hindrance and produce secondary infections.

The frequency of intestinal auto-intoxication in measles and influenza, the evident influence which these two diseases exercise in the causation of acute outbreaks in chronic enterocolitis, is thus easily explained.

B. CAUSES DIMINISHING THE ACTIVITY OF THE ANTITOXIC ORGANS

These causes are of the greatest importance, in fact, they are probably the most important of the factors in intestinal auto-intoxication.

As we have already studied in detail all of the means of defense and all the antitoxic organs, we may be brief. We have seen that they have to combat the phenomena of intestinal putrefaction, that they limit the absorption of its products, and that they modify these, so as to render them less harmful when absorbed, and finally that it is their office to eliminate them through the different emunctories of the body.

Whatever interferes with their action, whatever limits the functions of these organs and renders them insufficient, provokes or increases digestive auto-intoxication.

[1] Marvel: Am. Med. Assoc., 1903.
[2] Combe: Arch. de med. de l'enfance. 1899. p. 345.

CAUSES WHICH RETARD OR LIMIT THE TOXICOLYTIC POWER OF THE INTESTINAL MUCOUS MEMBRANE

Inflammatory swelling, such as observed in enteritis; the atrophy found in athrepsia; the presence of a coating of mucus and membranes on the mucosa, as noted in chronic muco and membranous enteritis; all of these causes by paralyzing the powerful toxicolytic functions of the mucous membrane, favor auto-intoxication.

All local or general diseases, that alter or diminish the action of the intestinal juices (gastric juice, bile, pancreatic), increase intestinal decomposition.

For, on one side, as we have seen, the insufficiency of these juices leaves a larger alimentary residue for the bacteria to prey upon; on the other side, it deprives the intestine of their important antiseptic action.

CAUSES WHICH LIMIT THE TOXICOLYTIC POWER OF THE LIVER

The second line of defense is constituted by the liver, the importance of which, from this standpoint, has already been described.

Causes of Hepatic Insufficiency

I. Congenital Insufficiency of the Mother

The intoxications (alcoholism, saturnism, etc.), as well as the toxinemias (tuberculosis, syphilis, typhoid, influenza, pneumonia, rheumatism, etc.), occurring in the mother during pregnancy, exercise a considerable influence on the functional integrity of the liver in the offspring.

Whether this is due to inherited cellular morbidity, or else to an infectious or toxic process, acting directly upon the hepatic cells through the placenta, the barriers of which the bacteria at times and the toxins always surmount; or whether it is an auto-intoxication of the newborn itself or else results from these united causes, is difficult to say. One fact remains, and that is the influence of the mother's diseases during pregnancy in the etiology of congenital hepatic insufficiency; this we have on many occasions clinically verified.

II. Acquired Insufficiency

1st. Auto-intoxication. Pregnancy: Poisons augment in the economy of the pregnant woman.

This is due to the greater toxicity of the oxidized products, to the decreased intestinal excretion, and to the diminished permeability of the kidneys. Finally, because pigmentation of the skin is less favorable to elimination. In consequence the liver, surcharged with fat and glycogen, becomes insufficient.

Splenic Anæmia, by conveying blood pigment in exaggerated quantities to the liver may render it insufficient from excess of work.

Intestinal auto-intoxication. The excess of enterotoxins, by fatiguing the hepatic cells and irritating its blood-vessels, gradually brings about insufficiency and engenders a vicious circle, which we very often notice in the dyspepsia of children.

2d. Intoxications. Alcohol and lead, like many other poisons, by altering the hepatic cells, paralyze their toxicolytic functions.

3d. Toxinemias. The same may be said of the toxæmias caused by infectious diseases, should their duration be prolonged.

4th. Parasites. *Ecchinococci* may, in exceptional cases, alter the hepatic parenchyma and render it insufficient.

5th. Diseases of the liver. Degenerations and multiple tumors of the liver are themselves accompanied by secondary changes in the hepatic cells, which, by limiting their function, render the organ insufficient.

Finally the liver may become incompetent owing to various forms of hepatitis and cirrhoses; all of these diseases exercise a harmful action on its powerful toxicolytic function and favor the consequent digestive auto-intoxication.

Causes Which Limit the Antitoxic Power of the Glands of Internal Secretion

The glands of internal secretion, veritable antitoxic organs, may also become altered, and by their insufficiency contribute to intestinal auto-intoxication.

Causes Which Limit the Eliminative Powers of the Emunctories

Lastly, the great emunctories, the skin and the kidneys, may become diseased and incompetent. Here again we will observe a series of symptoms, which, on ultimate analysis, will be found related to digestive auto-intoxication.

PATHOLOGICAL PHYSIOLOGY

The disorders due to auto-intoxication are frequent at all ages, but it is particularly in children that they have been most carefully studied.

During the last few years, several physicians have made it a special study, and we could only repeat what they have written, so much do their findings agree with ours. *Sevestre*, the eminent physician of the hospital *des Enfants malades*, a few years ago, wrote:

"It is not unusual to observe in childhood a series of morbid phenomena rather alarming in appearance, so much so as to make one fear the development of some grave condition (meningitis and cardiac affection), but which are far from having such a serious outlook.

"These accidents are rather variable in their manifestations, but in general they are characterized by a more or less intense headache, awakened or increased by mental effort; by an anæmic state, general lassitude and fatigue; at other times, they are characterized by outbreaks of fever or palpitations, finally by nervous troubles.

"These facts are already known, but perhaps not sufficiently so, for I have often seen well-informed physicians commit serious errors in this respect, as to the diagnosis and prognosis.

"In fact, it seems necessary to me, to insist, more than is done, upon the digestive troubles which accompany the accidents in question; for they appear to me to be of capital importance in their pathogeny as well as in their prophylaxis and treatment."

Le Gendre, who has investigated with so much talent the diseases of children and their digestive affections, sounds the same warning in a well-drawn report on *the dyspepsia of school-children* and after speaking of dyspeptic collegians suffering from

digestive troubles and who themselves attributed their com plaints to faulty digestion, he adds:

"Much more numerous in my experience, are those children and adolescents of both sexes, who, considering themselves free from digestive disorders, complain of certain nervous troubles; sometimes headaches, sometimes painful weariness or lassitude, or permanent coldness of the extremities; with it, inaptitude for work and concurrently no interest in play.

"Very frequently some loss of weight is noted, the complexion is yellow, the eyelids swollen, and slight transient albuminuria is found, outbreaks of acne or pharyngitis, seborrhea with coincident eczema of the seborrheic regions occur.

"In the collegians so affected I have always found upon a minute interrogatory (for they declare they have no digestive troubles), certain disorders of which they were not conscious; the need of unbuttoning their clothing after each meal, frequent hiccough, incessant thirst, a pasty mouth, infrequent stools, constipated and ovulated, or perhaps occurring twice daily, but unformed and peculiarly fetid.

"To this is added a bad breath inconveniently noticeable to those near-by, or else a peculiar odor of the cutaneous secretions, mawkish and nauseating."

We could multiply these citations, but the two quoted coming from physicians so qualified to speak authoritatively, will suffice to give a view of the problem.

As appears, the general symptoms of auto-intoxication are most frequently accompanied by digestive troubles, so evident that the relation between cause and effect is established without difficulty, and the diagnosis as well.

More rarely the general symptoms are alone evident, the intestinal cause being masked; it must then be sought by a careful interrogatory and examination of the digestive organs, aided by macroscopic and microscopic examination of the stools, and the ascertaining of the dosage of the sulphoethers and aromatic substances present in the urine.

If these means are neglected, the only ones that are positive, and if the intestinal flora is not examined, we run the risk of making an error in diagnosis and attributing these symptoms

and morbid state to entirely different causes. The interpretation of the morbid state we have roughly described, has in fact, until now, greatly varied according to different authors.

Many physicians have ascribed this morbid condition to nervousness, others to anæmia, others to arthritism, only a few connect it with intestinal auto-intoxication, which to our mind, is the true and sole cause.

Even unquestioned masters in modern pediatrics discuss its pathogeny as proved by the two following citations bearing upon the same symptomatic picture we have just described.

One is taken again from *Sevestre*, and we quote it first because its findings agree absolutely with ours.

Now our own interpretations are based not only upon clinical impressions, but in every case and without exception upon the examination of the stools and urine.

Sevestre says: "In the very large number of cases that I have seen (for they are far from rare), this is how we may understand the sequence of the phenomena.

"A child allowed too much liberty, introduces into his stomach badly divided or too great a quantity of food; in spite of which, digestion goes on, completes itself and for a variable length of time no appreciable trouble results.

"But, by the repetition of these same errors, the stomach becomes gradually overdistended and at the same time less active; the aliments remain longer in it and they undergo (at least those most easily altered) a decomposition which is continued in the intestine.

"The toxins resulting from this, and which are absorbed, are first destroyed by the liver.

"At the end of a certain time, however, this surcharged and overtaxed organ is itself altered and increased in size; it becomes unable to carry on its work of depuration.

"Then intoxication appears and is manifested by headaches, general fatigue, by vomiting and sometimes by fever, the latter denoting a more acute degree of intoxication."

The second explanation is that of *Comby*, the learned physician of the *Enfants Malades*. *Comby*[1] considers these same

[1] Comby: Arch. de med. de l'enfance. 1904.

symptoms as belonging to arthritism, and he has described them in two well-written papers, as **Symptoms of Arthritism in Children.**

These symptoms are so identical with those we have observed in intestinal auto-intoxication, that we might transcribe the entire work of *Comby* as the symptomology of intestinal auto-intoxication, without changing anything in it except the interpretation.

The notion of arthritism is admitted everywhere in France, because this morbid state really exists there, generally speaking, in most of the large cities and suburbs, at least in individuals comfortably situated.

They laugh at it in Germany, or rather they did up to a few years ago.

Slowly, however, the notion of a diathesis based upon the slowing up of the nutrition, is being discussed especially by the dermatologists, and in Berlin we have recently heard unquestioned authorities in German science admit the existence of arthritism, whereas eighteen years ago when, as a young physician, we followed the summer courses both in Berlin and Vienna, it was spoken of as "*the French idea*," and that with a more than sardonic smile.

This can be easily explained, for with the great general advance in wealth and comfort throughout Germany, the diseases which are the consequence of luxurious living and their symptomatic wake have begun to appear and forcibly claim the attention of the clinicians.

But the notion of arthritism has barely penetrated; hence the interpretation of *Comby* is admitted by no one in Germany.

In Switzerland, where we have two classes of patients, one composed of foreigners and the other made up from the local people, we are able to observe in the first, all the manifestations of arthritism; whereas in the second it does not exist or scarcely at all. Now, if the nervous, cardiac, cutaneous, trophic and other symptoms admittedly auto-toxic, are more frequent in the arthritic patients, it is because of two reasons; [1] in the first place, the arthritic owing to the incessant elimination of urates

[1] Combe: Traitement de l'entérite muco membraneuse. 1906.

and oxalates by the intestinal mucosa is naturally predisposed to digestive affections. Next, because the arthritic from matter of taste prefers meats, eggs, etc., and disdains or dislikes a vegetable diet; this greatly augments intestinal putrefaction, the cause of auto-intoxication. Furthermore the frequency of this morbid condition in arthritics is not proof of its arthritic origin.

On the contrary, the proof that arthritism only plays a predisposing part, is, that we observe in Switzerland in our patients belonging to the country and who present no trace of arthritism, exactly the same symptoms, nervous, cardiac, cutaneous, trophic, etc., described by Comby as being of arthritic origin.

We can understand quite well that *Comby*, who practices in Paris, cannot make the distinction which it is easy for us to make here, and which is as follows:

In the arthritic auto-intoxicated coming from foreign parts, we find in the urine *an exaggerated acidity and an excess of uric and oxalic acids*, and at the same time a considerable increase in the sulphoethers and aromatic substances.

In the non-arthritic auto-intoxicated belonging to the country, and who present exactly the same morbid symptoms, we find in the urine a *normal acidity and a normal quantity of uric and oxalic acids*, but a marked increase in the sulphoethers and aromatic substances, as with all auto-intoxicated individuals.

From this, we must conclude that the so varied symptomatic picture we have drawn, is due to intestinal auto-intoxication and not to arthritism as *Comby* maintains.

PATHOGENY OF INTESTINAL AUTO-INTOXICATION

The following is a brief *résumé* of the pathogeny of intestinal auto-intoxication.

A. Normal Digestion

In a normal digestion, thanks to the microbic symbiosis, we find in the intestine besides the peptones and crystalline bodies, aromatic substances and ptomaines.

These more or less toxic bodies are partly excreted by the stools, after having undergone a preliminary transformation in the intestine, into less harmful substances.

If their quantity is too great, they are swept out by diarrhea. The remainder partly neutralized by the digestive mucosa is changed in the liver and taken up by the circulation where it is still further modified by the action of the antitoxic glands.

The ultimate remainder is eliminated through the skin, the lungs and kidneys.

B. Pathological Digestion

If the products of a normal digestion are already toxic, there is nothing surprising if those derived from an abnormally developed putrefaction should also be.

As we know, it is the carbohydrates that ferment in the small intestine and the proteids that undergo putrefaction in the large intestine.

The nitrogenous bodies furnish the most toxic substances, particularly the ptomaines, and they also are the most potent factors in causing auto-intoxication.

I. Microbic auto-intoxication. Whenever the digestion of the albumins in the upper portions of the digestive canal is incomplete, whether due to nitrogenous suralimentation or insufficiency of the digestive glands.

Whenever there is exuberance of the bacterial flora—whatever the cause may be—there will be found a marked increase in the proportion of intestinal toxins.

In both cases we shall have a microbic auto-intoxication from hyperformation of enterotoxins.

The antitoxic and eliminative organs redouble their efforts, and, for a time at least, succeed in maintaining the equilibrium.

If one of the antitoxic organs becomes weak and incapable the others supplement its action; if one of the eliminative organs becomes obstructed, the others take its place and the signs of intoxication remain minimal.

The channel of elimination varies with the individual; in some it is the skin; in others the intestine; in still others the kidneys; it is a sort of special constitutional habit, a kind of idiosyncrasy found sometimes in all the members of one family.

But the overwork of these organs is not accomplished without wear and tear, and should it last, without lesions appearing. The liver becomes fatigued and augments in volume; the kidneys become slowly inflamed, and owing to the incompetency of these organs, the hyperproduction of toxins is no longer checked; then begin the symptoms of intestinal auto-intoxication. The enterotoxins only slightly modified and incompletely eliminated, accumulate and circulate in the blood, irritating the heart, the blood-vessels, the vascular glands, the nervous system, etc. These organs react by morbid symptoms which we shall shortly examine.

According to the individual predisposition, this or that organ will suffer; in one it will be the nervous system, in another the lungs, in a third the heart, etc. The gradual accumulation of these poisons in the organism, will, at variable intervals, determine crises of elimination according to the nature of the sufferer; at times a febrile access, at others a cutaneous outbreak, or an intestinal discharge, all of which leave the patient weakened but otherwise improved for a certain length of time, until a reaccumulation reproduces the same symptoms at necessarily varying intervals.

II. Organic auto-intoxication. Even with a normal digestion, or with a production of intestinal toxins within the physi-

ological limits; we may see auto-intoxication occur whenever one of the means of defense or one of the emunctories is defective or incapable.

From this results an organic auto-intoxication from hypo-destruction of the enterotoxins.

This form is naturally much more rapid and much more serious than the first.

Its symptoms are more grave, its crises more frequent and intense, and its prognosis more serious.

III. Mixed auto-intoxication. Finally it is easy to understand that these causes may be combined and that in certain cases the gravest and most serious of all, **we may have at the same time hyperproduction and hypodestruction of enterotoxins.**

SYMPTOMOLOGY OF INTESTINAL AUTO-INTOXICATION

We shall first examine the clinical forms of intestinal auto-intoxication and then take up their symptoms.

I. Clinical Forms

We may distinguish in digestive auto-intoxication three well characterized forms.

1st. The insidious form of intestinal auto-intoxication.
2d. The abortive form.
3d. The gastrointestinal form.

1st. The Insidious Form of Intestinal Auto-intoxication

This is the most frequent form and the one we should most learn to detect, for it is particularly observed in children.

General insidious form. Its evolution is effected so silently so insidiously, that parents are very often surprised when told their child is really ill. They have, of course, noticed that it was paler, somewhat thinner, had rings under the eyes, but they had ascribed these symptoms to accidental causes.

Undoubtedly the child had often complained of his head, his character had changed, he had become more nervous, more impressionable, more irritable than before, but that might be explained by the school, or by growing pains or else some other reason, but no one, not even the sufferer would have thought of accusing a bad digestion, which was not manifested by any outward sign.

Some parents notice that their child is not well; some children complain themselves of not feeling well, but without any idea as to the cause of the morbid trouble.

The aid of the physician is then sought and unless taught by experience, he will have much difficulty in making an exact diagnosis; embarrassed as he will be by the multitude of symptoms enumerated to him, and from the fact that they are related to the most diverse organs and systems.

Yet, it is precisely this multiplicity and this variety of symptoms which should awaken his suspicions and lead him to consider causes of a general character, and particularly digestive auto-intoxication. That alone should prevent him from being satisfied with the answer that ignorant or too busy physicians so often make: *It is nervousness! Don't worry about it.*

Nervousness? It may be true, but how often is the term wrongly applied.

Nothing but a careful interrogatory, only an examination of the patient, of the stools and urine, will settle the question.

The parents usually tell us: The child has been ill for some time, but we cannot tell since when. He has become pale and yellow, and has less vivacity than before. He has lost his appetite and complains of his head; he has dizziness and weak spells specially in school; he has even fainted several times.

He has palpitations and gets out of breath easily; he has itchings and eruptions of the skin at times.

His character has changed; he has become irritable and sullen; he cries for nothing; some days he has fits of anger, on other days fits of melancholia; his sleep is bad; he goes to sleep with difficulty, and has nightmares; it is hard to awaken him, etc. All of these complaints which we find noted in our observations; all these morbid phenomena upon which the parents insist, have occurred as isolated symptoms in children—which is rare —or have alternated at different intervals more or less long, or else have been simultaneous or combined in different manners in the same child.

It will be seen that this long train of symptoms involves all the organic systems and is silent on one only, that of digestive troubles.

Furthermore, if the parents are questioned, they will answer without hesitation, that the digestion of their child is normal, and the little sufferer himself will say that he does not feel

anything the matter with his digestive functions. This is an important character of the intestinal auto-intoxications; one that should awaken the attention of the physician. This multiplicity of symptoms, and these most diverse complaints seemingly have no relation to each other, so much do they belong to different systems and organs, so much do they escape general rules, and systematic arrangement. This of itself must induce the physician to examine the intestinal tract, and to seek the aid of the bacteriological chemist for the confirmation of his suspicions, by the examination of the stools and urine.

Such is the insidious general form of intestinal auto-intoxication.

Insidious local forms. Sometimes intestinal auto-intoxication manifests itself by a single symptom, or by a single group of particularly prominent symptoms; in which case the disease affects a special course.

This grouping is apparently due to some special predisposition, to a sort of systemic idiosyncrasy, whereby a greater impression is made upon some one organ or system than on the others.

We then speak of the *cephalgic form*, of the *neurasthenic form*, of the *pseudo-meningeal form*, of intestinal auto-intoxication. We can speak of the *cardiac*, the *febrile* and the *asthmatic* forms.

There exist besides the *cutaneous types* (strophulus urticaria, acne, etc.).

Some even mention *renal* and *gastrointestinal* forms of digestive auto-intoxication.

In a word it is possible to distinguish clinically as many types as there are predominating symptoms.

2d. Abortive Forms of Intestinal Auto-intoxication

In the abortive forms *we hear nearly the same complaints from the patient*, but the added intestinal symptoms are sufficiently prominent to strike, if not the parents, at least the attending physician.

In these cases the intestine, while not absolutely diseased, is never normal in its functions.

The tongue is frequently bad, specially posteriorly; the tip and the edges are red, often swollen and inflamed; the breath is bad and hiccough is frequently present after eating; the belly is often distended. These children have a capricious appetite, and a constant thirst, not only at meals but in the interim. The stools are irregular and obstinate constipation may alternate with looseness, in which the stools are soft and mushy. Very often the desire to stool comes on during meals, or else during the night, or on awakening in the morning; the desire is imperative, so that children may have difficulty in reaching the closet without accident. They often complain of bellyache at the level of the umbilicus; the pains being sometimes followed by mushy stools.

Finally, it is not rare to hear the patient say that his dizziness or weak spells are accompanied by abdominal pains, which are followed by urgent desire to defecate, after which all discomfort immediately disappears.

It is most frequently impossible to obtain any exact information as to the appearance of the stools, and we know how difficult it is to obtain even an approximative description from young people or their parents.

The interrogatory demands an examination. This will reveal varying signs of digestive troubles; generally a prominent belly, a distended and splashing stomach, an intestine overdistended by gas and often displaced, a festooned transverse colon, etc., a liver considerably augmented in size, exceeding its costal limits by several finger-breadths and with swollen borders. The inspection of the stools will show them to be made up of roundish masses, or ovulated, or long but of very small caliber with glairs and membranes, or else they appear mushy, dark in color; they are fetid, gluey and adhere to the vessel.

3d. Gastrointestinal Forms of Digestive Auto-intoxication

While the insidious and abortive types are accompanied by important general symptoms, and with almost no or only insignificant intestinal symptoms. The gastrointestinal types

on the contrary, are accompanied by slight general symptoms but by a considerable number of digestive symptoms.

These are constituted in the gastric forms by uncontrollable vomiting; in the intestinal by intense crises of diarrhea and by both in the mixed types.

To this group belong most of the acute crises observed in the chronic glairy and membranous enteritis we have already studied. As is demonstrated by the curve of the aromatic substances, we should consider these gastric and intestinal crises as veritable eliminative discharges of toxic matters, which the organism seeks to evacuate by these means.

It is for this reason and because of the violence of the elimination, of the vomiting, the colic, the diarrhea and the accompanying fever, that we prefer to designate these conditions as *the acute crises of chronic intestinal auto-intoxication*, so as not to confound them with the *acute* forms of intestinal intoxication. For, as we have already said in the introduction, the true acute forms of intestinal intoxications from milk or tainted foods, are always alimentary poisonings of exogenous or endogenous origin. *They are not auto-intoxications.*

II. Symptoms of Intestinal Auto-intoxication

External appearance. The auto-intoxicated is a suffering being, of pale visage, sometimes yellow, with a drawn face and a sad expression. The hair is dry, without luster; it is often split at the ends, the color is not frank, and the scalp desquamates. The eyes are sunken, the conjunctiva slightly yellowish at times, with some puffing of the lids.

The forehead and the cheeks are prematurely lined, and frequently covered with yellowish or brown spots.

The lips are red and thickened, much too red for the pale complexion with which they strongly contrast; at the time of of the crises this redness increases, and is accompanied by considerable tumefaction and heat, most disagreeable to the sufferer.

The thorax is emaciated, the abdomen is voluminous. The skin is dry, desquamates and has a dirty, grayish aspect. The hair on it is over-developed, but dry and broken.

The nails are soft, split, badly formed and often present transverse ridges indicating periods of crises. White spots are often found under the skin in the regions of the neck and axilla.

In the inguinal regions we can appreciate numerous movable and painless ganglions. The sufferer perspires easily during the day but particularly at night.

Digestive System

We must here distinguish between the digestive symptoms of the insidious forms and the gastrointestinal crises.

I. DIGESTIVE SYMPTOMS OF THE INSIDIOUS FORMS

We shall first examine the digestive symptoms:

A. Subjective Symptoms

Many auto-intoxicated subjects suffer from anorexia or from irregular appetite; others have a predilection for certain articles of food; many have a distaste for meat. Some have *parorexia* and swallow sand, earth, strings, plaster, etc. Others have *bulimia;* they eat too much and gluttonously. But the important symptom is the *polydipsia;* these patients have great thirst not only when eating but at all times. They often bloat after meals, and are obliged to loosen their clothing.

They often suffer from colic at and after meals, and this is frequently followed by an imperative desire to stool.

B. Objective Symptoms

The tongue is yellow or brown, coated posteriorly and red anteriorly, and at the margin the papillæ are swollen and prominent.

The breath is often bad, with an aromatic odor sometimes. The belly is swollen, the veins dilated, sometimes like the *caput medusæ.*

Very frequently at the level of the ninth and tenth ribs, we may find the *hepatic varicosities* described by *Buzzi* and *Schwenninger.* In children the liver is nearly always enlarged and descends

below the false ribs; while rare, this condition is not exceptional in the adult.

As to the gastric and intestinal signs, they vary with the individual, at times we find symptoms of gastric ptosis; sometimes those of spasmodic or organic stenosis of the pylorus; at others those of ptosis, or nervous or organic spasm of the colon; again those of chronic dyspepsia and enteritis. Hemorrhoids are frequent even in children.

C. Stools in Auto-intoxication

The stools are constipated, hard, ovulated or tubular, and of small caliber, or else soft and mushy; they frequently contain mucus, membranes, sand, and have a very marked fetid odor.

Macroscopic examination often shows the membranes characteristic of membranous enteritis.

Microscopic examination demonstrates dyspepsia and its nature, by the characters of the undigested alimentary residues; it will also reveal the ova of parasites, etc.

The physiological examination of the precocious fermentation will give information as to the intolerance for starchy foods.

Finally the bacteriological examination will show us the modifications in the intestinal flora, and the degree of putrefaction which it has developed.

Normal intestinal flora. We know that there exists a direct and intimate connection between the physiological intestinal activity and the composition of its bacterial flora.

Hence by following the evolution of the infant to the adult, we notice that as its activity becomes more complicated, the flora becomes likewise more complex.

In the normal child exclusively breast nourished, the microscopic picture as demonstrated by *Escherich* and afterwards by *Tissier* is most characteristic, in that it shows the great preponderance—almost exclusive—of a single species, the *Bacillus bifidus* of *Tissier*, or *Coli bleu* of *Escherich*. As the nourishment of the infant becomes more complicated, the bacterial picture becomes also modified and more complex.

In the infant nourished with cow's milk, the bacterial species

are not only different, but much more numerous than in the breast-nourished child. With the introduction of farinaceous foods, still other species (saccharolytes or amylolytes) will appear in the stools, while other species diminish or disappear. This permits us to say that the composition of the bacterial flora of the intestine depends directly upon the alimentation. If a certain kind of food predominates, the intestinal flora itself will be more uniform. A meat diet begets an entirely different flora from that rich in carbohydrates.

In the first case, the proteolytic anaerobics (*Bacillus mesentericus*, Proteus vulgaris, etc.) appear almost exclusively.

While in the second case it is particularly the saccharolytes and the amylolytes (*Bacillus acidi lactis aerogenes, Clostridium butyricum, Prazmowski*, etc.), which dominate. In mixed diet, by reason of the vital concurrence, there is established between the different antagonistic species, an equilibrium, corresponding to the physical and chemical conditions of the intestine.

The great and prolonged predominance of given types at the expense of others—a predominance caused by a too uniform and exclusive diet—will bring with it more or less grave inconveniences, from which intoxication may result.

This is particularly true of the proteolytes, which, owing to the toxins they secrete, may cause a nitrogenous digestive auto-intoxication.

It is equally true for the saccharolytes, but to a lesser degree; they give rise to acids and can provoke an acid intoxication of the organism or *acidosis*.

That is why the economy instinctively seeks to react against a too exclusive alimentation, and for that reason we see—as *Bunge* and *von Noorden* have called attention to—a constant and considerable augmentation in the consumption of sweets, go hand in hand with the modern diet, much too rich in nitrogenous elements (meats, eggs, etc.). This is an instinctive reaction on the part of the organism, intended to overcome or counterbalance the ills and the dangers which would result from a too uniform proteolytic flora, for this would be the unavoidable consequence. To ward off this danger instinct leads man to modify his regimen.

Hence, when alimentation is normal, that is, composed of mixed foods with carbohydrates predominating, there will be found in the intestine a mixed flora with a predominance of the saccharolytic and amylolytic aerobic bacteria.

Most modern authors fix the normal proportion of the saccharolytes at 65 per 100. These conditions no longer obtain in digestive auto-intoxication.

Intestinal flora in digestive auto-intoxication. The *first point*

FIG. 1.—STOOL IN INTESTINAL AUTO-INTOXICATION
(*Weigert Escherich* stain)

Proteus Vulgaris, Bacillus Putrificus, Bacillus Mesentericus, Bacillus Acidophilus, Enterococci.

to bring out is, that in the stools of auto-intoxication, there is found in all cases a distinct and notable diminution of the aerobic and facultative anaerobics (*coli*, *lactis aerogenes*), and a predominance of the strict proteolytic anaerobies; all of which *Grigoroff* found in appendicitis[1] and *Amann* in enteritis.

The second point is, **that the anaerobic flora is never uniform; it is extremely varied and variable according to individuals.** (Fig. 1.)

What are the strict anaerobies? They are for the most part the microbes of putrefaction or adjuvant organisms, as the

[1] Grigoroff: Thèse de Genève. 1905. p. 89.

investigations of *Bienstock, Achalme, Tissier* and *Martelly*, etc., have established.

It is thus that, among the numerous anaerobies, we usually find in examinations, the *Bacillus putrificus* of *Bienstock*, which attacks the albumins.

The *perfringens* was found like the *putridus* in decayed meats by *Tissier*.

En résumé, the analysis of the intestinal flora in auto-intoxication reveals the characteristic flora of albuminous putrefaction.

II. GASTROINTESTINAL CRISES

The elimination of the accumulated enterotoxins may take place through the mucosa of the digestive canal, under the form of periodic paroxysms.

It may take place through:

(*a*) The salivary glands; crises of periodic sialorrhea.

(*b*) Through the stomach; crises of periodic vomiting.

(*c*) By the intestine; crises of periodic diarrheas.

(*d*) Through both the intestine and stomach; periodic bilious crises.

A. Salivary Crises or Crises of Periodic Sialorrhea

This form is rare but of frightful intensity. We have observed but three cases.

One of them was in the child of one of our colleagues in the faculty. This young boy, then five years old, was seized every two or three weeks with acute crises, manifested by a febrile sialorrhea, lasting two or three days during which he sometimes eliminated as much as five liters of saliva.

B. Gastric Crises or Periodic Vomiting of Leyden

It is nearly twenty-five years, since Leyden described, under the name of periodic vomiting, a syndrome characterized by crises of uncontrollable vomiting, lasting from several hours to several days and occurring at intervals more or less far apart, and accompanied by headaches and gastric pain; although outside of these paroxysms the functions of the stomach were absolutely normal.

Clinically, these gastric crises manifest themselves as follows:

They return at varying intervals, but at nearly regular periods in the same individual, and present themselves under the form of crises of uncontrollable vomiting, lasting from a few hours to several days, and accompanied with headache and gastralgia, frequently severe. The vomit is at first alimentary but soon becomes limpid, ropy, and occasionally colored yellow or green by the bile. This liquid is hyperacid and contains a marked quantity of acetone.

Some hours, at times some days before the attacks of vomiting, acetonæmia appears; this is revealed by a peculiar sourish odor of the breath as well as by the increase in the urine of the quantity of acetone.

The temperature—sometimes normal—rises during the crisis to 38° or 39°C. (100.4 to 102.2 F.). Since *Leyden* first described this condition, many observations have been made both in children and adults and for their interpretation, many explanations of the most diverse kind have been made.

They have been attributed to tabes, to hysteria, neurasthenia, affections of the nervous system, some of which are accompanied by crises absolutely similar, essential crises, cyclical crises of nervous origin (essential neurosis of *Oettinger*), antitoxic crises of acetonæmia (*von Jacksch*), or by leucomainæmia (*Griffith*).

In all cases of periodic vomiting, as *Vergely* had already stated in a most interesting paper[1], we have found in the urine acetone and diacetic acid in varying quantities; we have even sometimes found lactic and oxybutyric acids.

The latter are products of the fermentation of the carbohydrates; the first of fatty bodies; both of them result from fermentations taking place in the small intestine.

These acids increase parallelly with the acidity of the urine and its ammonia content; they augment with the quantity of ammonia and diminish with it.

They are signs of acid intoxication (of **acidosis**), which, as *Cerny* and *Keller* have demonstrated, plays such an important role in the chronic dyspepsia and intestinal catarrh of children,

[1] Vergely—Rev. med. enf. 1898. page 1.

a true alimentary intoxication which takes its source almost exclusively in the small intestine.

In the next place in cases of acetonæmic vomiting, we have always found a considerable augmentation in the sulphoethers and aromatic substances, and in the few cases in which we were able to follow the complete daily curves of the phenols and indols, we were able to note the rise in the curves before, and their descent after the attack.

Our analyses of the urine coming from children suffering from periodic vomiting, show that acidosis is often combined with nitrogenous auto-intoxication, without there being the slightest parallelism between the two.

We therefore believe that these periodic crises are of autotoxic nature. They are crises of elimination of toxic matters, but it is impossible with our actual knowledge to decide whether these substances are derived from the fermentation of carbohydrates in the small intestine, or from the nitrogenous putrefaction in the large intestine. These crises are therefore absolutely comparable to those of periodic sialorrhea.

C. Diarrheal Crises

These, like the preceding, are crises of elimination, and they represent the most frequent form.

They are preceded by a prodromic period of anorexia, nausea, dizziness, during which the temperature rises.

Then suddenly the crisis begins with vomiting—not always present—then with colic followed by an abundant diarrhea more or less violent in character, and with or without fever.

The stools are soft with glairs, or else liquid and very abundant, always excessively fetid and sometimes bilious.

Gradually everything subsides and a period of comparative well-being follows, which lasts for some time.

D. Bilious Crises

As *Marfan* has well said: "What is characteristic of the pathology of childhood and separates it from that of the adult, is the greater solidarity of the stomach and intestine in children; their more intimate connection. While in the adult each one

of these organs conserves a certain independence, at least in its clinical expressions; it is rare to find such to be the case in children. Moreover, the liver nearly always takes part in the affections of the stomach and if it cannot always be demonstrated clinically, pathological anatomy brings it into evidence.

The digestive disorders of the child are therefore characterized by a variable but nearly constant participation of the liver, stomach and intestine.

That is what is observed at times in chronic auto-intoxication, when we see crises of elimination involving at the same time each of these organs.

We have observed a rather large number of cases in which the crises of elimination were manifested by vomiting at first alimentary, then mucus, yellow or green, and accompanied by green, polycholic diarrhea. These crises were of variable duration, and were preceded by a rise in the curves of the indols and phenols, these falling with termination of attack. They therefore are also crises of elimination.

III. ANGIOCHOLITIS

A. It is particularly in children that the liver takes part in gastrointestinal affections. It is not very exceptional to find an augmentation in its volume. This hepatomegaly frequent in the adult is nearly constant in the child; it varies in size and is frequently accompanied by splenomegaly.

The urine is highly colored and nearly always contains a very appreciable amount of urobilin, with often a considerable increase of ammonia and a diminution of urea.

In this first degree, there is a slight insufficiency of the liver with cholemia, for the examination of the serum reveals the presence of biliary pigments.

The influence of intestinal auto-intoxication is easily explained. The blood in the portal vein in auto-intoxication is charged with intestinal toxins and it is purified in the liver; this ultimately brings about a state of fatigue in the hepatic gland, and in consequence some functional incapacity.

Hence the brownish yellow aspect, the slight conjunctival jaundice, the yellowish color of the palms and soles of the feet

(palmo plantar signs of *Gilbert;* the itching, the various pigmented spots, the spots of xanthelasma around the waist line, which pale and disappear upon improvement of the intestinal condition.

This state of hepatism, as *Glenard* terms it, or familial cholemia as named by *Gilbert*, is found more or less accentuated in all auto-intoxicated children and in most adults. Hepatism is the consequence of auto-intoxication, and not the cause as *Gilbert* maintains.

B. Simple chronic icterus. Intestinal auto-intoxication, may, if it lasts a certain time, become complicated by this condition; isolated by *Gilbert* and well studied by *Rodocanachi*. It is characterized by all the symptoms of icterus and cholemia, and is frequently accompanied—but not always—by hepatomegaly and splenomegaly.

C. Hypertrophic cirrhosis. In some more serious cases, the hepatomegaly is accompanied by well-defined chronic icterus, but without venous stasis, in other words, without ascites, or collateral circulation and without hemorrhoids.

This icterus with hepatomegaly is frequently accompanied by splenomegaly.

We have thus all the symptoms of true biliary hypertrophic cirrhosis like those we observe in the attenuated ascending infections of the biliary canals, and caused by intestinal germs. We might connect with it those exceptional instances—several well-defined examples of which we have observed—of biliary hypertrophic cirrhoses consecutive to hepatic calculi (*Lereboullet, Gilbert, Legendre*, etc.), and which recognize the same origin—the ascending infection of the liver through intestinal causes.

Circulatory System

We know, since the researches of *His, Romberg*, etc., that the heart possesses an automatic motor system and that it obeys the pneumogastric and sympathetic nerves.

It is therefore certain that the toxic substances circulating in the blood must exercise an influence upon the heart. But it is none the less true, that we must take into account the reflexes of intestinal origin, for they modify the blood pressure considerably.

Lastly, the stomach can besides act mechanically when it is greatly distended; it crowds back the diaphragm and modifies the position of the heart, as the X-rays show.

Cardialgias

Simple cardialgias. We may see in digestive auto-intoxication *violent cardialgias*, marked by intense anguish, cold sweats and loss of pulse; terrifying phenomena which disappear as if by magic with the belching up of gas. *Ewald*, *Jessen*, and particularly *Schuster* of Nanheim who wrote a short monograph, report striking examples.

Pseudo angina pectoris (*Angina spuria* of the Germans). Like simple cardialgia, pseudo angina is more frequently observed in auto-intoxications of gastric origin, much more rarely in those of intestinal. It must be carefully distinguished from true angina due to sclerosis of the coronary arteries; from toxic angina (lead, tobacco); and from the angina of the neuroses (hysteria, neurasthenia, etc.). Pseudo angina of gastric origin may occur at any moment, but most frequently it comes on in the evening after a copious meal. The seizure is often preceded by a sense of weight in the epigastrium belching and nausea. Mental emotions, physical efforts (walking against the wind), may provoke it.

The seizure resembles in every respect that of true angina (*angina vera*). The pain is localized in the inferior half of the sternum and radiates to the left shoulder and arm. Sometimes it extends to the fingers, to the left side of the neck and the interscapular region.

The attack is accompanied by a *deadly anguish* extremely painful, by oppression, pallor, coldness of the extremities, cold sweats, and even fainting. Should it occur frequently, pseudo angina may be accompanied by hypotonia with symptoms of tricuspid insufficiency and dilatation of the right heart (*Potain*).

Tachycardia

We leave out here all febrile affections of the digestive system, which naturally present a more or less accentuated acceleration

of the pulse, and we shall speak only of the polycardia caused by digestive influence, mechanical, chemical or reflex.

Simple tachycardia. Digestion normally produces a slight acceleration of the pulse, with rise of the normal blood pressure.

This normal physiological polycardia may, nevertheless, be sufficiently marked to be perceived and to become disagreeable to nervous individuals of hysterical or neurasthenic tendencies. This condition may even weigh upon their minds to such an extent, as to make them forget their gastric troubles.

The characteristic feature of simple tachycardia or palpitations, is its immediate appearance after or sometimes during meals. Most of these patients complain of feeling the arterial pulsation throughout the body, with sensations of heat, vapors, and congestion most annoying to them. Simple tachycardia is absolutely harmless in the majority of cases, but it may become dangerous when the heart is the seat of valvular lesions, myocarditis, sclerosis, or fatty degeneration.

Paroxysmal tachycardia. This crisis—for it may assume that form—is no longer an exaggeration of a physiological process, but a deeper affection of the heart, occurring in dyspepsia, in gastrointestinal meteorism and especially in gastroptosis with abdominal protrusion.

These crises are accompanied by anguish, cold sweats, and considerable cyanosis and come on usually at night or in the morning.

Between the crises or preceding them, we often observe in intestinal auto-intoxication a *cardiac erethism*, characterized by the increased frequency of the heart beats and augmentation of systolic energy, so that the first sound often acquires a vibrating timbre.

This cardiac erethism is often noticed by patients who complain of feeling their heart beat.

The accentuation of the second sound is a very constant phenomena in these cases and is due to increased arterial tension.

Sometimes on auscultation, we may hear a galloping sound due to the greater tension of the general circulation over that of the pulmonary, which explains the double systolic sound.

Nervous reflex of Rosenbach. This reflex may be mentioned

in connection with the above; it is an affection characterized by crises which come on suddenly, either in the morning or at night, accompanied by intense tachycardia with intermittent and irregular pulse, pulsations of the carotids and abdominal aorta, great anxiety combined with extreme oppression and an urgent dyspnœa with cyanosis. The seizures which may last from several minutes to several hours, even days, are also accompanied by a marked bulimia, exaggerated sensitiveness of the stomach on pressure, and slight meteorism with constipation.

As it appears, this affection is like a transitional form between paroxysmal tachycardia which is purely cardiac, and dyspeptic asthma which is principally respiratory.

Bradycardia

Occurs normally in fasting and particularly in conditions of starvation.

Henoch and *Silberman* describe the bradycardia of children with gastric inanition.

Riegel, *Grob*, *Hirschsprung*, *Pick*, observed it in indigestion, dyspepsia, ectasia, in ulcer and cancer of the stomach. *Goltz*, *Meyer*, *Pribram*, noted it as following: mechanical, electrical, and chemical irritation of the gastric mucosa.

Bradycardia is therefore found more frequently in affections of the stomach, but not exclusively, for it is also observed in coprostasis, in the intoxication from the biliary salts in jaundice, and with intestinal worms.

Arrhythmia

In intestinal auto-intoxication, we often note intermittences, sometimes every two or three beats, recurring with variable frequency and appearing during the period of digestion. These intermittences are not influenced by physical effort and are sometimes noticed by the sufferer (palpitating arrhythmia of *LeGendre*), and sometimes not; they may be combined with tachycardia or bradycardia. Arrythmia may be observed in an absolutely normal heart.

Thus *Sommerbrodt*[1] observed it in himself twice during the

[1] Sommerbrodt: Arch. f. klin. Med., XIX.

same year after partaking of eels, although his heart was and is absolutely sound. *Bouchut*, *Barthez*, *Heubner*, *Comby*, etc., have reported numerous examples in children.

Fevers

Increase in temperature easily occurs in the auto-intoxicated.

Digestive fever. Digestion first and walking next, will easily cause a rise in temperature in the auto-intoxicated of from 37.8 C. (100 F.), even 38.3 C. (101 F.), and that without any other reason.

It is sufficient to modify the diet in the first case, and to keep the child quiet in the second to see the fever disappear.

Fever of exertion. If exercise or playing goes to the point of fatigue, it is not rare to see the temperature reach 39 C. (102.2 F.), or even higher.

Fever of absorption. This fever of irregular course, sometimes presenting the *inverse* type (maximum in the morning and minimum in the evening) is frequently noticed in intestinal auto-intoxication. It is easily subdued by a lacto farinaceous diet and by calomel.

Gastrointestinal intermittent fever. This curious manifestation of intestinal auto-intoxication has been very frequently described. *Comby*,[1] who gives an excellent description of it, looks upon it as a manifestation of arthritism.

Heubner, *Dinami*, and many others, have on the contrary, insisted upon its connection with the intestine.

For our part we find a large number of cases in our records. It is only a short time since we observed this curious type in a young Russian colleague who had for a long time been treated for malaria, notwithstanding the negative examination of the blood, and the failure of quinine to relieve, although given in large doses (3 to 4 grams daily). This morbid form is met with most frequently in children, but we have also observed it in adults.

The fever comes on in attacks separated by intervals of complete apyrexia; they present nearly always the three classic

[1] Comby: Arthritisme chêz les enfants. Sept., 1901.

stages; chills, fever and abundant sweats. They therefore present an unquestionable analogy with intermittent fever of malarial origin.

The affection begins after a prodromic period, lasting from a few hours to several days and characterized by an ill-defined discomfort. Then it breaks forth with vomiting in infants and by chills in older children and adults; the temperature rises rapidly to 39° (102.2 F.), or 40° (104 F.), or even higher.

The fever persists for ten or twelve hours, rarely more; it terminates by crisis and is accompanied by more or less abundant sweats.

The spleen remains normal in size or increases very slightly.

The attacks very rarely occur every day; most frequently they appear at intervals of two or three days, thus affecting the quotidian, tertian, or quartan types, etc.

Longer periods of apyrexia may be observed (from eight to thirty days).

During the period of apyrexia, children are pale, depressed and irritable.

The differential diagnosis between the digestive intermittent and the malarial intermittent fevers is easily made by examination of the blood and urine.

In the first the blood shows hyperleucocytosis, in the malarial the blood shows hypoleucocytosis and the plasmodia.

In the urine of digestive intermittent, we find a negative diazo reaction with many aromatic compounds, while in the malarial urine the reaction of *Ehrlich* is positive and the aromatic coefficients are but slightly elevated.

Finally, the spleen is enlarged in malarial fevers and more often remains small in the digestive.

Hypothermia

A certain number of auto-intoxicated are hypothermic. In some it is only during the periods of apyrexia; in others it is constant (the *cryesthesia* of *Dieulafoy*). This hypothermia is accompanied by sensations of coldness in the muscles and extremities, with more or less blueness of the hands and feet.

BLOOD PRESSURE

The arterial blood pressure measured with the apparatus of *Riva Rocci*, is nearly always increased in auto-intoxication, owing to spasm of the arterioles.

Arterio capillary pressure, measured by *Gärtner's* method, is diminished.

In fact, to the cardiac erethism corresponds an analogous erethism of the vascular system. This explains certain phenomena such as pallor of the face, coldness of the extremities, the dead finger and numbness of the hands, feet, etc.

It is also to the increased arterial pressure that the frequency of epistaxis may be attributed.

Œdemas without albuminuria. Very frequently the œdema is insignificant, transient, and limited to the eyelids, visible only on arising, for it quickly disappears.

In some cases, it is limited to the face and malleoli; more rarely it may involve all of an extremity, even both; it then presents a swollen, white and œdematous appearance in the inferior part of the affected member, or all over it.

Finally, we have observed in three cases a generalized œdema involving all of the body, in which there was neither albuminuria nor cardiac weakness.

These œdemas can only be explained by vasomotor agency.

Respiratory System

The respiratory apparatus is acted upon in two manners by intestinal auto-intoxication: first, by the digestive canal and then through the nervous system, this owing to the fact that the respiratory mucous membrane serves as excretory channel for certain intestinal poisons.

But apart from the anginas, which are very frequent, the respiratory manifestations of digestive auto-intoxication are rare.

Anginas

The frequent and repeated congestions of the throat, pharynx, and tonsils in their recurrent forms have been so often noted in our observations, that we feel called upon to mention them; for

the recurrent anginas constitute a noteworthy symptom of intestinal auto-intoxication, which should always be sought when in doubt.

Dyspeptic Asthma

First described by *Henoch, Silbermann,* and others, dyspeptic asthma is actually well known, but it is a rare form of which we have only seen three cases.

It nearly always follows upon an indigestion or dyspepsia; it diminishes or even ceases after vomiting, a liquid stool or after belching and the expulsion of flatus. The attack often commences with little dry coughs; then the breathing becomes sibilant both in inspiration and expiration; the respiratory muscles come into play and the child is obliged to remain seated on the edge of the bed, terrified, cyanosed and suffering from frightful orthopnœa.

The chest is painful, the heart agitated and the pulse rapid. The pulmonary elements, however, predominate greatly over the cardiac.

In the cases we have seen, the heart was absolutely normal, contrarily to the opinion of *Huchard.*

Upon auscultation, we hear ronchi and sibilant rales; the cough is incessant in some cases, of little importance in others.

The attack varies in duration from a few hours to a few days, and always terminates favorably if the origin is recognized.

With some patients the asthma is accompanied by urticaria, and always results from the ingestion of the same foods (strawberries, fish, etc.). Digestive asthma may be considered an internal urticaria.

Pneumonism

The febrile congestions of the lungs described by some authors are frequent in children, but we have not observed them in adults.

They are characterized by an acute fever ranging from 39 to 40 (102.2 to 104 F.), by a sighing expiratory dyspnœa with sometimes painful stitches in the sides. The duration of the congestion is from two to several days. The auscultative characteristic of pneumonism is the extreme mobility of the symptoms. On one day we may hear well-defined bronchial

breathing over the base of the left lung for example; the next day it will have disappeared, and we will hear rales instead, but bronchial breathing may be found at the apex of the opposite lung, etc.

The short duration, the *extreme mobility* of the serious objective signs(which is the important character of the affection), offer a very favorable prognosis if the etiological factor is recognized and pathogenic treatment is instituted by prescribing intestinal disinfections and a lacto-farinaceous diet.

NERVOUS SYSTEM

As the nervous manifestations would form too extensive a subject to be treated at length, we shall here limit ourselves to a *résumé*.

Neuroses

The auto-intoxicated, particularly in childhood, are all nervous. Their character changes; they are irritable, emotional, moody, quickly angered and at nothing, easily transported by a surprise, fear, or vexation.

They cry without reason and laugh without cause. They are bawlers, nuisances, and unbearable. They present in a word, all the symptoms of cerebral hyperæsthesia, which we have described in our work upon *la nervosité de l'enfant*[1], and which need not be repeated here.

The sleep of auto-intoxicated children is bad; they go to sleep with difficulty, and at late hours; they require some one with them, to sing to them, to hold their hand, etc. Their first sleep is extremely light; if a door opens, if somebody should speak, or should the mother withdraw her hand, they are instantly awakened and most frequently in tears. This light sleep is due to the fact that the too excitable senses are not completely at rest, and the ear perceives the noise, the eye the light, the hand the contact, etc.

These sensorial impressions, which are perceived in spite of sleep, either awaken the child or else he incorporates them during sleep into dreams, nightmares, from which he awakens with a

[1] Combe: La Nervosité de l'enfant. 1902. p. 33.

start, terror-stricken, crying and sobbing, with anguish and with palpitations, cold sweats, etc.

These crises of fear may lead to *nocturnal terrors* which are nearly always of autotoxic origin.

In other cases the sleep is not interrupted, but it becomes extremely agitated; the child laughs, chats, sings, weeps, yells; he turns this way, that way; if he has a bedfellow, he strikes the unfortunate one with his fists or feet; if he sleeps alone, notwithstanding the precaution of the mother, who has tucked him in bed, even tied him, he will be found in the morning with his head at the foot or lying crosswise. The second sleep, on the contrary, is heavy, deep, lethargic, more tiring than refreshing.

The awakening is very characteristic, slow and difficult; it is very hard to awaken these nervous children; they remain with their eyes open, in a subconscious state, not recognizing anybody and this for several minutes. They may even have hallucinations at the time and execute certain actions in a state of unconsciousness bordering on somnambulism.

Neurasthenia

We do not wish to take up the question of the origin of neurasthenia, which is being so warmly discussed at the present time.

We admit with *Dubois*—for we have seen many cases—that there are neurasthenics, who present the classical picture of neurasthenia, who, from their own admissions, suffer from predominating gastrointestinal symptoms and yet, upon examination, reveal a normal digestive system.

We find in the urine of these neurasthenics, the coefficients of auto-intoxication moving within physiological limits. But to pretend from this that all neurasthenias are of nervous origin is far from true.

Besides the nervous form of neurasthenia, we admit the existence of a much more frequent form, which is without doubt of toxic origin.

Who has not seen men in a perfect state of nervous equilibrium become neurasthenic, owing to a chronic malaria, latent tuber-

culosis, prolonged suppuration or a chronic insidious nephritis, from the abuse of alcohol or morphinism?

And yet these individuals presented such a faithful picture of neurasthenia in the slow, insidious, and progressive evolution of their morbid state, that eminent specialists in nervous pathology have made gross errors in diagnosis. Why, then, if the toxinemia in the first cases, the intoxications in the last, are capable of producing the symptomology of neurasthenia, why refuse this same ability to poisons of intestinal origin? Do we not actually see an evolution taking place in that manner, since *Chryssovergis*[1] has just described in a very interesting paper, *prenephritic neurasthenia* as being of dyspeptic origin; this, moreover, is in accord with the findings of numerous Italian authorities. We can note as *physical symptoms*, headaches, vertigo, visual disorders, ringing of the ears, lumbar pains, cramps of the calves, cryesthesia, pruritus, and vasomotor troubles.

The mental symptoms are those of sadness, fatigue, irresolution, depression, multiple phobias and particularly nosophobia.

As intellectual symptoms, the inability to concentrate the ideas, loss of memory. All these symptoms, which *Dieulafoy* described as the minor accidents of Brightism without nephritis, are observed in the dyspeptic auto-intoxicated, not at intervals far apart, but everyday nearly, and in a constant fashion, either as isolated symptoms or in different combinations. Moreover, it is a matter of common observation, to see these symptoms become either attenuated or aggravated, according to the modifications of the digestive troubles.

In the majority of cases these uncomfortable symptoms are undoubtedly transient. But they may persist for hours, sometimes for whole days, and they may recur for days and weeks, as long as the perversion of the digestive functions remain at a sufficiently accentuated degree.

Why should certain authors attribute the symptoms of neurasthenia to precocious manifestations of a uræmic intoxication, not yet dosable, for the kidneys are absolutely sufficient? Why should others connect them with digestive auto-intoxication if

[1] Chryssovergis: Sem. Med., 1904. p. 185.

the two autotoxic affections did not lead to the same result, the neurasthenic state?

Nervous Symptoms

Cephalgia. As *Sevestre* has so well remarked, the most common autotoxic phenomena is the headache, which is ordinarily frontal or may be localized in the brain itself.

It is an increasing headache. Sometimes moderately intense, but wearing from its persistence; at times it is accompanied by shooting pains and fixed points, as in frontal or temporal unilateral neuralgia. It comes on at any time during the day, sometimes in the morning, usually at the beginning of study.

Brain work always increases it or awakens it when it has ceased. Hence children, even the good scholars, feel a repugnance or an inaptitude for intellectual work.

They get behind in their studies, become depressed and worried, and may at times suffer from nervous complications.

These children have but little desire to play for fear of bringing on or augmenting their headache by the more or less violent efforts. The cephalgia may end in a few days, but it often persists for several weeks, or at least manifests itself when the studies are again taken up.

It, however, rarely occurs at night and it very rarely prevents sleep; although in children subject to headaches, we usually find sleep bad, agitated, troubled with grinding of teeth, moans, nightmares, etc. (*Sevestre.*)

Loss of memory, particularly for proper names, is frequently observed in autotoxic headaches.

Migraines. All the migraines are not of autotoxic origin, but a certain number are without doubt provoked by the enterotoxins. Migraine may be observed in the first years of life as light and but little characterized crises, for the digestive troubles are so prominent that we are tempted to consider them as simple gastric crises. The clinical characters of autotoxic migraine are as follows:

The attack comes on sometimes in the evening, sometimes in the morning; it begins as headache with vertigo and is accompanied by dread of light or noise, then vomiting super-

venes, which, in the morning is mucus and may in the evening contain food particles.

The vomiting, which has a strong acid odor, is repeated several times; it is not abundant and is only effected by painful efforts.

During the attack the little sufferer is greatly prostrated, the face is pale, and the pupils contracted.

The termination of the attack is as sudden as its beginning. All at once the little patient, who an hour before was so prostrated and who vomited all given him, becomes gay, lively, and eats with appetite. The first attack is followed by a second after an interval of three or four months. Then, unless appropriate treatment has been given, the crises become nearer to each other and as the child grows older, assume more and more their characteristic features.

Paroxysmal migraine. We see this form of migraine rather frequently in collegians, students and adults. It was first observed by *Rossbach*, and described by him under the name of *gastroxynsis*, and next by *Fenwick*. This form of migraine is only seen in neurotic individuals and is but an exaggerated type of the preceding. It is accompanied by paroxysmal hyperchlorhydria, which readily explains the gastric phenomena. We have observed a well-defined case in a celebrated publicist. The attack is usually announced by slight nausea with loss of appetite and constipation, and is ushered in with violent headache beginning in the frontal or occipital regions soon extending to the whole head; at the same time burning pain is felt in the epigastrium behind the sternum; this is accompanied by pyrosis, eructations, intestinal meteorism, nausea and shortly by the more or less abundant vomiting of strongly acid and acrid matters.

Sometimes the attack disappears after the vomiting, and the patient goes to sleep calmly and awakens completely restored. It is not exceptional to observe certain manifestations of a clonic, tonic or vasomotor nature with migraine.

The tonic manifestations consist in a general tension of the muscles near the seat of pain; hence we may note an exaggeration of the palpebral creases, a prominence of the cheek, a

dilatation of the nostril or an elevation of the labial commissure.

The clonic manifestations, much rarer, consist in slight tremors in the muscles of the eyelids and face.

The vasomotor manifestations are much more common. We frequently observe increased lachrymation or salivation, and a pallor of the face sometimes followed by an intense venous congestion, etc.

Nervous Autotoxic Crises

Quite a series of nervous crises have been pointed out, both with and without convulsions. They have been observed in auto-intoxicated children and may extend from mere dizziness to complete convulsions; these are the pseudo epileptic crises. They have been recognized for a long time, and have been differentiated from true epileptic seizures by numerous authors, among whom we may mention *Doctor Clozier* of Beauvais and more recently still, *Rachford*[1].

Crises of autotoxic petit mal. We can group these cases under the generic denomination of autotoxic petit mal from gastrointestinal toxæmia. We ourselves have observed several cases.

The attacks are preceded in the child by nervousness and extreme irritability, meanwhile his sleep becomes worse and worse. At the same time diverse gastrointestinal troubles become more and more evident, and the little patient becomes emaciated and anæmic. The attacks begin without prodrome by a more or less marked dizziness. Sometimes the child falls unconscious, at others he falls, but retains consciousness of what is going on. He never shows convulsive movements. At the expiration of a few minutes, he will get up, feeling nauseated and suffering from intense headache, which brings about an invincible drowsiness and sleep, from which he awakens, only after several hours. These attacks are often repeated several times during the month. A careful diet and intestinal disinfections bring about a rapid amelioration, and a definite disappearance of these nervous affections.

Crises of autotoxic grand mal[2]. Autotoxic eclampsia is not

[1] Rachford: Arch. of Ped. 1904.
[2] D'Espine: Eclampsie enfantile, Congrès de médecine de Paris. 1900.

very rare in children, and is sometimes observed in adults. At times the convulsive paroxysms take on the characters of seizures of grand mal, at other times they are more or less complete and again they may be more or less atypical.

Sometimes the convulsive attack will follow the ingestion of a same food, or it may come on irregularly and without apparent cause.

In all these cases a restricted regimen was sufficient to bring about the definite cessation of the eclampsias, which in some cases, recurred several times weekly.

Crises of tetany. We *actually* know that the removal or atrophy of the thyroid glands results in myxœdema and that the removal or atrophy of the parathyroids of *Sandstræm* causes tetany. The immediate cause of tetany is therefore not of gastrointestinal origin.

But what we also know, is that either in myxœdema or tetany, the symptoms are singularly accentuated when the extractive substances of meat or certain fats are ingested, whereas they diminish with a vegetable diet. The diet and digestive auto-intoxication therefore play a very important secondary role in the etiology of tetany, for they form toxic substances in such considerable quantities, that the already insufficient parathyroids cannot neutralize them.

Mental disorders. We shall only mention the importance of digestive auto-intoxication in the etiology of mental diseases; this is affirmed by *Pierret, Regis, Ballet, Voisin,* etc. Diseases of the mind do not enter into our subject, but in the course of auto-intoxication we have so frequently observed, phobias, somber ideas, misanthropy and even melancholia, that we are quite willing to accept its influence in psychic affections.

Paralytic troubles. We know that paralytic conditions of medullary or nervous origin are well-recognized facts in the acute digestive intoxications from ptomaines, and we have ourselves described in a thesis, a case of acute spinal paralysis in an adult following the ingestion of tainted mussels[1]. *Kouche*[2] has very recently cited several cases.

[1] Combe: Thèse de Genève. 1886.
[2] Kouche: Roussk. 1904.

But these cases are alimentary poisonings, and not disorders due to auto-intoxication of digestive origin.

We are not aware that there really exists any paralytic affection due to auto-intoxication.

GENERAL NUTRITION

The action of the intestinal poisons upon the general nutrition is undeniable; through their influence all the cells of the organism and particularly the blood cells are made to suffer.

Hence the anæmia and lack of development in auto-intoxicated children.

Anæmia. Our investigations of the anæmia of autotoxic origin have been quite extensive.

We have found in all our patients, the hematologic evidences of anæmia and noted that the degree of anæmia increased in proportion with the intensity of the auto-intoxication.

The hemoglobin diminishes from 80 per 100 to 70, and even 50 per 100. The **red blood cells** fall to 4,000.000, 3,500.000 and as low as 3,000.000. They are unequal in size, form and color (macrocytosis, poikilocytosis, ombrocytosis). In the young child it is not exceptional to find nucleated red blood cells (normoblasts).

The white cells are augmented in number (8,000 to 12,000). The polynuclears are mostly found in the form of transitional cells.

The lymphocytes are more numerous and myelocytes appear.

In glairy and muco-membranous enteritis, there is an increase of eosinophilic cells.

Our patients therefore have, in varying degree, all the signs of simple anæmia.

Pernicious anæmia. The grave forms of anæmia, and pernicious anæmia in particular, recognize multiple causes; among them gastrointestinal intoxication appears to take an important part.

The matter, as *Hunter* has demonstrated, is concerned with a toxic process and not with an infectious phenomena.

This question, having been greatly discussed lately, deserves more than mention.

W. Hunter, in his numerous papers on pernicious anæmia,

has, in fact, given a new development to the theory of auto-intoxication of gastrointestinal origin, which we maintain. What struck this author in the autopsies on auto-intoxicated subjects, was the existence of a large number of granules of blackish appearance in the hepatic cells. These granules are collections of extravasated blood pigment containing iron, as does the blood from which they are derived.

To prove this, *Hunter* makes use of different reagents, either a freshly prepared solution of sulphide of ammonium, or potassium ferrocyanide in the presence of dilute hydrochloric acid; this immediately stains the pigment granules giving them a Prussian blue color.

According to *Hunter*, these reagents have the advantage of reacting only upon the iron combined with the hemoglobin of the blood, which prevents any cause of error, even when the liver is congested.

In a series of experiments, *Hunter* has demonstrated where the destruction of the blood takes place normally, in infections and intoxications, and he has artificially provoked the latter by injecting into animals, various deleterious substances, such as pyrogallic acid and toluidindiamine.

Here are the conclusions derived from these experiments:

In the infections—**malaria,** for example—the destruction of the blood differs from that which takes place in pernicious anæmia. In malaria, the parasites attack the red blood cells, diminish their vitality, and are fatal to those stricken. The pigmentary debris are taken up and incorporated by the leucocytes and carried by them to the different viscera, the liver, spleen, etc.

In consequence, we find these pigmentary granules ordinarily enclosed within the leucocytes, in the capillaries, but they are hardly ever found in the hepatic cells.

In the intoxications, *pernicious anæmia*, for example, the destruction of the red blood cells takes place in the portal system, and consists in a dissolution of the cells with liberation of their coloring matter—the hemoglobin.

Hence the hemoglobin liberated in the portal vein is carried to the liver, where it is taken up by the hepatic cells. In them

the soluble hemoglobin is crystalized and forms the granules revealed by the chemical reagents.

It thus appears that in pernicious anæmia, the sanguineous granules are found only in the cells of the liver, as in the intoxications. This is proof for *Hunter* that the destruction of the red cells is of toxic origin and that the toxin is derived from the digestive canal, because, the destruction takes place in the portal system.

Hunter, in his researches in pernicious anæmia, sought for the poison in the urine, and he extracted from it two ptomaines identical with the cadaverin and putrescin of decaying meat, and a third poison, which appears to be a special diamine.

As we know, cadaverin and putrescin are both products derived from the bacteria of the digestive canal; this would seem to still further confirm the toxic digestive origin of pernicious anæmia.

In Germany, *Silbermann* was even able to produce pernicious anæmia experimentally in dogs by causing them to absorb toxic substances in small repeated doses; this experiment has been confirmed by the investigations of *Stadeleman*, *Bignani* and *Dionisi*, *Battistini* and *Rovere*, *von Voss*, *Tallqviste* and *Schaumann*, *Grawitz*, etc.

Grawitz shows that the toxic substance is formed in the intestine by the putrefaction of albuminoid matters. This fermentation may, moreover, be favorably influenced by the absence of hydrochloric acid secretion, noticed in many cases of pernicious anæmia. *Arslan*, furthermore, has studied a veritable epidemic of pernicious anæmia occurring near Padua in twenty-one children, and caused by duodenal ankylostoma. He arrived at the same conclusions as *Grawitz*, but by an entirely different method.

Several of these children had been considered tubercular, or to be suffering from some other cachexia. They all recovered after expulsion of the worms. *Arslan* made several interesting experiments which he describes as follows:

"In taking up the experiments conducted by *Lussana*, we were able to demonstrate that this anæmia forms one of the most beautiful types of intestinal auto-intoxication.

After having separated the toxin from the urine of two patients, by the method of *Brieger-Otto*, we inoculated rabbits with it in progressively increasing doses. These animals, from the first injections, presented all the symptoms characteristic of the anæmia in question; as soon as the injections were stopped, the rabbits gradually recovered in the same manner that recovery is observed in patients, after the ankylostoma have been expelled.

For control purposes, *Arslan* repeated the same experiments with urine from the same patients after expulsion of the worms, and with urine from individuals suffering from other forms of anæmia; not the least change occurred in the blood of the experimental rabbits. From all this, we may conclude that pernicious anæmia in at least one of its forms, is caused by an auto-intoxication of gastrointestinal origin. The influence of the poison in this disease extends simultaneously to the elements of the blood and to the bone marrow; upon the blood, by destroying it, on the bone marrow by exciting and stimulating its plastic activity.

Nutrition. Like all other cells those of the skin suffer from the general state of intoxication of the organism.

The skin becomes dry, rough and desquamates, the dead opithelial cells not yet replaced, give the skin a dirty color.

The hair is dry, badly nourished; it is prematurely gray or white from the destruction of its pigment by the *macrophages* (*Metchnikoff*), the hairs break easily and are often split.

The nails are also badly nourished, dry and easily broken, covered with white spots or with more or less deep ridges.

Premature senility. Intestinal auto-intoxication is often accompanied by all the signs of rapid old age.

The changes in the skin, the hair and beard prematurely whitened, the muscular fatigue, the stooping figure all give the auto-intoxicated the appearance of old age.

Even children very often look like little old men.

Since auto-intoxication retards evolution, it would be hardly possible to include this syndrome in *Weissman's* theory of senility, which, according to him, consists in the exhaustion of the limited reproductive power of the cells.

The theory of *Metchnikoff*, on the contrary, looks upon senility

or old age as a disease normally caused by the intestinal poisons stimulating the *macrophages* to eat up our pigments, to devour the higher cells, the cerebral, the muscular, the glandular and to gnaw our bones.

Whenever the toxins penetrate the organism (tuberculosis, syphilis), and whenever the intestinal poisons enter the blood in too great quantities, the phenomena of old age will take place before their time. According to the theory of *Metchnikoff*, we can readily understand why digestive auto-intoxication should cause premature senility.

Growth. The same suffering state of the cells in general and those of the thyroid in particular, is betrayed by the diminution in the growth of auto-intoxicated children, who remain below the size normal to their age.

Autotoxic dwarfism. In some cases the children remain so small that they may be truly called dwarfs.

We mean here a general diminution in the size and volume of the body, which remains small in all its parts.

The body remains well-proportioned, differing in this respect from myxœdematous and achondroplasic dwarfism and is more nearly related to the dwarfism of congenital heart diseases.

The explanation of these facts is found in the interesting experiments of *Charrin* and *Le Play*.

In a first series of cases these investigators by injecting intestinal products sterilized by successive tyndallizations, into pregnant females, obtained dwarfed offspring (*congenital dwarfism*).

In a second series they injected the same intestinal products into animals of the same litter reserving several for control purposes; in this manner they succeeded in producing dwarfism in the injected animals (*acquired dwarfism*).

While the weight of the control animals reached and exceeded 1,300 grams, that of the experimental remained at about 400 grams. The examination of the skeleton and of the different bones showed an enormous difference between those of the injected and non-injected animals, the radiographs indicating that in the injected animals the bones were more transparent and contained less solids, lime and phosphorus.

The digestive poisons, in fact, act in these cases upon the metabolism, which becomes imperfect and upon the thyroid and genital glands which become atrophied; these glands are necessary to set in action and stimulate the evolution of the organism.

It is therefore through a complex process that the digestive poisons engender dwarfism.

Urinary Apparatus

The kidneys, from their incompetency, may be one of the causes of intestinal auto-intoxication. But, likewise, digestive auto-intoxication may in its turn irritate and even inflame the kidneys, owing to a too continuous elimination of intestinal poisons.

Renal congestion. In the case of simple irritation of the kidneys, the insufficiency is only relative, and the albuminuria is minimal, frequently intermittent.

The examination of the centrifuged urine reveals no cylindruria nor renal epithelium.

This is termed, and with reason, *dyspeptic albuminuria.*

We have seen a number of these cases favorably influenced by a lacto-vegetarian diet, combined with a hypochlorized regimen, a combination easily effected.

Nephritis. When the morbid cause has persisted sufficiently long, *true nephritis* may be present, with all its symptoms, albuminuria, insufficient elimination of urea and chlorides.

In the urine of these cases, there is found granular casts, fatty granular casts and renal epithelial elements in great abundance.

III. THE URINE IN DIGESTIVE AUTO-INTOXICATION[1]

A. Physical and Chemical Properties

Daily quantity. There is in auto-intoxication a well-marked oliguria, to which *Boas* has called attention.

Although these cases eat and drink much, the total amount passed during twenty-four hours is very much reduced, ranging

[1] This chapter has been prepared in collaboration with Doctor Amann.

between 300 and 600 cubic centimeters and rarely attaining the normal, 1,200 to 1,500 c.c.

Concentration. Notwithstanding the reduction in quantity, the concentration of the urine is not increased, and its color is generally rather under than over.

The physico-chemical properties, which depend on the concentration in the urine of organic or inorganic matters (specific gravity, cryoscopic constant, vapor tension, etc.), present values generally lower than those of normal urines.

Specific gravity. The specific gravity is below the normal in the great majority of cases. Readings of 1,008 to 1,010 in children, and 1,010 to 1,015 in adults are common.

In certain exceptional cases and without glycosuria, we may find very high specific gravities; 1,032 to 1,035 with considerable azoturia.

Solid constituents. The solid content of the urine naturally follows the variations in the specific gravity; as a rule it is inferior to the normal.

Cryoscopy of the Urine

1st. **The cryoscopic constant Δ.** The freezing point rarely exceeds — 1°, 2, and is frequently lower than — 1°, 0.

2d. **The quotidian cryoscopic valence of Strauss** is the product of the total twenty-four hour quantity (expressed in cubic centimeters) by the depression Δ of the freezing point.

This valence in the healthy adult oscillates between 1,500 and 2,500; it is depressed in auto-intoxication to values ranging between 200 and 700.

3d. **The mean molecular weight.** Calculated from the functional point of freezing, is generally high.

While in normal urine, the molecular weight oscillates around 75, the values found in auto-intoxication frequently exceed 150.

4th. **The coefficient of von Koranyi** $\frac{\Delta}{\text{Na. CL}\cdot -}$ is *per contra* higher than the figure 1.7 conceded as normal by this author.

If we admit his theory of the formation of urine in the kidneys by equimolecular exchanges, we must conclude from the eleva-

tion of this coefficient that, as a rule, auto-intoxication produces a slowing of the renal circulation.

Electrical conductivity. The observations we possess relating to the electrical conductivity of the urine in the auto-intoxicated, are at present but few (about twenty). The results appear to show that the conductivity is generally greater in the auto-intoxicated than in the healthy; this would tend to confirm the elevation in the coefficient of demineralization, which we shall find further on. Nevertheless it seems to us—abstraction made of the small number of our observations—that the phenomena of electrical conductivity are too complicated and depend upon too many factors (concentration of inorganic molecules, their disassociation, the influence of non-electrolytes upon the disassociation and the rapidity of translation of the ions, etc.), to enable us to derive from it directly useful information.

Refraction of the Urine

We have *per contra* made a very complete study of the refractive properties of the urine, and we have reached the conviction *that the measure of the index of refraction of the urine* (taken, for example, by means of the immersion refractometer of *Zeiss*), is capable of furnishing to the clinician findings most useful in the diagnosis and symptomology of auto-intoxication.

We will state very briefly the conclusions at which we have arrived.

1st. Quotidian valence of refraction. That is, the product of the quantity of urine passed in twenty-four hours (expressed in cubic centimeters), measured by the difference in the index of the urine and distilled water; *this valence which may be considered as the measure of the ordinary urinary depuration, is nearly always lower in the auto-intoxicated.*

We have observed in intestinal auto-intoxication, readings generally lower than 8, sometimes below 2; this last figure would be equivalent to a urinary depuration less than one-fifth of the normal.

This insufficiency of urinary depuration in intestinal auto-intoxication is a consequence of the digestive toxæmia, which has not been sufficiently insisted upon.

The deficiency in the urinary depuration depends, in fact, upon the vitiated organic mutations and the slowing up of the normal metabolism; they give rise to the formation of abnormal and incompletely metamorphosed waste products; these being retained and accumulating in the tissues, add their cellular toxicity to the digestive toxæmia.

In some cases, and they are not rare, we may observe *polyuria*, at times *pollakiuria*, either from nervous origin or from local congestion. This signifies some more acute outbreak of auto-intoxication or else an eliminative crisis through the kidneys. But even in these cases, in spite of the increase in the quantity of urine, the urinary depuration measured by the valence of refraction, still shows that it is insufficient.

2d. Measure of metabolic insufficiency. The measure of the urinary refraction combined with the results of chemical analysis can furthermore give us exact information.

(*a*) Upon the presence in the urine of abnormal waste from nutrition and denutrition.

The nature of the waste, as a rule, completely escapes chemical analysis.

(*b*) Upon the proportion of the abnormal waste to the total waste.

This proportion of abnormal waste, which betrays and measures the imperfections of metabolism, is *very high* in the auto-intoxicated, in whom it forms 20, 30, even 40 per 100 of the total waste, whereas in the normal state it is about 10 per 100.

All that we know of organic mutations indicate that from the chemical standpoint the most general final result of the vital metabolism consists in scission of the large molecules introduced into the organism through alimentation, a scission which liberates the energy necessary for the maintenance of life.

We can therefore conclude that the presence in the nutritional waste of *large molecules*—which, as a rule, are *toxic* molecules—is a true indication of defective organic function.

3d. Specific volume of urinary molecules. It is known that molecular refraction may be considered a fairly exact measure

of the *molecular volume* (*Brühl*). We have found in the ratio $\frac{\Delta n}{\Delta d}$ a very easily and exactly measurable value, one which gives precise information upon the specific refraction and the mean specific volume of the urinary molecules.

This ratio is formed by the difference in the indices of urine and water, divided by that of the density of the two liquids.

The presence of these large toxic molecules in the urine of the auto-intoxicated should be expected *a priori*. This is, in fact, verified by the values obtained from the above-mentioned ratio (*specific differential refraction*); they are as a rule considerably higher than in the normal state[1].

4th. Superficial tension. In a work published in 1902[2], one of us showed that the measure of diminution of the superficial tension (lowering of the capillary constant) was susceptible of furnishing very useful data upon the presence and proportion in the urine, of certain abnormal constituents, which frequently escape chemical analysis, but are readily detected because of the property they possess, of lowering to a greater or lesser degree the superficial tension of the urine.

As the drop method by means of the *stalagmometer* readily permits the measurement of the capillary constant, it has been adopted by a number of hospitals and clinics.

From the point of view of our subject, we have found that in intestinal auto-intoxication, almost without exception, *the urine presents a specific depression of the capillary constant, either strongly or very strongly marked;* this depression is one of its most characteristic and most constant symptoms.

5th. Viscidity. One more physico-chemic property of the urine remains to be mentioned; its viscidity (or its inverse, fluidity) measured by the method of *Ostwald*. It is known that this property is in relation with the osmotic pressure and electrical conductivity, inasmuch as it influences the electrolytic disassociation and the rapidity of translation of the ions.

[1] The description of these new methods and the numerical results obtained, will be found in the work of Doctor Amann entitled (Étude sur la refraction des urines normales et pathologiques. Bull. Soc. vaudoise des. sc. nat., 1906.)

[2] Amann: Revue Médicale de la Suisse romande. 1902.

We have only a small number of observations relating to it. The fifty and odd measures of viscidity bearing upon intestinal auto-intoxication, have given us a coefficient of viscidity generally higher than normal.

We shall, moreover, complete this study and extend it to several other properties of the urine, such as the tension of vapors, specific heat, diffusion, compressibility, etc. We shall not include the results of spectroscopic, spectrometric and polarimetric examinations, as they do not offer sufficiently general characters from the standpoint of auto-intoxication.

B. CHEMICAL PROPERTIES OF THE URINE IN AUTO-INTOXICATION

Examples of Analyses in Auto-intoxication

	M. G.	M. de S. M.	M. B.
Quantity	750.c.c.	600.c.c.	1260.cc.
Specific Gravity	1017.0	1037.0	1015.0
	Grams per liter		
Solids dissolved	36.00	86.90	34.10
Mineral Substances	13.80	32.90	9.50
Acidity	1.10	4.10	1.20
Urea	16.10	47.40	19.20
Ammonia	1.20	4.70	0.47
Uric Acid	0.28	0.74	0.19
Ureic Nitrogen	7.50	22.10	9.00
Puric Nitrogen	0.10	0.26	0.07
Extractive Nitrogen	0.91	2.59	1.34
Total Nitrogen	9.56	28.94	10.80
Oxalic Acid	40.m.g.	115.m.g.	25.m.g.
Acetone and Diacetic Acid	45.m.g.	75.m.g.	20.m.g.
Chlorides	3.10	9.90	2.90
Phosphoric Acid	1.65	3.82	1.73
Total Sulphuric Acid	1.18	2.70	1.56
Sulphuric Acid of the Sulphoethers	240.m.g.	490.m.g.	152.m.g.
Phenols and Oxyacids	75.m.g.	95.m.g.	25.m.g.
Indols	20.m.g.	50.m.g.	20.m.g.
Urobilin	10.m.g.	80.m.g.	20.m.g.

Urinary Coefficients in Auto-intoxication

	Per 100	Per 100	Per 100
Coefficient of Bouchard	44.4	54.5	56.4
Coefficient of demineralization	38.4	37.9	27.8
Coefficient of acidity	3.2	4.7	3.5
Coefficient of nitrogenous	78.5	76.5	83.3
Coefficient $\frac{\text{Nitrogenous ammonia}}{\text{Total nitrogen}}$	10.9	13.5	3.6
Coefficient $\frac{\text{Puric nitrogen}}{\text{Total nitrogen}}$	0.3	1.1	0.7
Coefficient $\frac{\text{Extractive nitrogen}}{\text{Total nitrogen}}$	9.2	8.9	12.4

Coefficient of dephosphorization		17.2	13.2	16.0
Coefficient of desulphuration		12.3	9.3	14.4
Coefficient of dechlorization		85.4	34.3	26.7
Coefficients of Auto Intoxication	Baumann	12.1	18.1	3.8
	Amann	1.66	5.3	1.4
	Combe	993.0	450.0	324.0

As we cannot mention here all the characteristic features which detailed quantitative and qualitative analyses furnish and of which we possess several thousands, it will suffice to give an idea of them, to reproduce three of these analyses bearing upon three principal types of urine.

The first (M. G.) is that of a man with mediocre appetite and free from hereditary taint, while the second (M. de S. M.) is that of a large eater, arthritic and nervous; the third finally may be considered as about normal; it is that of a person (M. B.) in perfect health.

The age of the three persons was nearly the same, about twenty years. In the case of M. G. we notice that all the acts of nutrition are slower; the urea, the uric acid, the salts in general, the sulphur, the phosphorus, evidences of the protoplasmic disassimilation are excreted in lesser quantities than normal; this is the type common to the auto-intoxicated.

In M. de S. M., on the contrary, the acts of metabolism are exaggerated; this is the rarest type in intestinal auto-intoxication. Digestive auto-intoxication is manifest in both; *the sulphoethers, the aromatic compounds are excreted in excess*, which is the index of an abnormal formation and absorption of the products of microbic putrefaction of the proteids.

Let us add (although the matter is not clearly demonstrated) that the exaggeration in the proportions of acetone and ammonia excreted, leads to the supposition that there is also in them an increase in the microbic fermentation of the fats and hydrocarbons, which would suggest the diagnosis of a certain degree of acidosis.

C. URINARY RATIOS IN AUTO-INTOXICATION

To make positive deductions from a quantitative analysis, it is necessary to take into account not only the absolute quantities of matters excreted, but also the *ratios* **between these matters.**

The urinary coefficients upon which *Robin* has insisted with good reason, are, in fact, eminently fitted to demonstrate the abnormalities, the deficits in nutrition and the disassimilation.

COEFFICIENT OF BOUCHARD

Ratio between the Amount of Urea and the Total Residue

This ratio indicates approximatively how the organism oxidizes the circulating albumin, in other words, how the nutrition is effected.

COEFFICIENT OF BOUCHARD NORMAL = 50 per 100

In M. G.	44.6 per 100
In M. de S. M.	54.5 per 100
In M. B.	56.4 per 100

Statistics made in the laboratory of *Doctor Amann* from 606 cases of auto-intoxication, have given the following results:

Coefficient of *Bouchard* equal to or higher than 50 in 39.8 per 100 of cases and lower than 50 in 60.2 per 100 of cases.

These figures clearly denote the vitiation of metabolism, and the insufficiency of nutrition in the auto-intoxicated. The high values in ratio are generally found in large eaters.

COEFFICIENT OF DEMINERALIZATION

Ratio between the Inorganic Substances (Mineral Salts) and the Total Residue

This ratio has lately acquired considerable importance, owing to the interesting studies on the importance of the mineralization of the living cell, and the evolution of the salts in the organism.

In M. G.	38.4 per 100
In M. de S. M.	37.9 per 100
In M. B.	27.9 per 100

Statistics made by *Amann*, from this ratio, give values lower or equal to 30 per 100 in 9.36 per 100 of the cases.

Values higher than 30 per 100 in 90.64 per 100 of the cases.

From this, it appears that the exaggerated demineralization of the organism constitutes one of the most general manifestations of auto-intoxication.

COEFFICIENT OF DEMINERALIZATION OF THE PROTOPLASM (OF ROBIN)

Ratio between the Mineral Solids Elaborated (Dechlorized) and the Total Residue

This coefficient is obtained by deducting the weight of the sodium chloride from the inorganic residue, and dividing the difference by the total residue. It assumes particular importance if with *Gaube*, we admit that the mineral matters form the base of cytoplasm. On the other hand, we know that the recent discoveries made in the field of physico-chemistry, demonstrate that the salts play a major part in cell life, in that they govern in all the manifestations of cellular biology.

If we eliminate sodium chloride, the alimentary origin of which is unquestionable, the mineral remainder will, to a certain extent, be the measure of the cellular destruction.

Coefficient of Robin Normal = 9 to 10 per 100

In M. G. we find ..... 15.75 per 100
In M. de S. M. we find ..... 26.4 per 100
In M. B. we find ..... 19.4 per 100

This increase is the general rule in all cases of intestinal auto-intoxication, and is noted in its most diverse forms; it indicates a considerable degree of organic cell destruction.

COEFFICIENTS OF UTILIZATION AND CONSUMPTION

We reunite under this head several ratios of more than ordinary interest, but which have not the clinical value of those we have examined, because too many elements are involved.

In fact, they are under the direct dependence of alimentation, which is so variable, also under that of general metabolism, and they are furthermore influenced by the power of retention of the organism—and this must be taken into account. Finally, it must be said that the elimination of the different products is far from being uniform, as shown by the researches of recent years.

It is extremely difficult to take into account each one of these different factors and to calculate their value even

approximatively, and yet that would be the only way to draw from these ratios useful and truly scientific information.

I. NITROGENOUS RATIOS

Coefficients of the Utilization of Nitrogen

The researches of *Camerer*, *Rubner*, and others have demonstrated that in the normal subject the nitrogen waste is composed as follows:

(*a*) Nitrogen of urea . . . . . 83 per 100
(*b*) Nitrogen of ammonia . . . . . 5 per 100
(*c*) Nitrogen of purin bodies . . . . . 2 per 100
(*d*) Extractive nitrogen . . . . . 10 per 100

When the normal processes of nutrition and denutrition are disturbed, these ratios are more or less profoundly altered.

COEFFICIENT OF THE UREIC NITROGEN

Ratio of the Urea Nitrogen to the Total Nitrogen

This coefficient measures the activity of the nitrogenous nutrition, or better, the *utilization* of the proteids. *Urea*, in fact, represents the normal nitrogen waste of feeble molecular weight.

Coefficient of the Ureic Nitrogen Normal = 83 per 100

In M. G. . . . . 78.5 per 100
In M. de S. M. . . . . 76.5 per 100
In M. B. . . . . 83.3 per 100

The statistics made by *Amann*, from this ratio, give the following results:

Values equal to or higher than 83 per cent. in 7.6 per cent. of cases.

Values lower than 83 per cent. in 92.4 per cent. of cases.

It will be observed that in auto-intoxication the coefficient is almost always lower. This lowering is observed as well in M. G. the badly nourished auto-intoxicated with 9.56 gm., total nitrogen, as in the case of M. de S. M., a large eater with a nitrogen total of 23.94 gm.

COEFFICIENT OF THE PURIN NITROGEN

Ratio of the Purin Nitrogen (Uric Acid, and Xanthin Bases) to the Total Nitrogen

The purin bases (alloxuric), which are found in the urine, and the proportions of which interest the clinician for more than one reason, have a double origin.

Exogenous. Insomuch as they are derived from ingested *purinogenic* foods, that is, those containing a xanthin nucleus, coffee, tea, cacao, meat, meat extracts, brains, sweetbreads, etc.

In the healthy organism a good half of the ingested xanthin bodies appears to be burnt up into *urea*, while the remainder is transformed—and specially—into *uric acid.* It is strongly probable that the badly burnt portion increases considerably whenever the digestion and nutrition are interfered with.

Endogenous, derived partly from the disassimilation of tissues containing alloxuric derivatives, and partly from the functional activity of certain organs, which, like the liver, are the seat of the synthetic formation of uric acid, starting from urea and glycocol (*Horbaczewski*) or the ammoniacal salts and the amino acids[1].

On the other hand, if we consider that the alloxuric derivatives are contained especially in the cellular nuclei, we may, *a priori*, expect to see the ratio of the purin nitrogen present high values in all the diseases accompanied by great destruction of the leucocytes, and most particularly in those cases in which we meet very intense phenomena of leucocytosis and phagocytosis (leukæmia, certain toxæmias, bacterial infections), etc.

For that reason *Robin* terms it *the coefficient of leucocytic activity;* although it only takes in one of the sides of the question. From a general point of view, we must say that even in the physiological state, this ratio is much more variable than the preceding; the factors which influence leucocytosis being, as far as we know, very numerous and diverse.

[1] We here perceive some of those multiple and complicated ratios, which exist between intestinal auto-intoxication, uricæmia and arthritism.

Coefficient of the Purin Nitrogen Normal = 2 per 100

We have not yet made the statistics of this ratio in auto-intoxication, but we are in position to say

that, in the great majority of cases of enteritis, the values are higher than the conceded normal of 2 per 100, whereas they are frequently lower in simple auto-intoxication.

It would seem logical to admit that in enteritis, the intestinal mucosa is the seat of a constant and intense phagocytic reaction against the ever-menacing microbic invasion, favored by the superficial lesions of the mucosa.

This reaction must be accompanied by considerable destruction of the white cells, and this phenomena appears to be one of the efficient causes of the excessive formation of the purin bases, that we find in the urine of enteritis.

COEFFICIENT OF EXTRACTIVE NITROGEN

Ratio of Extractive Nitrogen to the Total Nitrogen

As the extractive nitrogen comprises the nitrogen from all the nitrogenous bodies usually neglected in ordinary analyses (kreatinin, hippuric acid, uroproteic, etc.), it is difficult to attach any very clear significance to the variations of this coefficient. As a matter of fact, these bodies have different origins and their physiological and pathological significance is very diverse; kreatinin, one of the most important among them, must be considered as one of the normal constituents of the urine; in certain proportions, the same may be said of hippuric acid.

Coefficient of Extractive Nitrogen Normal = 10 per 100

In a general manner, it may be said that this nitrogenous waste, which includes a large part of the *abnormal* waste, is increased in all cases in which digestion and nutrition are interfered with, hence in intestinal auto-intoxication.

II. INORGANIC COEFFICIENTS

PHOSPHATURIC COEFFICIENT

Ratio of Phosphoric Acid to the Total Nitrogen Waste

The proportion of phosphoric acid excreted depends upon three factors.

1st. The excretion of part of the alimentary phosphorus.

2d. Disassimilation of the phosphoric elements of the organism.

3d. Pathological retention of phosphorus in the organism.

Phosphaturic Coefficient Normal = 18 per 100

In M. G. ..... 17.2 per 100
In M. de S. M. ..... 9.3 per 100

The statistical results furnished by *Amann* are as follows:

Ratio higher than or equal to normal in 23 per 100 of cases.

Ratio lower than normal in 77 per 100 of cases.

The lowering of the phosphaturic ratio is therefore the rule in auto-intoxication.

It must be attributed to the nutritive defects in the phosphoric elements of the organism (nerve tissues among others).

SULPHURIC COEFFICIENT

Ratio of the Total Sulphuric Acid to the Total Nitrogen

The amount of sulphuric acid excreted depends upon how actively the disassimilation of the alimentary and tissue albumins takes place. With regard to this coefficient, nearly the same remarks can be made as for the coefficient of dephosphorization.

In almost all cases of auto-intoxication, this ratio will be found more or less lowered. The statistics give the following figures:

Coefficient Sulphuric Normal = 16 per 100

Ratio higher or equal to normal in 18.9 per 100 of cases.

Ratio lower than normal 81.1 per 100 of cases.

Here also we note that the lowering of the sulphuric disassimilation is the rule in auto-intoxication.

CHLORINE COEFFICIENT

Ratio of the Chloride of Sodium to the Total Nitrogen

Chlorine being essentially an alimentary product, its excretion depends immediately upon the abundance of the salt in the food. This abundance, as is well known, is subject to great variations.

Moreover, the retention of chlorides in the organism has been noted in certain pathological conditions. Notwithstanding the considerable part assumed by the chlorides in all the phases of cellular life, since they especially regulate the osmotic phenomena upon which all the nutrition depends; it is difficult to draw any certain conclusions from the chloride ratio.

Chloride Coefficient Normal = 70 per 100

We must limit ourselves to noting that in auto-intoxication, the ratio is generally inferior to the normal value of 70 per 100. It is not rare, however, to observe readings higher than normal, sometimes up to 90, 100, 120 per 100 in patients who make excessive use of salt with their food.

Coefficients of Auto-intoxication

These are:

The ammoniuric coefficient.
The coefficient of *Baumann*.
The coefficient of *Amann*.
The coefficient of *Combe*.

I. Ammoniuric Coefficient

There is formed in the intestine from the digestion of food, specially the proteids, relatively large quantities of ammoniacal salts. In the normal state the greater part of these salts, if not the totality almost, are transformed into urea by the liver.

The appearance of ammonia in the urine in exaggerated proportions may be due to several causes (we leave out, of course, those due to bacterial fermentation in the bladder).

1st. To an increased formation of ammoniacal salts, exceeding the converting power of the liver.

2d. To putrefactive processes in the intestine or elsewhere.

3d. To a modification in the functional activity of the liver, which may be physiological or pathological.

Physiological. Whenever the organism is called upon to defend itself against an excess of acidity, the liver appears to exercise a regulative action and neutralizes the acid excess by ammonia, which thus escapes transformation into urea; the ammoniacal salts appearing as such in the urine.

Pathological. The functional alteration of a diseased liver may bring about its insufficiency with respect to its uropoietic function.

In this case also, we find ammoniacal salts in the urine. It will be seen from this brief *résumé* that ammoniuria has multiple significations, which must be carefully considered before concluding upon any one of them. Nevertheless, this coefficient gives valuable indications.

Ammoniuric Ratio Normal=5 per 100

In M. G.	10.9 per 100
In M. de S. M.	13.5 per 100
In M. B.	3.6 per 100

In auto-intoxication, the ammoniuric ratio is always above normal.

Statistics have given the following results:

Ratio, below or equal to 5 per 100 in 11.6 per 100 of cases.

Ratio, higher than 5 per 100 in 88.4 per 100 of cases.

The extreme range observed up to now has been 26 per 100.

II. Aromatic Coefficients

The aromatic bodies derived from the nitrogenous putrefaction in the intestine (aromatic oxyacids, phenols, indols, skatol) combine in the liver, the greater part with sulphuric acid under the form of sulphoethers (or sulphoconjugated acids), a lesser part with glycuronic acid under the form of glycuroethers (or glycuroconjugated acids).

Sulphoethers

The dosage of the sulphoethers is therefore of great importance in the measurement of intestinal auto-intoxication, for they constitute its index.

Sulphoethers, Normal Figure = 100

In M. G. .....140.
In M. de S. M. .....490.

But the sulphoethers being proportional to the quantity of nitrogenous foods ingested, we cannot immediately conclude (as we might be tempted to) that the degree of intoxication is in proportion to the dosage of the sulphoethers, and that M. de S. M., for instance, is intoxicated three times as much as M. G. It is necessary for a correct appreciation, to compare the quantity of the sulphoethers with the amount of nitrogenous food ingested, and this brings us to the **aromatic coefficients.**

Coefficient of Baumann

Baumann, who conceived the first of these coefficients, takes as numerator the total sulphuric acid, and as denominator the sulphuric acid of the sulphoethers.

Coefficient of Baumann Normal = 10 per 100

The greater the degree of auto-intoxication the lower the reading, 10 per 100 being the normal; 5 per 100 represents an auto-intoxication twice as great, etc.

Coefficient of Baumann Reversed

Ratio of the sulphuric acid of the sulphoethers to the total sulphuric acid.

In order to have parallelism between the degree of intoxication and the coefficient, we have been in the habit of reversing the coefficient of *Baumann*, by taking the sulphuric acid of the sulphoethers as numerator, and the total sulphuric acid as denominator.

The reversed coefficient of Baumann increases with the degree of intoxication.

Twenty per 100 therefore represents an intoxication double that of the normal.

We shall have occasion to seriously criticise this coefficient in the chapter on diagnosis.

The ratio may, however, be used, but frequently its indications will not coincide with the other two.

Reversed Baumann Normal = 10 per 100

In M. G. 12.1
In M. de S. M. 18.1
In M. B. 9.8

The following statistics upon this ratio in intestinal auto-intoxication are from the laboratory of *Doctor Amann.*

Coefficient lower than or equal to normal in 5.4 per 100 of the cases.

Coefficient higher than normal in 94.6 per 100 of cases.

Coefficient of Amann

Ratio of the sulphuric acid of the sulphoethers to the total nitrogen.

Combe has designated, under the name of *Amann*, the coefficient which this chemist has originated, and which is a better measure of intestinal auto-intoxication. For, instead of being represented by a numerator derived solely from the aliments, and a denominator representing in great part the organism and the non-nitrogenized aliments as is the case with *Baumann's* coefficient; the coefficient of *Amann* takes as its numerator the sulphoethers, derived solely from the putrefaction of nitrogenous foods (excepting suppurations), and as denominator the total nitrogen derived almost exclusively from the alimentary albumin.

These two terms may therefore be easily compared.

Coefficient of Amann Normal = 1.4 to 1.5

In M. G. 1.6
In M. de S. M. 5.36
In M. B. 1.4

Coefficient of Combe

This coefficient indicates the number of milligrams of aromatic bodies per 100 *grams of total nitrogen.*

The coefficients of *Baumann* and *Amann* do not in all cases dose the totality of the aromatic bodies, because they are not all combined with sulphuric acid and that a part may be excreted under the form of glycuroconjugated acids, which are not dosed by the preceding methods.

To remedy this defect, *Amann* proposed the dosage of the

aromatic bodies in milligrams and their ratio to that of the total nitrogen. It is now ten years since he has denominated this ratio as the *coefficient of Combe.*

Coefficient of Combe Normal=200 to 250

In M. G. . . . . 993.
In M. de S. M. . . . . 580.
In M. B. . . . . 320.

Laboratory statistics give values inferior to or equal to normal in 2.4 per 100 of cases.

Values higher than normal in 97.6 per 100 of cases.

Our experience, actually based upon several thousand analyses, **has shown that the aromatic coefficients are always greatly higher in auto-intoxication.** Undoubtedly it is impossible to say that there always exists an absolute parallelism between the symptoms presented and the aromatic index; for, as in other intoxications, idiosyncrasies play here a large role, and we may observe serious symptoms with a feeble index or *vice versa.*

It is none the less true that based upon experience, we can state positively that **the measure of the aromatic coefficients furnishes us with valuable information upon the functions of the digestive tract, and its annexes from the standpoint of auto-intoxication.**

Autotoxic Cutaneous Diseases

Cutaneous diseases are frequent in all auto-intoxicated, but especially in intestinal auto-intoxications.

The question of the influence of the auto-intoxication, caused by abnormalities of digestion, metabolism and excretion upon the genesis of a large number of dermatoses, was recently discussed in Berlin at the last Congress of Dermatology and Syphilography.

The most authorized representatives of modern dermatological science resolved the question affirmatively. *Radcliffe Crocker* of London, *Duncan Bulckley* of New York, *Jadassohn* of Berne, *Brocq* of Paris, stated that in a large number of diseases of the skin, the lesions were caused by the cutaneous elimination of toxic substances.

Some act upon the skin by direct deposit, others by irritating the nerve terminations, others finally by their elimination through the cutaneous glands cause their inflammation. Undoubtedly these toxic substances do not all come from the intestine. The abnormalities in the nutritional exchanges (metabolism), the insufficiency of the antitoxic glands, the incompetency of the emunctories of the organism. All these causes may, like the intestine, produce toxic substances capable of reacting on the skin and determining in it the same disorders, the same eruptions, in a word, the same dermatoses.

Observations reveal; *Brocq* states—and his observations are based on more than 2,000 urinary analyses—that, if alimentation is excessive, or too scanty, of bad quality or not adapted to the surroundings and climate in which the individual lives; that if these aliments are badly digested, and particularly if badly elaborated in the organism (slowing of the albuminoid combustion), or if the excretory functions (kidneys, lungs) are vitiated, there will gradually accumulate in the fluids and organs of the economy, various excrementitious products more or less toxic, which leave the organism morbidly vulnerable, and this is manifested in the skin by various dermatoses.

From this it appears that, while intestinal auto-intoxication takes a pre-eminent part among the productive factors of autotoxins, it is by no means an exclusive one.

The appearance and the nature of the dermatosis but rarely indicates whether its origin is intestinal or not.

The cutaneous disorders are sometimes under the direct dependence of the intestinal infection, but more often not. While the intestinal toxins provoke more particularly certain dermatoses (*prurigo, strophulus, urticaria, acne, certain eczemas*), it would be a great error to conclude as to the cause from the nature of the lesion, for only the examination and analysis of the urine can definitely answer the question.

We shall limit ourselves to a simple *résumé* of the principal dermatoses observed in auto-intoxication.

Strophulus. Among the affections of infancy, strophulus takes an important part, for it is one of the most frequent.

Although of benign nature and never accompanied by fever

or general disorders, it is observed only in overfed children, who, notwithstanding their rotund appearance, present an anæmic aspect, a waxy pallor very indicative of auto-intoxication. It is especially in infants of three to nine months that it is observed; it is very rare after the second year.

Strophulus infantum is characterized by the appearance on the hands and feet—the palmar surfaces usually—upon the trunk and shoulders, sometimes on the face, of little papules about the size of a lentil, but capable of attaining the size of a pea, and strongly pruriginous.

Their number is variable; at times there are but eight or ten, at others they are very numerous.

The papules are of a clear red color, and their shape is circular, sometimes somewhat irregular. The papule does not form an abrupt elevation with flattened top, but it gradually rises in an acuminated form from its base to its summit, the center of which contains one or more vesicles rather deeply situated in the epidermis, and which can be better felt than seen. These vesicles are only ruptured by the scratching, which gives rise to little crusts, but very often the scratching will not suffice to rupture the vesicles so resistant is the epidermis.

Strophulus is exceedingly pruriginous; the warmth of the bed provokes an intense itching which disturbs the sleep of the little sufferer. During the day and if cool, the itching is less marked, and in light cases the disorder assumes an intermittent type, characterized by outbreaks separated by free intervals lasting from several days to several months.

In the more serious cases, new outbreaks may occur each day. When strophulus has existed for some time it is not uncommon to find in children enlarged ganglions, especially the inguinal, as a result of the secondary infection provoked by the scratching.

We have dwelt upon this affection because we have several times seen it confounded with the itch, to the great detriment of the poor infants, and yet a little attention suffices to make the differential diagnosis.

Pruritus (*lichen, prurigo*). There are a large number of subjects whose nervous systems are subject to disturbances of

either hereditary or acquired nature; these disturbances may be provoked or maintained by the general auto-intoxications or intestinal auto-intoxication in particular.

This nervous perturbation is principally revealed by a special cutaneous vasomotor disorder, which brings about pruritus and the multiple sensations of cutaneous hyperæsthesia.

In a skin thus prepared, the varied traumatisms, scratching in the first rank, provoke the outbreak of diverse lesions (circumscribed and diffused thickenings, papules, etc.).

It is to this *ensemble* of lesions, differing in aspect, but having a common basis that the dissimilar names of *prurigo* and *lichen* have been given.

The pruritus is anterior to and more important than the lesions, and the papule is neither the origin nor the cause. The itching outlives the papules; the papules do not outlast the itching, as *Besnier* well remarked.

This pruritus is of autotoxic origin, and frequently, but not always, of intestinal origin.

Urticaria. The intestinal origin of urticaria from alimentary toxæmias (shellfish, strawberries, eggs, etc.) needs no discussion. It is more discussed in the so-called idiopathic form of which we have observed several cases, either as chronic urticaria, or else as acute febrile crises with eruptions of the skin and mucous membranes; in all these cases the examination of the urine showed undeniable evidences of intestinal auto-intoxication.

We shall only cite two proofs; one of chronic urticaria, the other in the acute form.

Chronic urticaria. In a child, B. C., aged six years.

Coefficient of Combe=629

Phenols	55 mg.
Indol	40 mg.
Skatol	30 mg.
Oxyacids	65 mg.

Acute urticaria. M. J. B., age 18 years. For the last seven years has suffered from internal and external febrile crises, with asthma and muco-membranous enteritis.

Urine quantity	700.	c.c.
Specific gravity	1031.	
Solids	73.80	
Inorganic substances	26.70	
Organic substances	97.10	
Total nitrogen	25.50	
Urea	41.10	
Uric acid	41.10	
Ammonia	4.30	
Indol	35.	mg.
Phenols	55.	mg.
Skatol	25.	mg.
Oxyacids	70.	mg.
Sulphoethers	800.	mg.
Baumann	23.4	
Amann	3.1	
Combe	755.	

Seborrheic eczemas. In the infant these appear to have some connection with overfeeding, and many authors admit their intestinal origin.

But it seems to us much more probable that they are related to the acid auto-intoxications derived from the fermentation of the ternary bodies, the fats in particular, for we have seen several cures result from the use of a buttermilk diet.

Acne vulgaris. The dermatoses which involve the pilo sebaceous follicles or originate from them, are often accompanied by a cutaneous erethism provoked by the ingestion of food, the face being especially affected. The erethism of the skin is seemingly due to a temporary discharge of matters from the organism, these being excreted from the glands of that region bring about their congestion. (*Hallopeau.*)

Acne coincides most frequently with a pronounced seborrheic state, which is due to the same cause and represents the different modes of reaction of the pilo sebaceous system.

Many authors admit that besides predisposition, gastrointestinal auto-intoxication plays an important determining role in the pathogeny of common acne.

Furunculosis. Exactly the same may be said of furunculosis, which is besides too well known to dwell upon.

DIAGNOSIS

How can we diagnose intestinal auto-intoxication?

In a large number of cases the gastrointestinal symptoms predominate so greatly that the diagnosis is evident. But it is far from being always so.

In fact, the first difficulty is that it is not sufficient to say that the affection began with vomiting, colics, fetid diarrheas or constipation; in a word, with more or less accentuated digestive troubles; for these same intestinal disorders are met with in uræmia, septicæmia, and many other infectious diseases, in which they constitute symptoms secondary to the general infection.

Besides, as a second difficulty, there are, as we have seen, a certain number of intestinal auto-intoxications which are masked and are only characterized by disorders of the general nutrition, by anæmia, nervous phenomena, cutaneous eruptions, in a word, by variable and multiple symptoms, all of which may take place without the patient ever complaining of his digestive apparatus.

Only the multiplicity of the symptoms will awaken the suspicion as to a general cause, which might be an intestinal poisoning. As will appear from this simple exposition of facts, the diagnosis of intestinal auto-intoxication is not always easy, for the affection is not always accompanied by a precise and defined symptomatic picture, one carrying conviction; it sometimes assumes the appearance of other diseases, thanks to certain prominent symptoms which hide the slightly marked digestive symptoms. Briefly, at the side of *clear and well-defined forms*, the most frequent and easily diagnosed; there are masked and insidious forms, which must be considered and which we must know how to seek.

Undoubtedly, even in these cases, a careful anamnesis will awaken suspicion; no question but that a careful examination of the patient may bring confirmation, by the finding of unequivocal signs of an enteritis[1] or other signs of disorders clearly intestinal. But in some more obscure cases these signs fail.

We must then have recourse to more demonstrative, more convincing proofs, and these may be sought in the fæces, in the blood and urine of the auto-intoxicated.

I. THE FÆCES

Macroscopic Examination

The appearance of the fæces, their consistency, color, homogeneousness, odor and reaction give information of some importance, but present no certainty.

The macroscopic examination made in a vessel, with a white bottom, after the fæces have been triturated and diluted enables us to recognize mucus and in a gross manner, the undigested foods, which permits us to infer as to the greater or lesser gravity of the digestive trouble.

Microscopic Examination

The microscopic examination of the fæces enables us to recognize with certainty the numerous crystals present in them, to determine their form and nature; it also enables us to recognize intestinal sand.

But it especially enables us to study *and recognize the ingested alimentary residues*, with the aid of *Lugol's* iodine solution which colors the amylaceous matters.

Lastly, the examination easily reveals the eggs of parasites. The microscopic examination therefore serves to characterize, at the same time, the kind and degree of the dyspepsia, whether nitrogenous, fatty, or carbohydrate. This, of course, is of capital importance in the diagnosis and the dietetical treatment, but gives no assurance to the diagnosis.

Bacteriological Examination

The bacteriological examination of the stools give important results in enteritis as we have established elsewhere[2]. But,

[1] Combe: Traitement de l'entérite muco membraneuse. 1906. p. 95.
[2] Combe: Loc. cit., p. 40.

even in simple auto-intoxication, the results are not to be disdained.

In the adult and child the *Weigert-Escherich coloration* shows at first glance a considerable modification of the normal intestinal flora.

The *red flora* has given way to the *blue flora*, and there is found a diminution (often considerable) in the colon bacilli, which, by actual count may fall to 25 or 30 per 100, instead of the normal, 60 per 100.

A disappearance of the *Bacillus lactis aerogenes* is noted.

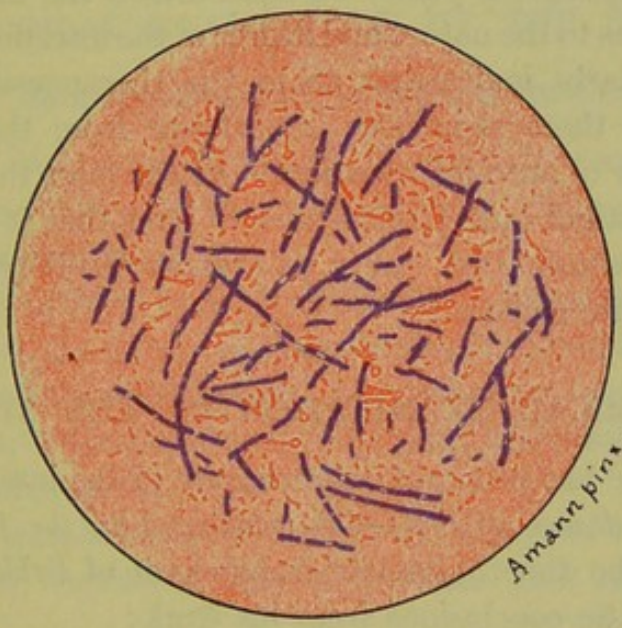

FIG. 2.—MUCO MEMBRANOUS ENTERITIS (*Bacterial Flora*)

Bacillus Mesentericus and *Bacillus Putrificus*. (Weigert-Escherich Stain. Specimen Prepared by Dr. Amann.)

All these aerobic bacilli have been replaced by a large number of strict proteolytic anaerobies, varying with the case; the *proteus, diplococcus, putrificus, putidus, mesentericus, subtilis*, etc.

The researches of *Tissier* and *Grigoroff*, *Massol*[1], have demonstrated that *the anaerobic flora is one of putrefaction* and that it requires an alkaline medium for its development. Hence this *flora always corresponds to a considerable increase in intestinal putrefaction.* In the infant at the breast in whom the intestinal flora is almost solely constituted by the *Bacillus bifidus* of *Tissier*,

[1] Tissier-Grigoroff: Massol. Loc. cit., p. 44.

we find in dyspeptic intestinal auto-intoxication a progressive disappearance of the *bifidus*, the *coli* and *diplococci* taking its place.

From a purely clinical point of view, what we require from the bacteriological examination of the **stools is not the determination of the bacterial species, but only to know if the intestinal flora is abnormal, and if the proteolytic anaerobic bacilli predominate,** *for these findings give important therapeutic indications.*

The microscopic examination of the stools is therefore of great importance. From the examinations we have conducted for more than fifteen years, we have drawn the most valuable indications, as to the nature and degree of the intestinal dyspepsia and particularly indications as to the therapeusis and diet.

But have these signs any importance from the diagnostic point of view of auto-intoxication? At the most they enable us to note intestinal putrefaction, and to infer that it is the cause of the auto-intoxication, but in no manner can they serve either to demonstrate or dose it.

CHEMICAL EXAMINATION OF THE STOOLS

Baumstark[1] has proposed as a measure of the intestinal putrefaction, *the dosage of the indols contained in the fæces* by the reaction of the dimethylamidobenzaldehyde of *Erhlich.*

Here are the conclusions from his work:

1st. The dosage of the indols in the fæces is easily accomplished by the method of *Ehrlich.*

2d. In cases of constipation, achylia, and hyperchlorhydria, there is found a considerable increase of indols in the stools, while in diarrheas a manifest diminution is noted.

3d. In order to dose the degree of intestinal putrefaction, the dosage of the indols in the fæces is not sufficient; it is necessary also, to dose the sulphoethers and indol contained in the urine.

4th. In fact there is often found in very grave cases of intestinal auto-intoxication but a small amount of indols in the fæces, whereas an enormous proportion is noted in the urine.

[1] Baumstark: Arch. f. Verdaunungs Krankheiten, IX, p. 201.

It may be added that *Bauer*[1] endeavors to show that *Ehrlich's* benzaldehyde reaction is due to the urobilinogen and not to indol, and cannot therefore serve to dose the indol as *Baumstark* maintains.

Be it as it may, we can see from the 3d and 4th conclusions of *Baumstark* that the dosage of the indols in the fæces may often serve—although not always—to dose the degree of intestinal putrefaction, but that it cannot serve to dose the autointoxication of the organism.

PHYSIOLOGICAL EXAMINATION OF THE STOOLS

A. Dosage of the Precocious Fermentation of the Carbohydrates

Schmidt of Bonn[2] has proposed in order to recognize and dose the fermentation of the carbohydrates that examination of the stools should be made.

As a matter of fact, it is very difficult to recognize and particularly to dose the degree of fermentation of the carbohydrates.

The fatty volatile acids derived from them are absorbed, and the greater part consumed in the organism, while only the lesser part is eliminated in the urine.

Those that remain in the stools and the dosage of which might be ascertained, represent only a minimal part of the total quantity.

The gases derived from the fermentation of the carbohydrates are partly absorbed (CO^2); they become mixed with the pulmonary gases and are not dosable. As for the other gases, they are mixed with those of the intestinal nitrogenous putrefaction. They likewise cannot be dosed. The diagnosis of the microbic fermentation of the carbohydrates, is therefore very delicate. To arrive at it *A. Schmidt* has proposed the following method: A normal stool kept at a temperature of 37° (98.6 F.) presents two fermentations; one, the *precocious fermentation* which lasts from twenty-four to forty-eight hours, the other, the *tardive fermentation*, which begins only on the third day.

The first is an acid fermentation with production of (CO^2);

[1] Bauer: Centralbl. f. inn. Med. 1905. p. 34.
[2] Schmidt: Zeits. f. phys. Ch. X, p. 230.

it is produced by the carbohydrates. The second is a nitrogenous putrefaction producing hydrogen, methane, phenol, indol and skatol.

There is in effect a sort of competition between the digestive juices and the microbes of the intestine; what the first do not utilize becomes the prey of the latter.

Moreover, if the intestine does not promptly absorb the transformed products—sugar, for example—the microbes bring about their fermentation.

In this incessant struggle the intestine brings into play all its resources of secretion, digestion, absorption and motility, so as to prevent stagnation and take away in the quickest possible manner, the digested products from the microbes.

Since only the free carbohydrates are subjected to the precocious fermentation, the result is that, it (the precocious fermentation) shows the function of the intestine from the standpoint of the digestion of the carbohydrates, and from the standpoint of their absorption.

When therefore in the stools from two individuals receiving the same food, we find in one a considerable and prolonged precocious fermentation, while in the other it is feeble, we can assert that the first suffers from insufficiency of the small intestine, because his stools contain a strong proportion of inutilized carbohydrates, which the slightest digestive power should have been able to digest and absorb.

Schmidt, through his experiments, has been able to show that there exists a complete parallelism between the intensity of the intestinal fermentation and that of the stool; and this is probably because the fermentative products are the normal excitants of peristalsis, and that the more the stools ferment the less time they remain in the intestine. *Doctor Strassburger*, from numerous experiments, has reached the conclusion that by giving the individual under examination a "febrile diet":

1st. We ought not to find any precocious fermentation in a normal intestine.

2d. That on the contrary, in all intestinal dyspepsias, and in all the functional and organic disorders of the small intestine, the precocious fermentations are intense.

3d. That affections of the stomach or of the large intestine, exercise no influence on precocious fermentation.

This method is therefore of great importance and fills a void, for with regard to the ternary bodies, it is much superior to urinary researches which are still incomplete.

It is more exact than either chemical or microscopical analyses, for the minimal quantities which they cannot detect are brought to light by the method of fermentation. Lastly, it alone, indicates the degree of digestibility of the ternary bodies remaining unused. In practice we use the apparatus of *Schmidt*, which is employed as follows:

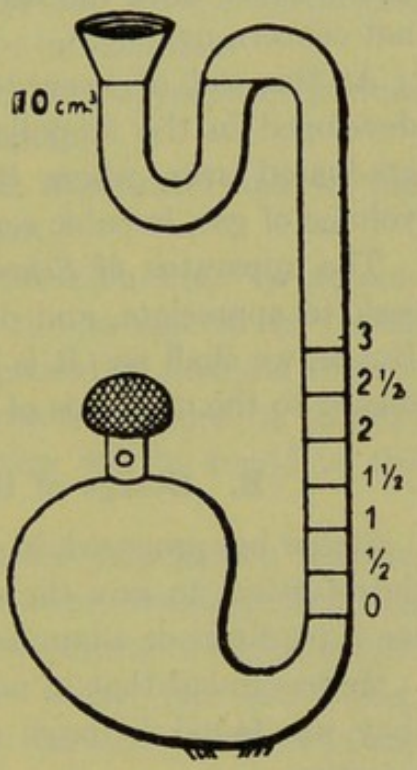

FIG. 3.—APPARATUS OF SCHMIDT.

The apparatus of Schmidt consists of a glass tube, bent so as to form a double U, one placed above the other and connected with each other through the straight arm. Fig. 3.

One of the branches of the inferior U has an opening which may be closed by a ground, hollow, glass stopper, having on one side a small hole corresponding to a similar aperture in the tube itself; immediately below the stopper, the tube is enlarged into an ampulla.

On the long vertical arm there is a scale divided into half cubic centimeters and whole cubic centimeters, to indicate the volume of gas given off by fermentation. The whole apparatus is fixed in a wooden support.

The same metallic spoon should always be used, so that the same quantity of fæces is always represented.

To use the apparatus proceed as follows: A certain quantity of the stool to be examined should be taken with the above-mentioned spoon and mixed with 10 c.c. of water, the whole is then poured into the inferior dilated portion or ampulla. Owing to the apertures placed both in the stopper and the neck of the ampulla, it is possible to bring the mixture to the degree marked

0 on the scale. This done, the stopper is turned so as to exclude all exterior communication.

This accomplished, the superior U having a funnel-shaped opening, is filled with 10 c.c. of water, and the apparatus is then placed for twenty-four hours in an incubator, at a temperature of 37° (98.6 F.).

At the end of twenty-four hours the apparatus may be taken out, as the precocious fermentation which alone interests us is terminated; later the tardive fermentation begins, but it does not concern us.

At the end of twenty-four hours the carbonic acid (CO^2) developed in the ampulla, forces the liquid mixture into the graduated arm, where the scale enables us to measure the volume of gas, in cubic centimeters.

The apparatus of *Schmidt* is hence most valuable when we seek to appreciate, and dose a dyspepsia from ternary bodies. But as we shall see, it is of more than relative usefulness with regard to the diagnosis of auto-intoxication.

B. Dosage of the Albuminous Putrefaction

Stutzer has proposed, in order to dose the degree of nitrogenous putrefaction, to mix the stool with gastric juice or trypsin to see if peptones or albumoses develop.

He has found that in normal cases none are formed, whereas they are found in large quantities in affections of the large intestine.

This method is much more complicated than *Schmidt's*, since we must seek chemically for the presence of the peptones, whereas in the carbohydrate method, the quantity of carbonic gas is directly appreciated.

It is therefore a laboratory method, rather than a clinical procedure.

Besides, from the clinical standpoint, the analysis of the nitrogenous putrefaction is much less useful than that of the fermentation of the ternary substances; because urinary analysis easily reveals albuminous putrefaction, while it only gives a very incomplete idea as to the fermentation of the ternary bodies.

From the foregoing, it will be seen that the direct, the microscopic, the bacteriological and even the physiological examinations of the stools, furnish most interesting and important results from the standpoint of digestion and dyspepsia, also with regard to the intensity of the ternary fermentation and nitrogenous putrefaction, *but none of these methods give us any idea of the degree of digestive auto-intoxication.*

For we may see individuals with excessively fetid stools, showing an advanced state of putrefaction, who, nevertheless, manifest no symptom whatever of auto-intoxication.

Whereas others, on the contrary, having apparently normal stools suffer from serious auto-intoxication.

This is owing to the differences in absorption and to the defense offered by the intestinal mucosa.

A strong degree of intestinal putrefaction may be accompanied by diarrhea, which diminishes the passage of the toxins into the circulation; it may be accompanied by lessened absorption, as for example, when the mucosa is covered by mucus; in these cases large quantities of toxins will be found in the stools, and but few in the blood.

In the second place a strong intestinal putrefaction may be accompanied by a good defense, by a considerable destruction of enterotoxins in the various lines of organic defense, which will diminish the penetration of the toxins into the blood. Here again we will find many toxins in the stools and few in the blood.

Whereas, if on the other hand we have a feeble intestinal putrefaction but increased absorption, owing to more or less deep ulcerations of the mucosa, or if we have insufficiency of the antitoxic organs, we shall find only few toxins in the stools but large quantities in the blood.

We can therefore see that what is really important from the standpoint of diagnosis and the dosage of the degree of auto-intoxication, is in no manner the absolute quantity of putrid matters contained in the stools, but solely the proportion of these substances that have been able to enter the blood; for it is this quantity, which alone can react on the entire organism and intoxicate it.

II. The Blood

Can we dose enterotoxæmia of intestinal origin by direct analysis of the blood?

Chemical Diagnosis

For reasons easily understood, the chemical analysis of the blood is practically impossible and specially so clinically.

On different occasions *Amann* has found the aromatic bodies increased in the blood of auto-intoxicated subjects, but the analysis is long and difficult, and, moreover, does not give any information which may not be more easily found by urinary analysis.

Physiological Diagnosis

The only means of dosing, not the aromatic substances present in the blood but the enterotoxins which circulate in it, would be to inject the blood of an affected individual into the veins of a healthy one, which of course, is practically impossible.

For, in fact, if human blood is injected into an animal, a number of morbid symptoms are always observed, even if the blood is from a healthy man.

How, then, can we pass judgment upon the symptoms produced by the injection of blood from a diseased individual?

The blood of uræmia, of eclampsia, is, in truth, hypertoxic, but its composition is also modified, its chlorides, sulphates, and urea content is increased, and that alone, without mentioning the toxins, might suffice to kill an animal.

On the other hand, observations have shown that the blood of diabetic coma acts indifferently. How, then, can we draw any conclusion from the physiological diagnosis of the blood?

III. THE URINE

The method of injection of blood from the auto-intoxicated, having failed to give any practical results from a diagnostic point of view, attention was naturally directed to researches bearing upon the principal emunctories of the body: the kidneys.

The enterotoxins present in the circulation are eliminated in small part by the respiration and perspiration, as we have already seen, but it is particularly through the urine that they are excreted, and it is in it that we must seek them and attempt to dose them.

For this purpose several methods have been proposed:

1st. The physiologic urinary diagnosis.

2d. The chemical urinary diagnosis.

3d. The physical urinary diagnosis.

PHYSIOLOGIC URINARY DIAGNOSIS

Bouchard, the first to take up this question, has studied it in all its aspects in a series of most interesting investigations. He demonstrated first that the urine was toxic and that even filtered and sterilized it affected or killed the animals into whose veins it had been injected.

He then made evident the many poisons which it contains, and the physiological analysis of their toxicity showed that it was composed of varied elements, such as convulsive poisons, poisons acting upon the pupils, diuretic principles, etc.

The necessity of having a uniform standard, which would allow the dosing of the urinary toxicity, and could also serve as a term of measure and comparison, naturally led *Bouchard* to establish the *urotoxic coefficient* (the number of urotoxies elaborated per kilogram in twenty-four hours).

The urotoxic is the quantity of urine necessary to kill one kilogram of living matter (of the experimental animal).

Provided with this measure, *Bouchard* made comparative studies from the standpoint of their toxicity, of the urines excreted in various diseases, and in particular those of gastro-intestinal auto-intoxication.

He thus succeeded in showing that the febrile urines, those of infectious diseases and eclampsia had a very high urotoxic coefficient.

Pursuing these studies upon the urine of auto-intoxication, *Bouchard* proved that in this condition, also, the urotoxic coefficient increased with the degree of intestinal putrefaction

and decreased when efficacious intestinal disinfection was practiced.

It thus appears that the urotoxic coefficient may, if need be, serve to dose intestinal auto-intoxication, but in no manner can it serve to diagnose it; for the reason that a high urotoxic coefficient is found in the most diverse diseases, and that the hypertoxic property of the urine is observed in all the infectious diseases, and in many nutritional affections. This was the first fault found with physiologic diagnosis; but a second one much more serious was soon discovered, and that was that the urotoxic coefficient not only indicated the toxicity of the urine, but that it comprised quite a series of other factors which we shall enumerate.

Beck and *Hymans v. den Bergh*[1], among the first, found in *Bouchard's* method many causes of error.

1st. The quantity of liquid injected increases the blood pressure; this, according to *Lesné*—a pupil of *Bouchard*—may cause thrombosis in the right heart and pulmonary embolism; these alone may cause death of the animal.

2d. The various species of rabbits, and even different individuals, show different degrees of resistance to the injection of the same quantity of urine.

3d. The salts of potassium and ammonia contained in the urine are the most harmful, for if the urine is made free of them it becomes almost harmless.

In fact, for *Charrin*, the urotoxic coefficient depends three-fourths upon the potassium salts, and for one-fourth only upon the extractive matters.

Lepine goes even further, for he states that 85 per 100 of the noxious action of the urine is due to the salts and only 15 per 100 to the organic substances.

4th. Lastly, the urine and the blood are far from being isotonic fluids; their osmotic pressure[2] is very different; while in

[1] Beck & Hymans v. den Bergh: Zeits. f. klin. Med., XXXV.

[2] The osmotic pressure or absorbent power of water, is proportional to the quantity of molecules in solution in a given volume of liquid (a liter).

(Abstraction is made here of the influence of the electrolytic disassociation by adding to the term *molecules* the acception molecules + ions.) This quantity of molecules in solution can be measured by cryoscopy, for the depression of the freezing point is proportional to the osmotic pressure.

Two liquids containing in solution the same number of molecules (of no

the blood it is equivalent to about 6 or 7 atmospheres, that of the urine is as a rule three to four timer greater.

The addition to the blood of a liquid, such as the urine, which possesses such different properties, must therefore produce considerable alterations by breaking the normal equilibrium between the various histological elements; first, in the blood cells and the serum. This forcible disturbance of the osmotic equilibrium suffices in itself to cause all the morbid symptoms observed by *Bouchard*, and to bring about the death of the experimental animals.

En résumé, in physiologic urinary diagnosis, osmosis exceeds the harmfulness of the toxins.

Bouchard[1] admits these objections; but according to him, the part played by the isotonic defect and the blood plethora resulting from the injection, represents only one-fourth of the total noxious effects. Hence, according to *Bouchard*, even when only the crude results of the intraveinous injection are taken into account, we still obtain valuable information.

Such is not the opinion of the German authors.

Schiffer, *Stadthagen*, and *Posner*, in order to determine the role of osmosis, made quite a series of experiments by making subcutaneous injections of salt solutions in animals, always of the same weight (white mice). With strong saline concentrations they obtained toxic effects as marked as those *Bouchard* noted from his intraveinous injections of urine.

By varying the degree of concentration, they observed symptoms proportional to it, and furthermore, with the same degree of concentration, the urine no longer produced any effect, and became harmless. *Brieger* was even able to inject into guinea pigs—in a single day—fifteen times their own weight of fresh urine rendered isotonic, without affecting them.

En résumé, the urotoxic coefficient cannot be considered, an exact measure of the quantity of enterotoxins contained in the urine.

matter what bodies) present the same osmotic pressure, and the same depression of the freezing point, and are said to be *isotonic*. It is thus, that the blood is isotonic with a solution containing 0.9 g. of NaCL per liter. (The former classical figure of 0.7 refered to frog's blood).

[1] Bouchard: XIII, Congrès international de Médecine. Paris. 1900.

It therefore cannot serve to dose the degree of auto-intoxication, much less to diagnose it.

Chemical Urinary Diagnosis[1]

To fully understand what are the diagnostic elements to be found by analysis of the urine, it is essential to clearly remember the substances produced in the intestine by the decomposition of the albuminous molecule, and to have a clear notion of those produced by the digestion of the enzymes on the one hand, and those produced by the action of bacteria on the other. For it is only in the latter that the elements of chemical diagnosis will be found.

These we shall recapitulate:

A. Digestion by the Enzymes. *Non-crystalline bodies:* albumoses, peptones, ammonia.

2d. *Acid crystalline bodies:* (diaminated acids).

(*a*) *Fatty series:* leucin, glycocol, alanin; aspartic and glutamic acids.

(*b*) *Aromatic series:* tyrosin, phenylalanin, indolalanin.

3d. *Basic crystalline bodies:* (monaminated acids) lysin, histidin, arginin.

B. Microbic digestion. The microbic digestion gives rise in the first place to the same bodies as the proteolytic digestion by the enzymes of the stomach and intestine.

1st. *Non-crystalline bodies:* albumoses, peptones, ammonia.

2d. *Acid crystalline bodies* (diaminated acids): leucin, glycocol, alanin, aspartic and glutamic acids, tyrosin, phenylalanin, indolalanin.

3d. *Basic crystalline bodies* (monaminated acids; lysin, arginin and histidin.

But the microbic digestion does not rest there, for besides, it gives rise to two other groups of bodies, one belonging to the fatty series, the other to the aromatic series.

4th. *Bodies of the fatty series:*

(*a*) *Ammoniacal salts*, butyric, caproic and valerianic acids.

(*b*) *Ptomaines.*

5th. *Aromatic series:*

[1] This chapter has been written in collaboration with Doctor Amann.

(*a*) *The aromatic oxyacids:* paraoxyphenylacetic and paraoxyphenylpropionic acids.

(*b*) *The phenols:* the phenols and cresols, principally the paracresols.

(*c*) *The indols:* indol and skatol. The bacteria act therefore on the albuminous molecule, by decomposing it into bodies of the fatty and aromatic series.

These bodies cannot be utilized by the organism; they are not burnt up in it with the liberation of heat. They are consequently excrementitious matters more or less harmful, and the economy seeks to get rid of them through its various natural emunctories, after having rendered them less noxious by combining them in the liver, with sulphuric and glycuronic acids. A glance at the two tables shows that it is among the bodies of the fatty or aromatic series that we must seek for the diagnostic elements.

Let us examine these different bodies from the standpoint of diagnosis.

Fatty acids. The fatty volatile acids are especially a product of the microbic fermentation of the ternary bodies; for the feeble formation of these volatile acids from the decomposition of leucin is too slight to be taken into account.

For these two reasons we must leave out the fatty acids as a means of dosing the nitrogenous putrefaction of the intestine.

Ptomaines. The ideal would be to have some sure, easy and simple chemical procedure allowing the dosing of the ptomaines.

For they alone are the true toxic substances causing intoxication, and their dosage would furnish the most exact method of appreciating intestinal auto-intoxication.

Unfortunately no such procedure is as yet known, and the practical method is still to be found.[1]

Aromatic bodies. We are therefore obliged to fall back on the aromatic bodies.

Undoubtedly these are not the real toxic substances, but like

[1] Dombrosky: (Semaine Med. 1902. p. 252) has indicated a method which not only permits the detection but the dosage as well of the toxalbumins in all urines whether normal or pathological. This should deserve attention and confirmation.

the ptomaines, they develop parallelly with the intensity of putrefaction.

They may therefore serve as index to the latter (the ptomaines).

For do we not do the same with carbon dioxide?

When we ascertain its quantity in our schoolrooms, we know perfectly well that it is not the true toxic substance that is dosed, but only its index.

Jaffé, *Baumann* and *Brieger* have shown that the products of nitrogenous putrefaction belonging to the aromatic series, are excreted almost entirely through the urine, in which they may be dosed.

Finally, *Baumann* has proved that these bodies with the exception of part of the oxyacids, are combined with either sulphuric or glycuronic acid. The first appear in the urine as sulphoethers or sulphoconjugated acids; the latter as glycuro-conjugated acids.

Hence we can chemically dose the aromatic compounds in the urine: (*a*) as sulphoethers; (*b*) as aromatic substances in nature.

A. Dosage of the Sulphoethers

Can we dose intestinal auto-intoxication by dosing the sulpho-ethers?

From this two questions arise:

1st. The first is:

Can the sulphoethers be looked upon as an index of intestinal nitrogenous putrefaction and of that only?

We need not refer here to the origin of the aromatic bodies, for we have already studied it.[1] That study permits us to state that:

Normally the sulphoethers may be regarded as an index of intestinal nitrogenous putrefaction, because they are derived only from the microbic nitrogenous putrefaction of the intestine. Naturally this does not include those cases where the body albumin undergoes local decomposition, as in an abscess, purulent collections, ulcerated carcinoma, etc. In these conditions, the

[1] See "Origin of the Aromatic Bodies."

same aromatic compounds are produced by the same bacteria, and are eliminated by the urine under the form of sulphoethers.

We can therefore conclude that:

Leaving out organic suppurations, the sulphoethers are solely derived from the microbic intestinal putrefaction produced at the expense of the proteids, the nucleo albumins, the pancreatic and intestinal juices, the bile and the intestinal mucus[1].

2d. The second question which arises is:

Is the quantity of the sulphoethers proportional to the degree and intensity of the putrefaction taking place in the intestine?

This question may be answered affirmatively, thanks to the later researches made by *Baumann*, *Nuttall* and *Thierfelder*.

Baumann[2], in a dog fasting for a long period, found only traces of the sulphoethers in the urine, and after disinfection of the intestine by means of strong doses of calomel, he found that the sulphoethers, indols and phenols had completely disappeared from the urine.

Nuttall and *Thierfelder*[3], by their beautiful experiments, gave the final solution of the problem:

They demonstrated that animals having a sterile intestine and who had received sterile food only, excreted a urine which contained not the slightest trace of indol, skatol, phenol, cresol, pyrocatechin, or of the sulphoethers.

The oxyacids, on the contrary, were found in slight quantities, owing probably to the organic digestion of the proteolytic enzymes.

Thanks to these experiments, it can be understood why the meconium and the stools of the newborn do not contain any aromatic bodies, while the urine contains sulphoethers communicated to it from the blood of the mother. It explains why, in the suckling, the stools contain but few aromatic substances and the urine but slight quantities of sulphoethers, for the intestine has but few microbes and the fæces do not remain long in it.

[1] See "Origin of the Aromatic Bodies."
[2] Baumann: Zeits. f. phys. Ch. XVI, p. 221.
[3] Nuttall & Thierfelder: Zeits. f. phys. Ch. XXII, p. 71.

Quite a series of experiments have been made since; all showing that a diminution of intestinal putrefaction always corresponded to a diminution in the sulphoethers and *vice versa*.

Morax[1], by means of intestinal antiseptics; *Rovighi*[2], by means of intestinal lavage with tannic and boric acid solutions, succeeded in diminishing in man the intensity of putrefaction in the large intestine and parallelly the proportion of the sulphoethers in the urine.

Poehl, Biernacki, Hirschler and *Winternitz* demonstrated that the same result may be obtained by modifying the diet and administering carbohydrates only, and that to the decrease of the intestinal putrefaction, there corresponded also a decrease in the sulphoethers, which fell to a third, even a fifth, of their previous quantity.

This was confirmed by *Tissier* and *Cohendy*, who administered bouillon cultures of bacilli lactis. On the other hand, *Mester* showed that high or tainted foods greatly increased the proportion of the urinary sulphoethers[3].

From all this we can conclude that:

The quantity of sulphoethers in the urine is proportional to the intensity of the putrefactive processes in the intestine, and that it enables us to measure them.

This conclusion, however, does not apply:

1st. To individuals taking medicines belonging to the aromatic series (salol, phenol, naphthol, etc.).

2d. To organic suppurations and infections, in which the bacteria destroy the albumin in the same manner as in the intestine.

Stern[4] has made an objection to this method which we cannot pass by. According to him, the quantity of sulphoethers in the urine is not proportional to the degree of intestinal putrefaction, but solely to the power of absorption, which varies greatly according to individuals. This is true, for even in an

[1] Morax: Zeits. f. phys. Ch. X, 318.
[2] Rovighi: Zeits. f. phys. Ch. XVI, p. 46.
[3] Mester: Zeits. f. klin. Med., XXIV., p. 441.
[4] Stern: Diss. inaug. Breslau. 1892.

intestine portions of which absorb badly, the sulphoethers may still be absorbed in considerable quantities by the parts remaining healthy.

But to this objection of *Stern*, we can oppose the fact that if the sulphoethers are badly absorbed, the *ptomaines will also be*, and, since it is only the substances *that are absorbed* that cause auto-intoxication, they are consequently dosed by the sulphoethers.

The objection of *Stern* thus falls of itself.

Dosage

Sulphuric acid is found in the urine under two forms:

(*a*) Combined as sulphates.

(*b*) Combined as sulphoethers.

I. Dosage of the total sulphuric acid. Urine 50 c.c. + 5 c.c. of strong hydrochloric acid + 10 c.c. barium chloride solution (barium chloride 30.5 to one liter), heat over flame for fifteen minutes.

The hydrochloric acid decomposes the sulphoethers into aromatic bodies and sulphuric acid. The latter combines with the barium and forms a precipitate of barium sulphate.

The sulphuric acid of the sulphates does the same.

Allow sedimentation to take place, then filter, follow by washing sediment, drying, calcining and weighing.

The weight found (I) corresponds to the total sulphuric acid.

II. Dosage of the sulphuric acid of the sulphates. Urine 50 c.c. + 5 c.c. of acetic acid (which does not decompose the sulphoethers) + 10 c.c. barium chloride solution.

Heat slightly; the sulphuric acid of the sulphates combines with the barium and precipitates. Allow sedimentation, filter, wash, dry, calcine and weigh.

The weight found (II) corresponds to the sulphuric acid of the sulphates.

The difference (I – II) multiplied by the constant factor, 6.8692, gives in milligrams the quantity of sulphoethers contained in one liter of urine.

Normal Quantities of the Sulphoethers during 24 Hours

	Grams
Newborn	0.000[1]
One to five years	0.50 to 0.80[2]
One to fifteen years	0.80 to 0.100[3]
Adults	0.100 to 0.150[4]

A. Physiological Variations

	Grams
Time, 8 A.M.	0.061 per 1,000[5]
Time, Noon	0.027 per 1,000
Time, 8 P.M.	0.147 per 1,000

Diet

1st. Diminution of the Sulphoethers

Vegetarian regimen. *Hoppe-Seyler*[6] points out the marked influence of a vegetarian diet, on the diminution of the sulphoethers.

Lactose. *Strauss*[7] observed a decrease of more than one-half in the proportion of the sulphoethers, by adding 100 grams of lactose to the diet.

Before Addition of Lactose	After Addition of Lactose
Sulphoethers 0.290gm.	Sulphoethers 0.180gm.
Sulphoethers 0.412gm.	Sulphoethers 0.240gm.

Milk. *Biernacki*[8], *Matteoda*[9], *Winternitz*[10], noted a decrease in the sulphoethers with a milk diet.

Sour milk. *Poehl*[11] showed the influence of sour milk in the diminution of the sulphoethers. This property has since been made a matter of common knowledge by *Metchnikoff*.

[1] Senator: Zeits. f. phys., Ch. IV, p. 1.
[2] Rovighi: Zeits. f. phys. Ch. XVI, p. 31.
[3] v. de Velden: Virch. Arch. No. 72, p. 345.
[4] v. de Velden: Virch. Arch. No. 72, p. 350.
[5] Poehl: Petersburg. Med. Woch., LXXXVII, p. 50.
[6] Hoppe-Seyler: Zeits. f. phys. Ch. XII, p. 36.
[7] Strauss: Zeits. f. klin. Med., XXIV, p. 441.
[8] Biernacki: Deutsch. Arch. f. klin. Med., XLIX, p. 87.
[9] Matteoda: Diss. Genève. 1894.
[10] Winternitz: Zeits. f. phys. Ch. XVI, p. 17.
[11] Poehl: Maly's. 1887. p. 277.

Kephir. *Rovighi*[1], *Embden*[2], observed a considerable decrease in the sulphoethers by the use of kephir.

Farinaceous foods. *Rothmann, Gottwald, Krauss*[3], *Hirschler*[4], etc., demonstrated the diminution of the sulphoethers with a farinaceous diet.

2d. Increase in the Sulphoethers

Bunge[5] found the sulphoethers increased fourfold with a meat diet; *Rovighi, Mester, Hirschler*, etc., confirmed these findings.

B. Pathological Variations

Stomach. The normal acidity of the gastric juice diminishes the proportion of the ethereal sulphates. In hypochlorhydria and anachlorhydria the sulphoethers increase considerably. The administration of hydrochloric acid greatly decreases their quantity, as noted by *Biernacki*[6]. The prolonged administration of sodium bicarbonate augments the urinary sulphoethers[7]. If the administration of alkalis is prolonged, the quantity of sulphoethers augments considerably and in a durable manner; according to *Kast*[8], *this is the one cause of alkaline cachexia.* At all events these experiments demonstrate the retarding or bactericidal influence of hydrochloric acid; they have been confirmed by those of *Wasbutzki*[9], who noted that in all gastric conditions with hypoacidity, there was a considerable increase of the sulphoethers.

Bile. *Biernacki*[10] has shown that as soon as the bile can no longer flow into the intestine, as in icterus, the sulphoethers are quadrupled.

Intestine. In acute catarrhs with diarrhea, the sulphoethers diminish, while they augment with constipation[11].

[1] Rovighi: Zeits. f. phys. Ch. XVI, p. 30.
[2] Embden: Ibid, XVIII, p. 223.
[3] Rothmann, Gottwald, Krauss: Zeits. f. phys. Ch. XII, p. 16.
[4] Hirschler: Ibid., X, p. 35.
[5] Bunge: Handbuch, p. 315.
[6] Biernacki: Arch. f. klin. Med., XL, p. 87.
[7] Stadelmann: Diss. Stuttgart. 1890.
[8] Kast: Festschrift. 1889.
[9] Wasbutzki: Arch. f. exp. Path., XXVI, p. 133.
[10] Biernacki: Centralbl. f. med. Wiss. 1890. p. 49.
[11] Brieger: Zeits. f. klin. Med, III, p. 465. Gava Ungar: Arch. f. med., p. 288.

Bartoschevitsch[1], in an enteritis, with alternations of diarrhea and constipation found in:

Periods of Diarrhea	0.332	Sulphoethers
Periods of Diarrhea	0.261	Sulphoethers
Periods of Constipation	0.456	Sulphoethers
Periods of Diarrhea	0.190	Sulphoethers
Periods of Constipation	0.627	Sulphoethers
Periods of Diarrhea	0.286	Sulphoethers
Periods of Constipation	0.410	Sulphoethers

Stagnation is accompanied by considerable putrefaction; in consequence it is not surprising to note that *Hoppe-Seyler*[2] found an increase of sulphoethers proportional to the stagnation and varying with the matters causing it.

Constipation. In constipation *Pfungen*[3] found a great increase in the sulphoethers, but only when there was atony with stagnation of matters in the *upper portions* of the intestine.

Hoppe-Seyler, on the other hand, showed that in simple constipation there is no increase of the sulphoethers in the urine.

Perityphilitis. Stokviss and others have studied the proportions of the sulphoethers in perityphilitis, which is accompanied by stasis in the upper part of the bowel, and they found a very marked increase in the sulphoethers; this we have confirmed in all the cases we have observed.

Peritonitis. Salkowski[4], *Hoppe-Seyler*[5], found in peritonitis a great increase in the sulphoethers.

Intestinal obstruction. Salkowski was able to note that in intestinal obstruction the augmentation in the proportions of sulphoethers was enormous, not exceeded in any other disease.

We have ourselves observed in a case of cæcal invagination occurring in a young girl of six years, 935 milligrams of sulphoethers.

B. Dosage of the Aromatic Bodies in their Natural State

The research of the sulphoethers, while not exactly difficult, requires, nevertheless, delicate manipulations, which demand time and experience, and can hardly be done except by a chemist.

[1] Bartoschevitsch: Zeits. f. klin. Med., XVII, p. 56.
[2] Hoppe-Seyler: Zeits. f. phys. Ch. XII, p. 31.
[3] Pfungen: Zeits. f. klin. Med., XXI, p. 118.
[4] Salkowski: Zeits. f. phys. Ch. XII, p. 85.
[5] Hoppe-Seyler: Zeits. f. phys. Ch. XII, p. 31.

Hence it is very desirable to have at command some easy clinical procedure which may be confided to an interne, and which allows the making of daily dosages; in order to note the progress of the auto-intoxication, and to compare them with its course, so as to draw from this double curve the necessary therapeutic indications. We desired another method all the more, because the dosage of the ethereal sulphates does not give an absolutely complete idea, of all the processes of intestinal putrefaction.

For, in fact, there are bacteria: the bacterium of *Eberth* and the streptococcus, for examples, which do not form either indol or phenol at the expense of albumin.

Secondly, the curve of phenol is not absolutely parallel to that of indol or skatol. *Odermatt* maintains that skatol normally occurs in larger quantity than indol, and that, in prolonged putrefaction, indol diminishes and the phenols alone increase.

It is besides known that indol already begins to form in the small intestine and phenol only in the large intestine. A great disproportion in their reciprocal quantities may consequently have some importance in the regional diagnosis of intestinal obstruction, for example:

In our case of cæcal invagination we found:

Indols	0.880 grams
Phenols	0.045 grams
Skatols	0.035 grams

The enormous disproportion between the indols and phenols, and the fearful quantity of indols, led to the supposition that stasis existed in the inferior part of the small intestine; this was in fact, verified by the operation. We may therefore infer that the proportions of the different aromatic bodies may give certain indications as to the course and locality of the putrefaction.

In the third place, it sometimes happens that when the available sulphuric acid is exhausted, the phenols and indols are not found in the urine in the form of sulphoethers, but in the form of glycuroconjugated acids.

Lastly, but particularly, the sulphoethers contain only a slight part of the oxyacids, the rest being eliminated as such.

Neither the glycuroethers nor the oxyacids are measured by the sum of the sulphoethers.

For all of these reasons, it is useful to seek for the phenols, indol and skatol independently of the sulphuric and glycuronic acids with which they are combined, and dose them separately.

Thanks to *Amann*, we are now able to make this dosage, for he has found a method and devised an apparatus for the purpose.

The apparatus has received the name of *Amann's Chromometer*.

The Chromometer of Amann

This apparatus, intended for the colorimetric dosage of the aromatic bodies is copied from *Fleischl's* hemoglobinometer. It is composed of a mounted lens, and is provided with a movable stage, bearing a blue prism for indol and a red one for phenol, skatol, and the oxyacids.

FIG. 4.
CHROMOMETER OF DR. AMANN

The prisms are cut at such an angle that the color intensity will vary according to the thickness of the bevel, so that it suffices to move the stage in one direction or another to bring about a gradual variation in color.

Above the prism there is placed a cell lighted from below and divided into two equal parts; one of the divisions is placed above the prism; this is filled with filtered water, the other receives the colored solution to be examined. The stage is then moved and the intensity of the color varied, until it corresponds as nearly as possible to that of the solution.

The thickness of the colored glass is then ascertained from the scale, and in the tables which accompany the instrument, will be found the quantity of the aromatic body sought for.

To establish these tables, *Amann* made long comparative researches between the colorimetric and the chemical methods; *Kossel* and *Penny*[1] employed the latter for the phenols, and for indol and skatol they used the method of weighing after evaporating and purifying the solution. The oxyacids were measured

[1] Kossel & Penny: Zeits. f. phys. Ch. XVII, p. 117.

colorimetrically by a centinormal solution of paroxybenzoic acid.

By comparing these findings with those of the chromometer, *Amann* succeeded in establishing a scale sufficiently exact for clinical purposes.

The analyses are performed as follows:

I. The Aromatic Oxyacids

According to *Baumann* tyrosin is transformed in the lower portion of the small intestine and in the large intestine—but almost exclusively by microbic action—into *paraoxyphenylacetic* and *paraoxyphenylpropionic* acids, the first splitting up into paracresol, the second into paracresol and phenol.

The oxyacids are therefore intermediary products of intestinal putrefaction, and they increase with its intensity.

They are eliminated through the urine, mostly in state of nature and in small proportion as sulphoethers.

Normal quantity of oxyacids per liter = 0.010 to 0.020.

Normal quantity of oxyacids in 24 hours = 0.015 to 0.030.

Dosage of the Oxyacids

Fifty cubic centimeters of urine + 5 c.c. of concentrated hydrochloric acid are heated in a porcelain cup and concentrated to half.

The salts of the oxyacids are thus decomposed into free oxyacids while their bases are converted into chlorides.

The sulphoethers are also decomposed at the same time into phenols, indols and skatol; a part of the phenols being volatilized. The liquid is allowed to cool and is poured into a graduated tube marked No. 1; to it is added 10 c.c. of ether and the tube is rotated or shaken for fifteen minutes so as to dissolve the oxyacids, the phenols and the indols.

The ether is then removed by means of a pipette and dropped into a tube similar to the first and marked No. 2. The pipetting is repeated three times, so as to remove all of the ethereal solution which is added to the contents of tube No. 2.

For the elimination of the phenols, add to the ethereal solution in tube No. 2, 5 c.c. of decinormal solution of caustic soda and

10 c.c. of distilled water, rotate or shake tube as before; by this means the oxyacids form their sodium salts in aqueous solution, while the ether retaining only the phenols and indols may be pipetted and cast aside.

The aqueous solution is acidulated with 15 c.c. of decinormal sulphuric acid; this decomposes the salts and again sets free the oxyacids. To the acidulated solution, add 10 c.c. of ether and rotate or shake tube as before; in this manner an ethereal solution of the oxyacids is obtained; this should be evaporated in a porcelain cup and the residue taken up by adding 20 c.c. of distilled water. Then add gtt xx of *Millon's* reagent and heat until the maximum color is obtained and examine with the chromometer.

II. The Phenols

The phenols, that is to say, phenol and paracresol are products of the putrefaction of tyrosin from its conversion into the oxyacids.

The phenols are never produced in the small intestine, but only in the large intestine.

Diseases and stasis of the small intestine do not increase the phenols, whereas stagnation in the large intestine is accompanied by abundant production of phenols.

They are eliminated in the form of sulphoethers, a part being oxidized in the system.

Normal quantity of phenols per liter = 0.010 to 0.015.

Normal quantity of phenols during 24 hours = 0.015 to 0.030.

This proportion augments :

1st. *In all organic suppurations:* Empyæmia, putrid bronchitis, pulmonary gangrene, pyæmia and puerperal fever, etc.

2d. *In stasis of the large intestine:* Simple and tubercular peritonitis, perityphilitis, narrowings caused by bridles, acute flexures, tumors, chronic invaginations, paralysis, dilatation, intestinal obstruction or high constipation, which is most frequently spasmodic.

3d. *In all exaggerations of intestinal putrefaction.*

Dosage of Phenols

The phenols found in the urine as sulphoconjugates, must be decomposed into free sulphuric acid and phenols.

For this purpose, heat 50 c.c. of urine with 5 c.c. of hydrochloric acid until reduced to half volume, then add water, 10 c.c., and distill over slow flame; only the phenols will pass over.

The distillation should be conducted so as to leave about 20 c.c. of distillate, which is then diluted so as to bring it up to 50 c.c.

Take 20 c.c. of the liquid, and heat it after having added gtt xx of *Millon's* reagent[1] (should any trouble occur add gtt ii or iii of nitric acid).

Heat to maximum color and allow it to get cool before examining with chromometer.

III. The Indoxyls

A. Indol is formed under the influence of intestinal putrefaction; its formation taking place before that of phenol and beginning in the lower portion of the small intestine, where it appears to be largely absorbed.

Stagnation and obstructions of the ileus largely augment the production of indol, while at the same time the phenols remain normal.

Indol is eliminated by the urine as a sulphoether.

Normal quantity of indol per liter = 0.005 to 0.015.

Normal quantity in 24 hours = 0.010 to 0.025.

This proportion augments :

1st. *In all organic suppurations.*

2d. *In all conditions of stasis of the small intestine;* simple and tubercular peritonitis, perityphilitis, strictures of the small intestine through bridles, adhesions, acute flexures, spasms, chronic invagination, paralysis and tumors.

3d. *In all exaggerations of intestinal putrefaction.*

[1] Millon's reagent consists of 10gm. of mercury dissolved in 20gm. of nitric acid; this is diluted with equal volumes of water; it gives a red color with proteids and benzene and naphthalene derivatives (tr).

B. Skatol occurs under the same conditions as indol; it increases and diminishes parallelly with it.

Normal quantity of skatol per liter = 0.005 to 0.010.

Normal quantity in 24 hours = 0.010 to 0.015.

Dosage of the Indoxyls

The derivates of indol occurring in the urine under the form of indoxylsulphuric acid, give rise through their oxidation, to coloring matters, the principal ones of which are indigo blue and indigo red. The method of oxidation and extraction indicated by *Amann* is as follows:

Clear the urine by adding 10 per cent. of its volume of lead acetate solution and filter.

Take 55 c.c. of the cleared and filtered urine (corresponding to 50 c.c. of the original urine) and add gtt v of a saturated aqueous solution of *sodium persulphate*, then 10 c.c. of *crystallizable benzene* and finally 30 c.c. of *dilute sulphuric acid* (50 per cent. solution of concentrated $H^2 SO^4$).

Cork or stopper tube, *and carefully* turn upside down for ten times without shaking, and remove stopper each time, so as to allow gas to escape; wait fifteen minutes and repeat as above.

Then keep tube at rest until the benzene has completely collected at the surface of the liquid.

The benzene solution may appear as follows, and indicate:

(*a*) *Without color:* absence of indol and skatol.

(*b*) *Blue:* indigo blue only.

(*c*) *Violet:* indigo blue mixed with indigo red or skatol.

(*d*) *Rose:* indigo red mixed with skatol.

In the cases of (*b*) (blue appearance) and (*d*) (rose appearance), the solution may be at once dosed with the chromometer, using the blue or red prism.

In the case of (*c*) (violet appearance) the solution is pipetted as completely as possible, then evaporated over a water bath in a small porcelain cup, after having added a small crystal of sodium carbonate. The dry residue is then washed with 20 c.c. of dilute alcohol (30 per cent.); this dissolves the red coloring matter, leaving only the indigo blue. The red solution is examined with the chromometer and dosed.

The indigo blue residue is redissolved in 20 c.c. of benzene, and likewise examined with the chromometer.

In many cases, the operation may be simplified by omitting the clearing of the urine with the lead acetate, for this is only necessary with highly colored urines.

If it is desired to neglect the red coloring matter, and only take into account the indigo blue, it is sufficient to purify the original benzene solution by the addition of a few drops of rectified alcohol (until it clears). By this means there is obtained in most cases a clear blue solution.

Clinically. We are satisfied with establishing the curve of the indols and phenols, renouncing the dosage of the oxyacids which is too complicated.

C. Coefficients of Auto-intoxication

Of these there are three:

1st. The coefficient of *Baumann.*
2d. The coefficient of *Amann.*
3d. The coefficient of *Combe.*

The Coefficient of Baumann

As we have seen, the quantity of the sulphoethers varies according to the time of day; errors may be avoided by examining the urine of the twenty-four hours. It varies also according to the food, increasing with albumin, meat, etc., in a word, with a nitrogenous diet and it diminishes with a vegetarian one.

The normal quantities vary with the individual, and for that reason, it is necessary to admit wide normal limits for the sulphoethers, as with the total nitrogen.

Baumann has attempted to eliminate these physiological variations, by comparing the sulphuric acid combined with the sulphates (*sulphuric acid A or the sulphates*), which is also derived from the alimentary albumin, to the sulphuric acid combined with the aromatic bodies (*sulphuric acid B or sulpho-conjugate*). This coefficient has received the name of *Baumann.*

The sulphuric acid of the sulphates A = 1.50.
The sulphuric acid of the sulphoconjugates B = 1.50 at the maximum.
} In normal cases.

Coefficient of Baumann Normal $\frac{A}{B}=\frac{1.50}{0.150}=10$

B. diminishes in inanition and diarrhea; it augments with exaggerated putrefaction.

The coefficient is lowered in the latter condition. It may therefore be said:

That the non-reversed coefficient of Baumann is in inverse ratio to the intestinal putrefaction. It diminishes when putrefaction increases.

We have been in the habit with *Amann*, of reversing this coefficient and multiplying it by 100. In this new form it indicates the proportion of the sulphuric acid of the sulpho-conjugates to the 100 grams of the total sulphuric acid. *This constitutes the coefficient of Baumann reversed.*

It is proportional to the intensity of the putrefaction.

It increases when the putrefaction augments.

Reversed Coefficient of Baumann Normal $\frac{B}{A}=\frac{0.150}{1.50}=10$

But *Baumann's* coefficient cannot and should not, at the present time, be considered as the sole measure of intestinal auto-intoxication.

It could be such, only when the alimentation remains absolutely the same (*experimental alimentation*). For any change or variation in the food exercises a considerable influence upon the sulphur of the urinary sulphates.

In the first place, the sulphur content of the albumins is not constant; it varies from 0.20 to 2 per 100, and, moreover, it is not proportional to their content in nitrogen which only varies from 15 to 16 per 100.

In the second place, the urinary sulphur is derived not only from the alimentary albumin, but also—and in large proportion—from the decomposition of the organic albumin.

It results therefore that the coefficient of *Baumann* compares two things which offer no comparison, because they depend upon altogether different factors. The sulphur being at the same time a result of the functional disassimilation of the organic albumin and of the alimentary albumin; while the

sulphoether sulphur is derived from the putrefaction of the proteids only.

In consequence, the *Baumann* gives but very approximative information. Nor is it very difficult to find, even in the works of the partisans of *Baumann's* coefficient, the proofs of what we advance. In the works of *Rochmann* and in those of *Rovighi*, we may see that the *non-reversed Baumann* is diminished by feeding dogs with zwieback. This diminution is not due to an increase in the sulphoethers, for they have diminished, but to the fact that the total sulphur decreases greatly with that kind of alimentation.

In the work of *Winternitz*, we notice in several places that he obtained with his milk and meat diet the same *Baumann*, although the sulphoethers had been quadrupled.

Hence we notice that most authors: *F. Müller*[1], *von Noorden*[2], *Salkowski*[3], *Kast* and *Boas*[4], express doubts as to the value of *Baumann's* coefficient.

They arrive at the conclusion that this coefficient has only a very relative value, and that only the quantity of urinary sulphoethers can be considered as a measure of the penetration into the blood, of the products of nitrogenous intestinal putrefaction.

We therefore agree with *Schmitz*[5] when he asserts **that as a measure of digestive auto-intoxication, it is better not to take the absolute quantity of the sulphoethers into account, than to compare them with the total sulphur as the Baumann does.**

Nevertheless, *Baumann's coefficient* may be retained, on condition that it is not solely consulted, for only a comparative value should be attributed to it.

In the case of chronic intestinal invagination, already cited, the *Baumann* rose to 28.8.

2d. Coefficient of Amann

This coefficient is much more exact, for it compares the sulphoethers with the total nitrogen, and for some time past we have

[1] Müller: Zeits. f. klin. Med., XII, p. 63.
[2] Von Noorden: Zeits. f. klin. Med., XVII, p. 525.
[3] Salkowski: Zeits. f. phys. Ch. XII, p. 85.
[4] Kast & Boas: Munich Med. Woch. 1888. p. 51.
[5] Schmitz: Zeits. f. phys. Ch. XIX, p. 384.

given it the abbreviated designation of *Amann's coefficient.* The ratio indicates the quantity of sulphoethers to the total nitrogen output.

$$\text{Amann's Coefficient Normal} = \frac{\text{Sulphoethers}}{\text{total nitrogen}} = 1.4 \text{ to } 1.5$$

These two terms are comparable. The numerator, *the sulphoethers,* is solely derived from the aliments while the denominator, *the total nitrogen,* is nearly all derived from the same aliments; lastly, the proportion of nitrogen is almost the same in all albumins: 15 per 100.

Our experiments have demonstrated the great usefulness and the valuable indications furnished by this coefficient.

In the case of invagination we found:

$$\text{Amann's Coefficient} = \frac{935 \text{ mg.}}{22.6} = 4.1$$

3d. Coefficient of Combe

Amann has designated under our name the coefficient which he has proposed, and which is obtained by taking the sum of the weight (expressed in milligrams) of the aromatic bodies; phenols, indols, skatol and oxyacids and dividing the sum by the urea or the total nitrogen (expressed in grams).

The coefficient of Combe indicates how many milligrams of aromatic bodies, the urine contains to the 100 grams of urea or total nitrogen.

Phenols	10 to 15mg.
Indols	05 to 15mg.
Skatols	05 to 10mg.
Oxyacids	10 to 20mg.
Normal aromatic bodies	30 to 60mg.
Normal urea	15 to 25gm.
Total nitrogen normal	10 to 15gm.

Coefficient of Combe Normal = 150 to 250.
Coefficient of Combe Normal = 250 to 300.

We by no means claim that the coefficient comprises all of the aromatic substances, but the principal ones are included and they complete quite well the information furnished by the sulphoethers.

In the case of chronic invagination the *Combe* was 4,250.

Physical Urinary Diagnosis

It is now some years since those extremely delicate physical methods, which have transformed modern chemistry by the application to solutions of the laws of the kinetic mechanism of gases, have been applied to the urine.

It is especially from the standpoint of their osmotic pressure that the two physiological fluids, the blood and the urine, have been studied. The simultaneous cryoscopic study of these two fluids have given remarkable results, by furnishing information upon the renal functions.

For some time also two other properties of solutions have been studied by physicists, and they have given most interesting results; we refer here to the refraction and the superficial tension of fluids, studied by the drop method. While cryoscopy and, better still, the refraction of a liquid give information as to the molecular concentration of a solution, and the *number of molecules* it contains; its superficial tension measured by the drop method instructs us as to the *complexity and dimensions of these same molecules.*

For a number of years we have made use of *Amann's stalagmometer* in our service.

We will briefly recall the principles and the application of stalagmometry.

Superficial Tension

The molecules of all fluids are attracted to each other proportionally to their mass, and in inverse ratio to the square of their distance; they therefore do this, in an extremely limited space, spherical in form and of very small radius, which has been termed their *sphere of activity.* Attracted on all sides by equal forces, the molecules of the fluid remain in a state of equilibrium. It is not the same at the surface; the superficial molecules are in equilibrium in the horizontal plane but not in the vertical, for there the atmospheric molecules cannot exert the same attraction as the liquid. All the molecules at the surface are therefore drawn toward the interior, and in consequence the surface always tends to occupy the minimum area.

The tension at the surface of the liquid is called *its superficial tension.*

To use a simile of *Quincke*, everything passes as if the surface of the liquid were covered over by a thin sheet of rubber always stretched and always ready to contract, so as to present a minimum area.

It is owing to the superficial tension that hydrometers float instead of sinking; it is because of it that a drop of oil immersed in a medium of the same density assumes a spherical form presenting a minimum area, etc.

If the bottom of the vessel containing the liquid is pierced at its base by a capillary orifice, the flowing out of the liquid will not take place in a continuous stream, but only drop by drop, owing to the superficial tension which tends to push back the molecules at the surface of the drop toward the interior.

There is, so to speak, a struggle between the weight of the drop, which tends to make it fall, and the superficial tension which seeks to crowd it back to retain it.

It will be easily understood that the greater the superficial tension, the heavier will be the drop before falling, and the smaller will be the number of drops, necessary to empty a given volume. This is expressed by **the two laws of Tate.**

1st. For a same liquid, the weight of the drops is proportional to the perimeter of the orifices (*first law*).

2d. For different liquids, the weight (and the volume) of the drops is proportional to the superficial tension of the liquid (*second law*). The drop counter or stalagmometer can therefore be used to measure the superficial tension of liquids, provided that the capillary tube is always of the same perimeter at the orifice.

The works of many authors have shown that certain relations exist between the superficial tension and the composition of the liquid. *Quincke*, *Valson*, *Rodenbeck*, and specially *Duclaux* and our countryman, *Rillet*, have demonstrated that the stalagmometer can very well serve to determine the molecular weight of liquids. *Duclaux* has shown that the stalagmometer can be used for the dosage of alcohol in wines, and *Quincke* also, from his researches of the fatty acids, which diminish the superficial tension, the more so as their molecular weight is greater.

For the fatty acids (as example), we have in 5 c.c. of a solution 1:50.

Distilled water	100 drops
Acid formic	101 drops
Acid acetic	105 drops
Acid butyric	152 drops
Acid caproic	263 drops

From these examples, it will be seen that the superficial tension gives very different information from that furnished by osmotic pressure and refraction.

Osmotic pressure is measured (as a matter of fact, not very accurately) *by cryoscopy*, while *refraction is measured by the refractometer of Zeiss, with remarkable ease and with a still more remarkable accuracy. The point of freezing and the index of refraction* are both depressed by all of the molecules present, and this depends *consequently upon the number of the molecules and not upon their nature.*

The superficial tension measured by stalagmometry depends on the contrary, *on the nature of the molecules, and not on their molecular weight.*

Some of the molecules elevate the superficial tension and diminish the number of drops; these are generally the inorganic molecules.

Others (the organic molecules) generally lower it and increase the number of drops, the more so as their molecular weight is greater.

Amann has applied this method, both so simple and exact, to the study of the urine, and he has been able to find that the constituents of the urine may be divided into two categories:

Some elevate the superficial tension; consequently they diminish the number of drops from the stalagmometer; they are principally constituted by the inorganic salts; the chlorides, phosphates and sulphates.

These form about 30 per cent. of the solids in solution.

Others act almost indifferently: these are: urea, sugar, albumin. The urea represents about 50 per cent. of the solids in solution.

The last depress the superficial tension.

These are: uric and hippuric acids, the fatty acids, the aromatic bodies, etc.

What is important to remember, **is that, generally speaking the *normal* constituents of the urine (leaving out albumin and sugar) *elevate* the superficial tension, while the bodies constituting the *abnormal* waste products of the badly burnt, organic exchanges all depress the superficial tension.**

This simple enumeration, necessarily very incomplete, demonstrates that the inorganic compounds generally *elevate* the superficial tension, and that the normal organic compounds (urea) depress it in an insignificant degree, whereas the incompletely oxidized organic substances, the clinkers of the nutrition, depress it markedly.

Hence the degree of depression in the superficial tension may be considered as a measure of the increase in the abnormal products in the urine.

These abnormal products comprise precisely the bodies which, without any doubt, play a preponderating role in auto-intoxication.

To measure the degree of depression, it is above all necessary to take into account the influence of the inorganic constituents of the urine (chlorine, sulphur, phosphorus) and eliminate it in the calculation of the depression.

Chlorine varies greatly in the urine and exercises but a very insignificant action in the depression of superficial tension. A difference of more than 10 grams of chlorides per liter of urine only diminishes the dropping by about one-tenth of a drop in 100 drops.

The influence of the chlorides is therefore negligible.

The sulphates and phosphates in the urine vary much less, for their quantity seldom reaches one gram, but their influence on the dropping is much more important.

Sulphuric acid. Each additional gram of sulphuric acid in the state of neutral sodium sulphate diminishes the dropping by one drop in 100.

Phosphoric acid exercises about the same influence; each additional gram of phosphoric acid in the state of bisodic phosphate, diminishes the dropping by about one drop in 100.

But it is relatively easy to rapidly dose the amounts of sulphuric and phosphoric acids, and this allows of correction being made.

In this manner, the depression of the superficial tension due only to organic bodies, may be obtained.

For some time past, we have taken up this study in our clinic and the results, while not definite, are most interesting, particularly if they are confirmed by time.

1st. **In infectious diseases the depression of the superficial tension measures the degree of intoxication,** and as it runs nearly parallel with the intensity of the disease, its measure may be utilized from a prognostic point of view.

2d. **In all pure intestinal auto-intoxication, the curve of superficial tension depression is frequently parallel with the curve of the phenols and indols.**

Whether the determination of this depression by the drop method may not in the future—to a certain extent—take the place of the dosage of these bodies, is a question. From a clinical point of view, it would present great advantages for measurement by means of the stalagmometer is performed with remarkable ease and rapidity. Let us mention, however, that *Billard*[1] asserts that the phenols exercise only a slight action on the depression of the superficial tension.

The Stalagmometer

Description and method of using. The stalagmometer of *Amann* in its simplest clinical form consists of a gauged glass pipette with a spherical expansion blown in its upper part, and having at some distance below it a ground-glass stopcock.

To the inferior extremity, there is connected by means of small rubber tubing, a specially constructed capillary tube, intended to regulate the dropping.

The upper extremity of the pipette is bent at right angles, and is provided with a rubber tube serving to fill the instrument by aspirating. The whole is fixed in an appropriate support. Above and below the spherical expansion are two marks etched

[1] Billard: Soc. biol., LVIII, p. 991.

in the glass. The quantity of distilled water comprised between the two marks furnish 100 drops exactly.

To measure the capillary constant of the urine, it is sufficient to fill the pipette with the urine to be examined, so that its meniscus will correspond exactly with the upper mark.

This is done by first removing the capillary adjustment, then open the stopcock and plunge the inferior extremity of the pipette in the filtered urine, and aspirate through the rubber tube until it (the pipette) is completely filled.

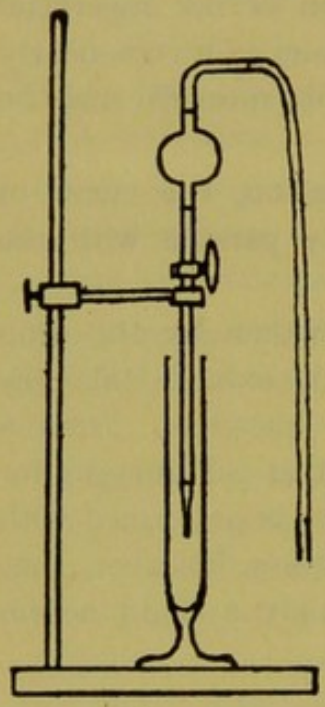

FIG. 5.—STALAGMOMETER.

The capillary tip is then adjusted, care being taken to see that it hangs straight; the stopcock is opened and the urine is allowed to flow out, until its meniscus is exactly even with the upper mark. The stopcock should then be closed, and the excess of liquid at the capillary point removed with filter or blotting paper.

All is now ready for the measurement; open the stopcock and count the number of drops N as they fall, until the precise moment at which the meniscus of the urine corresponds exactly with the lower mark.

Precautions to be observed. The urine must be filtered through filter paper. The capillary tip must be protected from dust and carefully cleaned and washed in distilled water after each examination, to avoid its becoming foul or obstructed.

The time necessary for the complete emptying should be about the same for the urine as for water. The temperature should not vary greatly from 15 c. In case of sensibly different temperatures, it is better to determine first, the number of drops of distilled water under the same conditions, and to base the proportion of the urinary drops to each 100 drops of distilled water. (See example No. iii.)

Calculation of Results and Capillary Constant

In the foregoing, one of us proposed as an expression of the capillary properties of the urine, the ratio Δ/E, that is, the depression of the capillary constant Δ to the weight of the extractive matters E contained in one liter of urine.

The calculation of this formula, while presenting no difficulty, might appear somewhat complicated and require the use of a table; to obviate this, we have proposed a method of notation and representation, which is much more simple and reduces the calculation to its simplest form.

We can, in fact, consider as measure of the depression of the superficial tension of the urine, the difference between the number of drops observed in the urine and that of the drops of water, which, according to the construction of the instrument is 100 drops.

$$\Delta = N - 100$$

That is to say, the number of drops for the urine, less 100 (the number of drops for water). But this measure alone is not sufficient. It is necessary in all cases to take into account the degree of urinary concentration so as to obtain comparable results for different urines. We therefore divide the difference $N-100$ by the weight $-W$ in grams of the liter of urine (at 15° C.), less 1,000 grams (the conventional weight of a liter of distilled water); this quantity is designated by the letter Σ.

$$\Sigma = W - 1{,}000$$

The weight W of the liter of urine is immediately given by the specific gravity taken with the areometer or otherwise, and multiplied by 1,000.

We shall have at the end, as characteristic of the capillary properties of the urine, the following formula:

$$\text{Capillary Constant } C = \frac{\Delta}{\Sigma} = \frac{N - 100}{W - 1000}$$

Hence the following rule may be formulated, one very easily remembered:

In the normal state, the number of urinary drops less 100, is half the number represented by the decimals of the specific gravity.

Normal Capillary Constant = 0.5

Example

I. Temperature	15° C.
Specific gravity of urine	1,020
Σ = 1,020 − 1,000	20
Number of drops for the urine	110
Δ = 110 − 100.	10

$$C = \frac{\Delta}{\Sigma} = \frac{10}{20} = 0.5 \text{ (Normal Urine)}$$

In auto-intoxication of intestinal origin, the capillary constant is, as a rule, relatively very high: 0.8; 1.0; 1.5 above.

Examples

II. Temperature	15° C.
Specific gravity of urine	1,018
Σ = 1,018 − 1,000	18
Number of drops for urine	128
Δ = 128 − 100	28

$$C = \frac{\Delta}{\Sigma} = \frac{28}{18} = 1.56 \text{ (Urine in Auto-intoxication)}$$

III. Temperature	25° C.
Specific gravity of urine	1,015
Σ = 1,015 − 1,000	15
Number of drops for urine (at 25°)	117
Number of drops for water (at 25°)	104
Δ = 117 − 104	13

$$C = \frac{\Delta}{\Sigma} = \frac{13}{15} = 0.87 \text{ (Urine in Auto-intoxication)}$$

IV. DIAGNOSIS OF HEPATIC INSUFFICIENCY

Hepatic insufficiency is one of the first among the causes of auto-intoxication.

It is therefore very important to know how to diagnose it.

A. Chemical Diagnosis

The chemical diagnosis of hepatic insufficiency is based upon the diminution of urea in the urine, and upon the proportion or abnormal presence of uropoietic substances in it.

Hypoazoturia

Following *Brouardel*, the French clinicians have for a long time considered the variations of urea, or more strictly speaking, its diminution in the urine (*hypoazoturia*) as one of the most important elements of the urological syndrome of hepatic insufficiency.

But while it is certain that the liver is the most important seat of urogenesis, it is almost as certain that uropoiesis is a biochemic process, which may—in small part at least—be carried on outside of the liver.

The absolute and relative diminution in the secretion and excretion of urea in the urine, may therefore and up to a certain point, be considered as proportional to the degree of anatomic and functional failure of the liver.

But before concluding, it is always necessary to carefully consider the relation between the alimentary regimen and its urea output; for many observations on hypoazoturia are in reality cases of hypophagia.

It is precisely this double relation, that the coefficient of the ratio of urea to the total nitrogen output measures. (The coefficient of nitrogenous utilization.)

The depression of the nitrogenous coefficient below 83 per 100 is a sign of hepatic insufficiency.

Accumulation of Urogenic Substances

In order to signify hepatic insufficiency, the diminution of urea must be accompanied by an augmentation of ammonia, uric acid and purin bases; and by the appearance in the urine of amino acids (leucin and tyrosin), for these bodies are all transformed by the liver into urea.

Ammonia. More or less pronounced increase of ammonia always exists in the functional insufficiencies and degenerative affections of the liver. (**Hepatogenous Ammoniuria.**) But the significance of ammoniuria is equivocal, for it occurs in acid intoxication in which there is most frequently no trace of hepatic insufficiency, the ammonia serving to neutralize the acids. (**Ammoniuria of acidosis.**) Lastly, it occurs in nitrogenous intestinal putrefaction. (**Enterogenous Ammoniuria.**)

In consequence, hypoazoturia accompanied by ammoniuria proportional to the depression of the nitrogenous coefficient, cannot reveal with certainty a uropoietic insufficiency of the liver, as long as it persists in spite of an alkaline treatment, or if it increases with the administration of ammoniacal salts. (**Experimental Ammoniuria.**)

Ammoniuria is then a sign of profound functional and organic failure of the liver.

For the uropoietic power of the liver is independent of its mass, and it may be preserved in all its integrity in portions of the organ (however small they may be) provided these zones are spared by the morbid process.

Normal Ammoniuria Does Not Excceed 5 per 100

Uric acid. A part of the uric acid appears to be transformed in the liver into urea by the action of a *uropoietic ferment* (*Richet* and *Chassevant*) or better *uricolytic* as *Schittenhelm*[1] terms it. Consequently there is noted an increase of the urates and uric acid in hepatic insufficiency, as pointed out by *Salaskine* and *Rowaliskaia*.

But on one side we should not trust to the sediment to arrive at that conclusion, for it does not indicate the true quantity of uric acid, but only the portion precipitated and only its dosage can testify to its increase.

On the other side, as *Schittenhelm*[2] has demonstrated, uricolysis does not belong to the liver alone, for *Wiener*, *Buriau* and *Ascoli* have shown the presence of the uricolytic ferment in the muscles, the liver, and the kidneys, and that furthermore, these organs supplement each other in their uricolytic functions.

As may be seen, the increase of uric acid is neither a constant or specific symptom of hepatic insufficiency.

Xanthin and hypoxanthin. Besides its uricolytic function, the liver has also a uricopoietic one, performed at the expense of xanthin and hypoxanthin and this, thanks to a ferment discovered by *Buriau*[3] (*xanthinoxydase*), which converts hypoxanthin into xanthin, the latter into uric acid.

[1] Schittenhelm: Zeits. f. phys. Ch. XLV, p. 161.
[2] Schittenhelm: loc. cit.
[3] Buriau: Zeits. f. phys. Ch. XLIII, p. 497.

Consequently, in all cases of hepatic insufficiency, xanthin and hypoxanthin appear in the urine.

But here again it is not a question of a special function, for the spleen, the kidneys and the intestine share this property with the liver; at least, in the presence of oxygen[1].

Leucin is transformed by the action of the hepatic cells into urea, which, in normal conditions alone appears in the urine; whenever the hepatic cells are destroyed or incompetent, leucin appears in the urine, while the quantity of urea diminishes.

An abundant appearance of leucin in the urine is a sign of hepatic insufficiency.

Urobilinuria

The elimination of the biliary coloring matters and of the hematin chromogens is in relation with the failure of the hepatic function.

In the examination of fifty patients all suffering from cholemia, *Gilbert* and *Lereboullet* found:

Marked urobilinuria in 25 cases.

Feeble urobilinuria in 20 cases.

Complete absence of urobilinuria in 5 cases.

These authors concluded that urobilinuria must be considered a diagnostic point in cholemia, as much so as the cholemic color, the palmo plantar sign and the diverse pigmentations, resulting from the transformation of the biliary pigments into melanin, at the surface of the epidermis. But the question is far from being as simple as *Gilbert* supposes, and it merits development. Urobilin, discovered by *Jaffé*[2], is with urochrome, the most important biliary coloring matter; it is characterized by its fluorescence and its spectroscopic absorption.

It gives the urine its yellow color (at least in part); whenever urobilin is present in large quantity, the urine becomes brown and its foam yellowish.

Has urobilin several sources, or are there several kinds of urobilins (urobilinoids) having the same chemical and spectroscopic reactions as *Lehobel* asserts? We incline to the last hypothesis:

[1] Schittenhelm: Zeits. f. phys. Ch. XLV, p. 121.
[2] Jaffé: Virch. Arch., XLVII.

1st. The hemoglobin derived from the normal destruction of the red cells, is transformed in the liver into bilirubin.

When the liver is insufficient from degeneration or cirrhosis, the hematin passes into the blood and is converted in the kidneys into urobilin (*hepatogenous urobilin*).

2d. One of the urobilins is identical with hydrobilirubin (stercobilin). It is a derivate of bilirubin, which, under the influence of albuminous putrefaction is transformed in the intestine, into stercobilin (*enterogenous urobilin*). As proofs may be given: first, the identity of stercobilin with the urinary urobilin, and next the fact that it is not present in the newborn and in alcoholics; finally its parallel augmentation with intestinal putrefactions.

3d. A third urobilin, or a third source of urobilin is formed whenever an outpouring of blood takes place in the organism, and each time that a large quantity of blood cells is destroyed by the introduction of blood poisons (acetanilid, antipyrine, etc.), or by infections (toxins) *hematogenous urobilin*.

The latter is probably identical with the *febrile urobilin*.

Hoppe-Seyler, *Lehobel*, *Nencki* and *Sieber*, obtained a urobilinoid by reduction of hematin and *MacMunn* by oxidizing it, obtained urobilin.

It is possible that in the organism this conversion may take place in the kidneys. (*Gilbert* and *Lereboullet*.)

It is thus seen that to assert the existence of hepatic insufficiency, it is not sufficient to make a diagnosis of urobilinuria.

But that is not all, for to measure the urobilin content by its fluorescence and the appearance of its absorption band, is difficult, owing to the fact that the reaction does not attain its maximum until twenty-four to fifty hours after it has been made, and that this duration varies with the origin of the urobilin.

In fresh urine, urobilin exists only under the form of urobilinogen, which becomes oxidized under the influence of light into urobilin. It is the rapidity of oxidization which varies according to the source of the chromogen.

Hematogenous urobilinogen oxidizes very rapidly; in consequence the characteristic reactions are very quickly obtained.

The hepatogenous and enterogenous urobilinogens oxidize much more slowly; the urine is frequently clear in spite of its large urobilin content; it only becomes darker very slowly upon exposure. Even when the urine is shaken with chloroform and there are added nine large drops of an alkaline solution of zinc, hardly any rose color is noticed while the spectroscope shows no absorption band.

It is only after two days that the decanted urine assumes a rose tint, fluoresces, and shows a very marked absorption band, as *Jaffé* and *Wirsing* have demonstrated[1].

It is thus seen that the syndrome of urobilinuria must be looked at with circumspection, for it is no wise identical with any sign of hepatic insufficiency.

Indicanuria

It is certain that the aromatic substances increase in the urine of subjects suffering from hepatic insufficiency. But it is the digestive fermentations, which above all register indicanuria. Although the liver has a certain influence upon the evolution of indican, it is prudent not to base an assertion that the liver is at fault upon the presence of indicanuria.

Ethereal sulphates. As much may be said of the variations in the sulphoconjugates.

A marked increase in the sulphoethers and aromatic bodies indicates auto-intoxication to a certainty, but permits no conclusion as to its enterogenous or hepatogenous origin.

B. Physiological Diagnosis

Diminution of the Antitoxic Function of the Liver

The consequence of an antitoxic insufficiency of the liver, being an incomplete neutralization or destruction of toxins; the urinary toxicity will necessarily be increased, as soon as the hepatic cells are impaired. This toxicity may be measured by the *urotoxies*.

But as we have seen, this method is open to many serious

[1] Jaffé & Wirsing: Verhandl. der phys. med. Gesell. Würzburg. 1882. p. 32.

objections; hence it is not actually possible to draw from it any conclusion as to hepatic insufficiency.

Insufficiency of the Glycogenic Function of the Liver

The examination of this function is made by means of *experimental alimentary glycosuria.*

The glycogenic function of Schiff. The liver converts intestinal sugar into glycogen. If preliminary ligation of the portal vein is made and sugar is introduced into the intestine, glycosuria will result (*Claude Bernard*); this indicates the absence of the function of the liver.

We have the greater interest in carrying out this experiment, since it allows us to ascertain the arresting action exercised by the hepatic cells upon the toxins. The investigations of *Roger* have, in fact, demonstrated the connection between the glycogenic and antitoxic functions of the liver.

A liver which no longer forms glycogen at the expense of the carbohydrates, becomes also incapable of exercising its protective action against the poisons traversing its parenchyma. One hundred and fifty grams of glucose must be considered as the normal experimental dose (*Achard*); this amount must be quickly absorbed, so as to avoid its partial conversion in the intestine, which would render the experiment valueless and negative.

In order to appreciate the value of a positive result, it is necessary to know if the glycogenic insufficiency is purely hepatic or if it is due to the *ensemble* of the tissues.

Lastly, it is necessary to dose the renal permeability and its output.

It is only at the price of all these precautions that alimentary glycosuria becomes one of the best signs of hepatic insufficiency, one which according to Chauffard[1] informs us best as to the anatomic and functional state of the hepatic cells.

For other investigators however, *Charrin*, *Linossier*, alimentary glycosuria is not a sure sign of hepatic insufficiency because all hepatic impairments, by no means bring about glycosuria.

[1] Chauffard: Traité de path. generale de Bouchard, V, p. 49.

This finding conforms to the general notions of physiology, by virtue of which a fragment of healthy gland, thyroid, pancreas, etc., suffices to prevent any appearance of myxœdema or diabetes.

How can we then admit that the liver alone presents an exception?

Alimentary glycosuria is therefore rather a sign of general insufficiency of the liver than one of grave and profound incompetency.

Intermittent elimination of methylene blue. According to *Chauffard*[1] the intermittent character which the elimination of this stain assumes in hepatics, is one of the best indications of hepatic insufficiency.

The urine must be collected every two hours; the number of intermittences may vary from one to five; the most precocious may appear from the third to the sixth hour, while the tardive may not appear until the fortieth and up to the forty-fifth hour.

Their minimum duration is from one to two hours, ten at the maximum, the average being four to five hours.

In a general manner it may be said that, the more precocious and the more numerous the eliminative intermittences, the more gravely involved will be the functions of the hepatic cells. (Chauffard.)

This is the explanation given by this eminent observer.

In the healthy man in whom the functional integrity of the liver and kidneys is normal, the glomeruli and the uriniferous tubules operate synchronously. The elimination of water and soluble materials takes place and follows parallel curves; the methylene blue is eliminated in a continuous manner and not prolonged, the same as urea and the salts in solution. In the hepatic subject the intestinal poisons and other toxins irritate and intoxicate the convoluted tubes particularly, thereby producing partial inhibitions, the glomeruli being less affected; in consequence the secretory rhythm is profoundly modified.

The activity of the glomeruli suffers relatively less (except in grave cases of anuria and oliguria) and becomes disassociated

[1] Chauffard: Loc. cit., p. 55.

from the secretion of the convoluted tubes. In this manner there occurs a disassociated type of elimination in which the excretion of a large quantity of water corresponds to a secretion, containing but little urea or soluble matters, and a disappearance of the biliary pigments and of the methylene blue, which was simply intended to demonstrate the intermittence more clearly and visibly.

Such are the signs of hepatic insufficiency.

They all correlate with the normal functions of the gland, while indicating the pathological counterpart.

They are not all of equal value, and it is only by consulting them all that we may obtain an idea of the degree of hepatic insufficiency.

TREATMENT

Intestinal auto-intoxication is, as we know, partly due to the nitrogenous putrefaction occurring in the intestine and partly to the insufficiency of the antitoxic organs of the body.

Hence the indications in the treatment derive from two principal sources:

1st. To diminish the nitrogenous putrefaction in the intestine so as to bring it back to normal, if the antitoxic organs are competent.

To bring the nitrogenous putrefaction in the intestine to a point below normal, if the antitoxic organs are insufficient.

2d. To stimulate the antitoxic and excretory functions of the organism, when they have become insufficient.

I. TO DIMINISH NITROGENOUS PUTREFACTION IN THE INTESTINE

We have seen elsewhere that nitrogenous putrefaction is due to the activity of the proteolytic anaerobic bacteria.

The vitality of these bacteria is enhanced, thanks principally to the favorable culture medium in which they live, feed and multiply.

The therapeutic indications derived from these facts are the following:

1st. **To modify the intestinal culture bouillon in which the intestinal proteolytic bacteria thrive.**

This indication may be carried out in three ways:

A. **By introducing into the intestinal culture bouillon an anti-putrefactive lacto farinaceous diet.**

B. **By introducing antagonistic bacteria into the intestinal culture bouillon.**

C. **By introducing bacterial ferments into the intestinal culture bouillon.**

2d. **To diminish the vitality of the proteolytic bacteria in the intestine by means of germicidal medicines.**

3d. **To evacuate the proteolytic bacteria and their toxins by means of intestinal lavage.**

II. TO MODIFY THE INTESTINAL CULTURE BOUILLON IN WHICH THE INTESTINAL PROTEOLYTIC BACTERIA THRIVE

A. By modifying the alkaline culture bouillon of the intestine by means of an antiputrefactive regimen.

This is the best and surest of the means we possess, and it can be easily obtained by combining a regimen which will furnish the number of calories necessary to the life of the individual, and at the same time modify the alkalinity and nutritive properties of the intestinal culture bouillon, but too favorable to the putrefactive microbes. We shall therefore study:

(*a*) The caloric value of the antiputrefactive regimen.

(*b*) The alimentary composition of the antiputrefactive regimen.

Caloric Value of the Antiputrefactive Regimen

As we shall see, the treatment of intestinal auto-intoxication is above all alimentary, and as such, it must conform to the dietetic rules, which we will briefly examine.

Caloric Value of the Daily Ration

Professor Müller[1] of Munich formerly of Basle, has occupied himself for many years with the question of dietetics, upon which he delivered a most interesting inaugural discourse from which we shall borrow largely. Thanks to recent works, it is actually possible to exactly measure the amount of force and heat liberated in the organism, under the influence of the nutritive exchanges. It is therefore possible to measure in calories, the potential necessary for an individual to conserve his animal heat and satisfy his physical needs.

Johannesen[2] was able to calculate by means of the apparatus of *Tigersted* **that a healthy man in complete repose or during sleep required one calorie per hour and per kilogram weight; that is, 24 calories per day and per kilogram.**

With a moderate amount of work this figure rises to 44 calories per kilogram and per twenty-four hours.

[1] Müller: Antrittsrede, Basel.
[2] Johannesen: Arch. Scand. de phys., VII, p. 123, and VIII, p. 85.

With a great amount of work this figure rises to 54 calories per kilogram and per day.

An adolescent weighing 50 kilograms, therefore requires 1,200 calories per day when in repose; which implies that when at work from 2,200 to 3,000 calories will be necessary to him, according to the amount of work. Now, in order to supply this caloric value, an alimentation capable of furnishing it is necessary, else the organism will be compelled to draw upon its own muscles, fats, etc.

Rubner has proved that the aliments furnish to the organism through their oxidation as many calories as when they are burnt up outside of the organism; it is therefore possible, thanks to this method to measure the potential, that is to say, the nutritive strength of the food from the quantity of calories it furnishes.

The calculation of the caloric value of the daily ration is hence of the highest importance in establishing a regimen.

Very frequently, in fact, in calculating the daily ration of patients who catechize themselves, and who are persuaded that they eat too much, one is often surprised to find that, either from lack of appetite or from bad choice of the food, that they fall much below the necessary ration, which explains to a certain extent their progressive emaciation.

At other times, on the contrary, the calculation shows a ration much greater than required, and we are forced to conclude that the progressive emaciation of the patient is due to some digestive or assimilative trouble or that some more grave disease exists (tuberculosis, malignant disorder, etc.).

Rubner later demonstrated that from the caloric point of view, the alimentary substances: albumin, carbohydrates, and fats, may replace each other according to the quantity of calories they furnish.

1 gram of albumin gives ..... 4.1 calories
1 gram of carbohydrates. ..... 4.1 calories
1 gram of fats ..... 9.3 calories

One gram of albumin is then said to be *isodynamic* with one gram of carbohydrates.

But it should be recognized that alimentary isodynamy is not perfect.

It is exact, only in so far as it seeks to maintain normal oxidation and prevent loss of weight.

For as soon as it is a question of suralimentation and increase in weight, it is no longer so. In such case an excess of fats in the alimentation would be much preferable to even isodynamic quantities of albumin and carbohydrates.

Whenever, on the contrary, it is a question of sparing the albumin, an excess of carbohydrates, which oxidize with extreme facility, will be much more indicated than an isodynamic amount of fat.

At all events, isodynamy is never absolute, for a certain proportion of albumin is essential to life, and this quantity cannot be replaced by any other aliment.

Life may be sustained by albumin only; but we cannot live upon fat only, nor upon the carbohydrates solely. Albumin is absolutely indispensable to the life of the organic cells, for it constitutes their framework. Living matter is, in fact, of albuminous nature, and even an albuminoid substance like animal gum cannot take its place.

Leaving aside the indispensable albuminous ration, the daily alimentary ration may be composed entirely of albumin or solely of isodynamic quantities of fats or carbohydrates; lastly, it may be formed of a mixture of the three substances, provided that the sum of their potential is equivalent to the number of calories necessary to maintain the vital equilibrium.

The last is certainly the best method. According to *Rubner*, the ideal daily ration should be composed of a mixture of:

Albumin	16 per 100
Fats	17 per 100
Carbohydrates	67 per 100

There is no necessity for considering the other elements, such as water and the salts, for the indispensable quantities of these substances occur naturally in the food.

But as *Rubner* remarks, these figures should only be considered as averages, and in practice too much schematizing should be avoided.

Take albumin, for example, very frequently it may be given, and it is given in practice in quantities of less than 16 per cent.

Nature does this in the breast-fed infant, for woman's milk contains only:

Albumin	10 per 100
Fats	47 per 100
Carbohydrates	43 per 100

The same may be said for the fats and carbohydrates, the reciprocal proportions of which vary and change with customs, habits and even days.

Rubner[1] has collected and formed into a table, the number of calories necessary to the different periods of life, and to the varying degrees of human activity, as well as the ordinary proportions of albumin, fats, and carbohydrates required to furnish them.

		Calories (gm.)	Albumin (gm.)	Fats (gm.)	Carbohydrates. (gm.)
	Infant at the breast	344	8	17	37
	Child 20 kg. weight	1524	63	37	225
	Child 40 kg. weight	1913	80	47	280
Moderate work	Adult 50 kg. weight	2102	90	37	262
Moderate work	Adult 70 kg. weight	2631	123	46	327
Hard work	Adult 50 kg. weight	2472	96	44	409
Hard work	Adult 70 kg. weight	3094	118	56	500
	Old man 60 kg. weight	2111	91	45	322

Composition of the Daily Ration

Let us examine each of the alimentary bodies, from the standpoint of the minimum and maximum dose, and also the laws which preside over its fixation in the body; for each one of these points must be considered in the establishing of regimens, which seek to bring together at the *same time* maximum doses for some aliments and minimum doses for certain others.

ALBUMIN

The question of albumin is of great importance in a regimen based upon a reduction of proteids, as ours is; consequently we shall study it in detail, by first seeking the minimum dose of albumin which may be incorporated in the daily normal ration, and then examining the influence exercised by exaggerated amounts in normal man.

[1] Rubner: Ernährungswissenschaft, p. 32.

Minimum dose of albumin. We have already seen that, while the fats and carbohydrates may be replaced—at least for some time—by isodynamic quantities of albumin, the last is indispensable to man and cannot be completely replaced by any other aliment.

As soon as the quantity of albumin ingested falls below the *indispensable minimum dose*, the albumin of the organism is put under contribution, especially that of the muscles; in consequence there occurs a nitrogenous deficit in the organic cells.

This minimum dose also termed *the minimum ration of nitrogenous equilibrium* (Stickstoffgleigewicht's minimum) is intended to make up the albumin loss in the organic cells, and every normal regimen should carry at least **the minimum ration of nitrogenous equilibrium.**

Minimum ration of nitrogenous equilibrium. The minimum ration was fixed by *Voit* at 118 grams of albumin in twenty-four hours.

Gautier lowers it to 109 grams.

Müller, Cedercreutz, Emberg, Hirschfeld, Klemperer, Peschell, Siven, Landengren, have published works of great importance upon this question of the minimum albumin ration, which have completely changed our notions, and have demonstrated that a hyponitrogenous regimen has a sound physiological basis.

Hirschfeld[1] shows that a nitrogenous equilibrium is obtained with an amount of albumin much inferior to that admitted before his researches.

Müller[2] asserts that the minimum nitrogenous ration has been fixed too high, and that 60 grams of albumin should be considered as the minimum.

Rubner[3], in his interesting work, calls attention to the necessary quantity of albumin, which he states is very small and may be fixed at 5 per cent. of the daily necessary potential; this would correspond to about 35 grams of albumin for an adult man in whom growth was complete. In the child, *per contra*, who needs albumin for his development and for the

[1] Hirschfeld: Pflügers Arch., XLI, et Virch. Arch. Bd., CXIV.
[2] Müller: Antrittsrede, Basel.
[3] Rubner: Ernährungswissenschaft, p. 25.

formation of his tissues, a slightly larger quantity may be necessary.

Klemperer[1] obtained nitrogenous equilibrium with 33 grams of albumin by giving at the same time, it is true, a strong proportion of fats and carbohydrates.

Siven[2], in his interesting work, and *Peschell*[3] in his inaugural dissertation, prove that nitrogenous equilibrium may be secured, with an alimentation containing only 40 grams of albumin, and that, under these conditions, the organism does not draw in the slightest manner upon its own albumin, provided the quantity of calories lacking is made up by the fats and carbohydrates. *Landengren*[4] sought to determine the necessary ration, in a manner altogether different from that of his predecessors. He withdrew albumin entirely from a diet rich in fats and carbohydrates, which he gave to healthy men who continued their usual work as before the experiment. Under these conditions all of the necessary albumin ration was drawn by the organism from its own tissues and was revealed in the urine by its nitrogenous content which could thus be dosed.

By this method *Landengren* showed that in man the minimum nitrogenous ration is from 3 to 4 grams; this would nearly correspond to between 30 and 40 grams of albumin found by the other methods. These experiments were repeated by *Siven*[5] and by *Cedercreutz*[6]; they found 3.4 nitrogen for the minimum and 4.49 for the maximum, results completely confirming the experiments of *Landengren*. *Ernberg*[7], in his excellent inaugural dissertation, repeated the experiments of *Landengren* upon bedridden subjects; his figures, somewhat lower on that account, are 2.38 minimum nitrogen to 3.1 maximum.

A summary of all these researches shows that modern investigations have completely and absolutely vindicated the vegetarians, the Europeans and particularly the Japanese, who assert that the nitrogenous ration may be diminished without disadvantage.

[1] Klemperer: Zeits. f. klin. Med. Bd. XVI.
[2] Siven: Skand. Arch. f. Phy., Bd., X.
[3] Peschell: Dissertation. Berlin. 1890.
[4] Landengren: Skand. Arch. f. phys., Bd., XIV.
[5] Siven: Skand. Arch. f. Phys., Bd., XI.
[6] Cedercreutz: Dissertation. Breslau. 1902.
[7] Ernberg: Dissertation. Stockholm. 1905. p. 4.

Therapeutically, we are justified in applying these findings to certain diseases in which it is needful to lower the proportion of albumin in the food.

Thus in nephritis and in intestinal auto-intoxication, it is possible for the greater benefit of the patient to establish regimens carrying only 40 to 50 grams of albumin; these are therapeutic regimens, and for the time being only.[1]

Exaggerated dose of albumin. What is the effect of a quantity of albumin greater than the so-called minimum dose?

Is this excess of albumin, *this nitrogenous ration de luxe*, preserved in the body in the form of muscle, blood cells and is an individual nourished with a surplus of albumin likely to become stronger, more vigorous?

Such was the conclusion of *Pflüger*[2], who admitted that an albuminous surplus increased the cellular substance almost double.

This was also the opinion of *Herbert Spencer*, who maintained the physical superiority of the meat eater over that of the eater of rice, the Japanese, Russians, etc.

The experiments of *Pflüger* were performed on cats, and led to false deductions.

Muscular work, is in fact, a physiological stimulant to the deposition of nitrogen in the tissues, and under its influence, osmosis increases as *Loeb*[3] has shown, and the muscular fibers become thicker without increasing in number.

That is why a cat, always in movement, has large muscles; and for the same reason also, a vegetarian workman has larger muscles than the carnivorous scientist.

But under normal conditions, the nitrogenous surplus is burnt up at once, without fixation and only an acceleration of the oxidizing processes results from it.

The absorption of oxygen, the excretion of carbonic dioxide, and the production of heat are augmented; they bring about a prodigality of nutritive exchanges, as confirmed by *Magnus Lewy*[4], and by *Pflüger* himself[5], who adds:

[1] *See* Combe: Beiträge zur chlor und stickstoffarmen Ernährung bei Morbus Brightii, Monatschrift f. Kinderheilkunde, IV, 1 and 2.
[2] Pflüger: Archiv., LXXVII, p. 424.
[3] Loeb: Pflüger Arch., LXIX, p. 32.
[4] Magnus Lewy: Pflüger's Arch., LV, p. 1.
[5] Pflüger: Arch., LXXVII, p. 159.

"The albuminous excess increases the oxidations beyond need, and the great effort exerted by the organism to rid itself of this valuable nitrogen surplus, is most remarkable. For it is accompanied by excess of body heat, tachycardia, quickening of respiration and great nervous excitement."

For this reason, excess of nitrogen should be avoided in all nervous subjects or those pathologically excited as are the digestive auto-intoxicated.

Fixation of albumin. Under ordinary circumstances, all ingested albuminous surplus is burnt up and the organism has no means of storing it and keeping it in reserve.

In the adult there is but one exception to this rule, and that is when the body has suffered from grave disease or inanition, and there consequently exists a deficit of nitrogen in the cells.

It is not here a question of forming new cells, but only of filling up with fresh juice the old cells as well as the depleted and weakened muscular fibers, so as to give them back their strength and former volume.

Numerous experiments have demonstrated that in the convalescence of grave diseases the body may retain as much as 20 grams per day, of the albumin in the food, and most remarkable of all, without any increase in the fat or weight of the convalescent.

In the child, on the contrary, fixation of the albumin is observed, **even in the physiological life during development.**

Keller[1] has, in fact, found that at this period of life the nitrogenous retention of the organism may rise to 1 gram, even to 1.60 grams per day, that is, from 5 to 12 per cent. of the ingested nitrogen.

This quantity of nitrogen, *Rubner*[2] states, is intended for the formation of new cells, for the formation of the blood, its coloring matter and the lymph; it besides supplies the cells of the skin, of the mucous membranes, the bones, cartilages and hair.

The nitrogen retained in the child is therefore the mother substance of all the albuminous and albuminoid substances formed in the organism during development.

[1] Keller: Centralbl. f. inn. Med., XIX, p. 545.
[2] Rubner: Loc. cit., p. 28.

In the diseased child the quantity of nitrogenous material absorbed may be so slight that its retention ceases and growth is arrested; this is what happens in athrepsic sucklings and in the atrophy of older children.

In the healthy child the nitrogenous retention takes place, even when the quantity of food ingested is too feeble to suffice for the production of animal heat, and it is obliged to draw upon the fat of the organism as both *Rubner* and *Heubner*[1] have shown.

The healthy cell alone is capable of fixing the nitrogen and of multiplying. Therefore in order that nitrogenous fixation may take place there is required on the one hand, the cellular attraction of the healthy cells in a state of convalescence or of development, on the other, the necessary amount of nitrogenous food. The young cells, the organs in the period of growth have the faculty of attracting the nitrogen of alimentary origin circulating in the blood and present in the tissues and of making use of it for their own formation; if the food does not contain enough, the young and growing cells will go to the point of robbing the organism of its nitrogen, to the detriment of the muscular tissues which rapidly atrophy.

This nitrogenous migration to the point of maximum growth has been demonstrated by *Miescher*.

En résumé, nitrogenous fixation normally occurs at the expense of the proteids, owing to the physiological stimulus of the nervous system upon the convalescing muscles, and in the next case to the stimulus exercised by growth upon the young organic cells[2].

Albumin in the Antiputrefactive Regimen

It is therefore in these two classes of cases, convalescence and development, that the regimen must exceed the minimum of nitrogenous equilibrium.

Hence in the antiputrefactive regimen intended for cachectic auto-intoxicated, we have fixed the daily albumin ration, not at 40 grams, but at 50 grams giving 205 calories.

In regimen No. II. The soups and puddings contain 1,500 grams of milk, that is, 52.50 grams, of albumin.

[1] Rubner & Heubner: Zeits. f. Biol., XXXVI, p. 391.
[2] Rubner: Wachstumskrafft. 1906. p. 26.

In regimen No. III., in which a somewhat larger quantity of albumin is admissible, the proportion rises to 70 grams of albumin, that is, 287 calories.

	Albumin
100 grams roast meat	22.95 grams
50 grams ham	12.50 grams
1,000 grams milk (soups and puddings)	35.00 grams
	70.45 grams

Fat

The fat absorbed in the intestine is burnt up in the body, *pro rata* with the calorific needs of the organism, which regulates also (and for the same reason) the absorption of oxygen and the excretion of carbonic dioxide. The calorific need is the amount of heat necessary to maintain the animal heat in a state of equilibrium, and to furnish the amount of work demanded of the heart, the lungs, and particularly of the muscles.

The excess of fat ingested, contrarily to albumin, is retained and fixed, the surplus being deposited in the living cells of the organism.

These cells take up the fat from the blood, in which it circulates in a soluble form and no longer in the shape of droplets, as in the chyle. In fact, the liver, which is the depot for the fatty bodies, only allows them to enter the circulation very gradually and then only by combining them with lecithin; the latter keeps them in solution in the plasma, and it is under this form that the cell protoplasm absorbs them and reconverts them into fat.

Whenever there is need in the organism of calorific bodies, the cell protoplasm retransforms the fat into soluble combinations and returns them to the blood, in which they are consumed. The cell produces these transformations, thanks to the soluble ferments it contains.

Fats in the Antiputrefactive Regimen

In regimen No. II. we have with the three meals:

	Butter	30 grams = 30 grams
1,590 grams of milk =	butter	54 grams = 54 grams
	Fats =	84 grams = 781 calories

In regimen No. III:

30 grams of butter =	30 grams
100 grams of meat and 50 of ham =	23.32 grams
1,000 grams of milk =	36 grams
Fats =	90 grams = 837 calories

The Carbohydrates

The starches, dextrine and sugar transformed in the intestine into glucose and absorbed as such, accumulate in the liver in the form of glycogen and are returned to the blood as sugar, but in such a manner that the quantity never exceeds the normal.

The carbohydrates ingested in excess may be converted into fat (*Voit, Tscherwinsky, Meissel, Strœhmer*), perhaps because the carbohydrates burn up easily and thus preserve the fats from oxidation.

The Carbohydrates in the Antiputrefactive Regimen

REGIMENS II AND III

Cereal flours Alimentary pastes Zwieback Sugar and lactose	300 to 500 grams that is 1,230 to 2,050 calories

Caloric Value of the Antiputrefactive Regimens

In our regimens we have on an average:

Albumin	50 to 70gm. =	205 to 287 calories
Fats	84 to 90gm. =	781 to 837 calories
Carbohydrates	300 to 450gm. =	1,230 to 1,845 calories
		2,216 to 2,969 calories

Alimentary Composition of the Antiputrefactive Regimen

How may the regimen modify the intestinal culture bouillon, and what should be the composition of the antiputrefactive regimen?

Antiputrefactive Regimen

For this purpose two regimens have been proposed:

A. The aseptic regimen.

B. The lacto farinaceous regimen.

A. Alimentary Asepsis

Aseptic regimen. As soon as the principles of surgical antisepsis were understood by physicians; they very naturally fixed

their attention upon the absolute cleanliness of alimentary hygiene.

In intestinal auto-intoxication, this is even more essential, so as to prevent the further entrance of large quantities of putrefactive microbes.

Raw articles of diet should therefore be avoided for they serve as vehicles for the intestinal parasites, besides being laden with innumerable bacteria derived from all sources.

In spite of washing, etc., raw vegetables, such as salads, radishes, watercresses, etc., such fruits as berries, grapes, cherries, plums, etc., that are eaten with the skin, all of these are soiled by dust, earth, manure and fecal matters which contain very frequently noxious microbes, particularly saprophytes.

Bienstock has found in the soil of his strawberries the spores and bacilli of tetanus. It is true that he did not find them in his digestive canal where they had been destroyed by antagonistic microbes.

But we should not rely too much upon the bactericidal power of the intestine, and it is much preferable and advisable in cases of digestive auto-intoxication to absolutely avoid the use of raw vegetables and fruits and to use them only in a cooked state; when all, or at least the very great majority of micro-organisms they contain will have been destroyed. This rule should apply to meats, which should always be well done and never used in the raw state or even underdone or rare.

Lastly, all suspicious or slightly tainted meats should be at once rejected; those susceptible of easy fermentation should likewise be eliminated.

The water, unless from an absolutely pure source should be boiled. The regimen we propose is therefore an aseptic one, avoiding as it does all raw or suspicious aliments so as to prevent the entrance into the body of the microbes of putrefaction, the deleterious actions of which are unquestionable.

Sterilized Regimen. It has been attempted to go further by proposing a sterile regimen with the object of obtaining intestinal asepsis.

This regimen was first studied by *Stern* in 1886[1], and con-

[1] Stern: Arch. f. Hygiene. 1886.

sisted in administering to patients completely and absolutely sterilized nourishment.

With the same object in view, *Ferrand* gave a sterile regimen, followed by the use of laxatives, which it is true, diminished but did not suppress intestinal putrefaction; for a true intestinal asepsis was by no means obtained, as the bacteria decreased only one-half and the sulphoethers but two-thirds.

Huchard, for the same purpose, preaches enteroclysis combined with a milk diet; both excellent means but incapable of bringing about intestinal asepsis.

Albu[1] applied these methods under rigid control and this is what he found:

"Repeated examinations demonstrate that the introduction of aseptic or sterile foods modify the proportions of bacteria but very slightly, and produce almost no change in the quantity of the sulphoethers.

It is only by combining this method with free purgations and enteroclysis that a veritable diminution in the intestinal flora and the sulphoethers is observed; but such methods would be difficult to apply in practice and are, moreover, of doubtful utility; they are good adjuvants but do not suffice to render the intestine aseptic.

B. Lacto Farinaceous Regimen

To disinfect the intestine more and better than the preceding is needed; we must be able to saturate the intestine from top to bottom, even its smallest recesses and corners with a substance inoffensive to man but offensive to the bacteria, one capable at least of inhibiting them and preventing their putrefaction of albumin. This substance can only be alimentary.

This end is attained by completely changing the culture medium, in which the proteolytic microbes of the intestine live.

This notion of the great influence a change of regimen exercises upon the vitality of the intestinal flora is not new, for it is a long time since *Escherich* brought it to light, and it has been employed since then in pediatric practice for the treatment of dyspepsia. This method does not therefore seek to directly destroy the

[1] Albu: Deuts. med. Woch. 1897. p. 509.

intestinal microbes nor even to destroy them in part. It simply seeks to modify the medium in which they thrive, nourish themselves, secrete their toxins and multiply; it also seeks to cut off their food supply, thereby diminishing their vitality, their activity and virulence.

What must be done to accomplish this?

1st. To find among the natural aliments themselves those that favor the vitality of the putrefactive microbes and those that are harmful to them. The first are the putrefactive aliments, the second the antiputrefactive.

2d. To diminish in the regimen and in as great a measure as possible the putrefactive aliments, and *per contra*, increase as much as possible the antiputrefactive ones.

What Are the Putrefactive Aliments?

Nitrogenous foods. A long series of investigations have demonstrated the great influence exercised by nitrogenous foods upon intestinal putrefaction.

From their researches *Salkowski*[1] and *Jaffé*[2] both concluded that intestinal putrefaction increased parallelly with the quantity of albumin ingested.

Müller first, *Ortweiler*[3] next, showed that with a meat diet the products of microbic intestinal putrefaction, the aromatic bodies, indol and phenol particularly, were present in the urine in large quantities. *Backmann*[4] repeated these experiments and completed them by studying the action of egg albumin; his results are as follows:

		Sulphoethers
1st	Series ordinary food	0.167
2d	Series ordinary food + 200 grams eggs	0.184
3d	Series ordinary food + 120 grams meat	0.234

It thus appears that the sulphoethers increase with eggs but much less than with meats.

Mester[5] pursued these investigations by comparing the effects of fresh and tainted meat.

[1] Salkowski: Deuts. Gesell. 1876. p. 138.
[2] Jaffé: Virch. Arch. LXX, p. 370.
[3] Ortweiler. Diss. Kœnigsberg.
[4] Backmann: Zeits. f. klin. Med. XLIV, p. 409.
[5] Mester: Zeits. f. klin. Med. XXIV, p. 453.

	Sulphoethers
1st Series ordinary food	0.058
2d Series ordinary food + meat	0.113
3d Series ordinary food + tainted meat	0.328
4th Series ordinary food + strongly tainted meat	0.694

It may be concluded from these researches:

1st. That a meat diet considerably augments intestinal putrefaction, the more so, if the meat is not fresh.

2d. That the white of eggs exercises the same action, but to a much lesser degree.

The fats. What is the influence of fats upon nitrogenous putrefaction?

It was thought for a long time that they had none, but modern researches have on the contrary, shown that they exercised a very appreciable action.

Pemosch[1] had already demonstrated that the presence of fat in the alimentation of rabbits increased the proportions of indol.

Nasse[2] made quite a series of experiments upon dogs with the following results:

1st DOG:	Sulphoethers
1st Series: meat 1kg.	0.155
2d Series: meat 1kg. + 500 grams fat	0.284

2d DOG:	Sulphoethers
1st Series: meat 1kg.	0.185
2d Series: meat 1kg. + 500 grams fat	0.241

Backmann[3] completed these investigations by studying the influence of more digestible fats than those of meat (cream and butter.)

IN MAN:	Sulphoethers
1st Series ordinary food	0.237
2d Series ordinary food + 135 grams butter	0.284

IN MAN:	Sulphoethers
1st Series ordinary diet	0.165
2d Series ordinary diet + 181 grams cream	0.193

The conclusions being:

1st. That the addition of fats to the alimentation notably increases intestinal putrefaction.

[1] Pemosch: Diss. Kœnigsberg. 1877.
[2] Nasse: Pflüger's Arch. XXI, p. 170.
[3] Backmann: Zeits. f. klin. Med. XLIV, p. 469.

2d. That butter and cream exercise the same action, but to a much lesser degree.

What Are the Antiputrefactive Aliments?

The antiputrefactive alimentation is a lacto farinaceous diet. This is not an empirical method, but one based upon a scientific knowledge derived from many investigations, of which the following is a brief *résumé.*

MILK

The first author to speak of the antiputrefactive action of milk was *Poehl*[1].

The use of raw milk, even that of cooked milk, he states, notably diminishes the urinary sulphoethers.

A few years later *Biernacki*[2] took up these experiments by examining the urinary sulphoethers.

	Sulphoethers
Before using milk	0.693
With milk diet	0.441
With milk diet	0.331

	Sulphoethers
Before using milk	0.772
With milk diet	0.750
With milk diet	0.230

In these experiments the intestinal putrefaction diminishes on an average one-half and even two-thirds with a milk diet. The following experiments give these averages:

1st	Ordinary diet	0.142
	Milk diet	0.098
2d	Ordinary diet	0.125
	Milk diet	0.092
3d	Ordinary diet	0.158
	Milk diet	0.070
4th	Ordinary diet	0.149
	Milk diet	0.068
Average with ordinary diet		0.142
Average with milk diet		0.068

The milk diet therefore diminishes intestinal putrefaction to a great extent about 70 per cent. on an average.

But while these authors noted these facts and called attention to the very interesting results, they did not seek the reason.

[1] Poehl: Mahli Jahresbericht. 1887. p. 277.
[2] Biernacki: Deuts. Arch. f. klin. Med. 1892. p. 102.

The first to take up the question were *Hirschler* and *Winternitz*. *Hirschler*[1] (whose interesting work upon farinaceous foods we shall presently cite), in discussing the results of *Biernacki*, attributed them to lactose, which, according to him, ferments more readily than albumin and would in that manner absorb the fermentative faculty of the intestinal bacteria.

Winternitz[2] began by comparing the proportions of the sulphoethers between a meat diet and a milk one, in the same individual.

4 days upon milk diet	Sulphoethers	0.086
	Sulphoethers	0.078
	Sulphoethers	0.073
	Sulphoethers	0.073
4 days upon meat diet	Sulphoethers	0.344
	Sulphoethers	0.360
	Sulphoethers	0.355
	Sulphoethers	0.366

	Sulphoethers
Average with milk diet	0.079
Average with meat diet	0.358

There are therefore four times as many sulphoethers with a meat diet than with a milk one; in the milk-diet stools, leucin, tyrosin and the oxyacids were found, but no trace of indol, skatol or phenol; this is what is noted in the stools of the suckling. Pursuing his experiments, *Winternitz* showed that of all the proteids, milk was the one which resisted putrefaction the best; it is only after five days that tyrosin is found, paraoxyphenylpropionic acid after seven days; indol, phenol and skatol cannot be detected even after twenty days.

Lastly, *Winternitz*[3] showed that it suffices to add a certain quantity of milk to a meat diet, in order to attenuate its harmful effects and to diminish digestive auto-intoxication.

	Sulphoethers
Meat diet	0.344
Meat + half liter of milk	0.268
Meat + one liter of milk	0.264
Meat + one liter of milk	0.236

Hence, Winternitz was able to conclude that, not only did milk resist putrefaction, not only did a milk diet diminish the phenomena of intestinal putrefaction, but that it was also an antiputrefactive food, for added to a meat diet it greatly lessened the toxic effects.

[1] Hirschler; Zeits. f. phys. Ch. X, p. 306.
[2] Winternitz: Zeits. f. phys. Ch. XVI, p. 460.
[3] Winternitz: Zeits. f. phys. Ch., XVI, p. 463.

To explain these facts *Winternitz* advanced the two following hypotheses, that (as *Hirschler* believed), the lactose forestalled the intestinal bacteria, thus preserving the casein or else it was owing to the products of the lactose fermentation, the lactic and succinic acids, which inhibited the proteolytic bacteria whose office it is to putrefy casein.

Bienstock[1], having shown that there exist special bacteria for the decomposition of the casein, and that they are in no manner affected by lactose, *Winternitz* then completely eliminated the hypothesis of *Hirschler*.

Continuing his researches still further, he demonstrated that the resistance of milk to putrefaction is not due to its fat nor to its casein, for if milk is deprived of its lactose, casein putrefies with the same rapidity as other albuminous substances.

It is therefore due *to the presence of lactose*, the only substance contained in milk capable of preventing its nitrogenous putrefaction.

But it was reserved to *Blumenthal* to furnish the proof that the antiputrefactive action of lactose was not due to *sugar of milk in a state of nature*, but to the *lactic and succinic acids derived from it*. They are the agencies which protect casein against putrefaction.

By neutralizing these acids the artificial putrefaction of milk can be brought about. (*Blumenthal*).

En résumé, milk is an antiputrefactive aliment, thanks to the lactose it contains, and which under the influence of the aerobic bacteria of the small intestine (**"coli bacillus and lactis aerogenes"**) **is decomposed into lactic and succinic acids.**

These are the *acids*, which *prevent* the **proteolytic anaerobic bacilli of the large intestine,** from putrefying either the *casein of milk, or the albumin of the proteids in their immediate vicinity.*

Hence milk resists putrefaction and it is therefore an antiputrefactive aliment.

But to conclude from this that milk is capable of rendering the intestine aseptic is a far stretch.

Upon this point the following is the opinion of *Albu* and

[1] Bienstock: Zeits. f. klin. Med. VIII, p. 1.

Blumenthal, both of whom have devoted many long years to the study of intestinal auto-intoxication.

"Is it possible to obtain complete asepsis of the intestine by means of a milk regimen? The results of our experiments show that no more than sterilized foods can milk, raw or cooked, prevent the development of intestinal putrefactions.

"*Schmitz* found the same results by giving animals milk, both raw and boiled.

"It is therefore impossible to secure *asepsis of the intestine* by means of a milk diet.

"By administering an absolute milk diet a diminution in the intestinal putrefaction is effected, but it does not completely disappear.

"Milk is at the present time the only agent which may be usefully employed in intestinal antisepsis." (*Albu.*)

Soured Milks

There exist a certain number of milk aliments which all contain lactic and succinic acids in greater or lesser proportions, and which if the hypothesis of *Winternitz* were exact could like milk but better still fill the antiputrefactive function pertaining to it.

They are the soured milks:

Curdled milk	Pot cheese
Whey	Koumys
Buttermilk	Kephir

Curdled Milk

Curdled milk sometimes called sour milk is ordinary milk, which, abandoned to itself, turns under the influence of a microbe termed *Bacillus acidi lactis aerogenes* and coagulates into a creamy whitish mass slightly gelatinous, having a very palatable acid taste.

In many places, in order to obtain a rapid coagulation of the milk, dry or liquid rennet preparations are employed; these are sold commercially by the large dairy establishments of Germany and Denmark.

Mode of preparation. *Milk curdled naturally.* A liter or a half liter of milk is poured into a bowl or dish, which should be covered to avoid contamination by dust, etc., it should be placed in a rather warm spot (before the stove or fire) to favor microbic action but not warm enough to hinder it.

It is allowed to remain there until the milk is curdled, which, in summer, requires usually about twenty-four hours, considerably longer in winter; the action can then be hastened by adding one or two spoonfuls of the previous day's curdled milk.

Artificial curdled milk. To a liter or a half liter of milk made lukewarm (25° to 30° C.), add a small quantity (what would cover the point of a knife) of powdered rennet (from Witte, of Rostock) and stir well into the milk.

Or else a liquid preparation may be used, for example, *the liquid rennet of Hansen* of Copenhagen. Place the bowl or vessel in a warm spot or before the stove.

The milk will curdle and be ready to use in from one to two hours. Milk prepared by either of these two methods will be sweet and at the same time acid if immediately taken.

By allowing a longer time, which is preferable from the viewpoint of its action, the acidity increases and in from twenty-four to forty-eight hours, the milk becomes decidedly acid.

It should then be taken with a little sugar or flavored with cinnamon; although many of our country people prefer it in its natural state; owing to its thick consistency it is best taken with a spoon. Whenever it lies heavily on the stomach, we usually have the cream removed wholly or in part before curdling the milk.

Curdled milk is an extremely widespread aliment. It has been used in Switzerland from time immemorial and particularly in German Switzerland, where it is taken before meals or after, as a dessert.

In Germany also, it is greatly used as a food by the people, and also in the numerous sanatoria (Naturheilanstalten) of the country.

In France curdled milk, much employed in ancient times, had fallen into disuse, but owing to the great authority of *Metchnikoff* and thanks to the writings of *Monteuuis* (the eminent

physician of the Sylvabelle Sanatorium[1]), it is rapidly regaining in favor and will again occupy its place—and with reason—in French dietary.

Chemical composition. Curdled milk contains about the same elements as ordinary milk. The lacto casein, the lacto albumin, the butter, the salts are not modified; the lactose alone is diminished and but slightly, the lactic and succinic acids taking its place.

	Fresh Milk	Curdled Milk (Orla Jensen)
Casein	3.55	3.55
Butter	3.70	3.70
Lactose	4.88	3.9 to 4.50
Salts	0.71	0.71
Water	87.17	87.17
Lactic acid	.0	0.60 per 100

Digestibility. Curdled milk is much more easily borne by the stomach than fresh milk, and it is not unusual to see patients who have never been able to take fresh milk get along admirably with curdled milk.

Monteuuis himself had this experience, for he, who could never take fresh milk, which he could not digest, became able to take curdled milk at both his morning and evening meals with great benefit. He gives the following explanation:

Milk, owing to the fact that it is curdled, no longer coagulates in a mass in the stomach, and does not inhibit its own digestion nor that of the other aliments forming part of the same meal.

This explains why it may be taken without detriment at meals, and we have in practice met numbers of patients who could not tolerate fresh milk but suffered no inconvenience from the use of curdled milk.

Curdled milk is not only more easily borne, but it is more acceptable than fresh milk. Its thick consistency which permits its being eaten with a spoon instead of drinking it, its cool and acid taste make it a dish that most patients like at once, while others very quickly get accustomed to it.

Manner of using. The dose of curdled milk varies greatly; we generally begin with a cupful twice daily at the end of a dry meal.

Later the amount is increased to a bowlful twice a day; it

[1] Monteuuis: Lait caillé, élixir de longue vie. 1905.

may be taken in its natural state, or sweetened with milk sugar.

This method of giving curdled milk with meals is that adopted by the Orientals, most of the German sanatoria and is the one we prefer. Curdled milk is very easily taken with puddings.

Many prefer it fasting: *Monteuuis* prescribes it on arising and on retiring; others at 10 A.M., at 4 P.M. and 10 P.M., instead of liquid refreshments.

As may be seen, the time of taking is of secondary importance.

Therapeutic action. Curdled milk is a complete food and like milk, it is diuretic owing to its milk sugar content.

Per contra, owing to its content of lactic and succinic acids, it has the advantage over fresh milk of being an intestinal excitant. Its daily use is generally accompanied by great regularity of the stools, thus overcoming one of the great disadvantages of a milk diet.

Action upon intestinal auto-intoxication. Until now this action has been very little studied.

Poehl[1], who has examined the question from this point, claims to have seen very beneficial results.

We can absolutely confirm this, and in all cases of *digestive auto-intoxication of non-enteric nature*, we have always employed it with the greatest satisfaction. Since the use of yoghourt has become more practicable, we have employed it as much as possible and in preference to curdled milk, for as we shall see, the Bulgarian preparation acts not only like curdled milk but also by introducing in the digestive canal bacteria antagonistic to the proteolytic bacilli of putrefaction. In the country where curdled milk may always be prepared at small expense, we continue to recommend it as a most excellent antiputrefactive food.

Whey

The name of whey is frequently given to the clear or opalescent liquid remaining after the removal of the thickened portion of curdled milk. This is an error for what remains is nothing but the *serum of the curdled milk.*

True whey is the liquid left in the milk after it has been

[1] Poehl: Mahli-Jahresbericht. 1887. p. 277.

coagulated by rennet and the removal of the coagulum, which contains the greater part of the casein and butter.

Whey is therefore a cheese milk. It is a clear, transparent liquid of a greenish yellow color, with a sweet but at the same time slightly acid taste, due to its lactose and lactic acid content.

Whey is still greatly used in Germany and Switzerland as a hygienic beverage and as a dietetical agent in the sanatoria of both countries. The whey cures (*Molkenkur*), formerly so much used and in vogue, have declined in the last ten years, perhaps owing to the difficulty of securing milk from healthy cows, free from tuberculosis and properly kept.

A mistaken idea, for the micro-organisms in the milk are largely, if not totally, precipitated by the coagulation of the milk and remain in the butter and casein.

A distinction is made between whey from cow's milk and that from goat's or ewe's milk, but their properties differ very little. Whey is sometimes combined with alum (1 in 200) or with tamarinds (4 of tamarind pulp to water 200). The first is used in diarrheal cases, the second where constipation exists. Arco, Aussee, Baden Baden, Homburg, Reichenhall, Gries near Bozen, Ischl, Kreuznach, Levico, Meran, Wiesbaden, are the most celebrated localities in Germany for the whey cures.

Mode of preparation. A half liter of milk is poured into a bowl and kept at a gentle heat by placing bowl over warm ashes or in a larger vessel filled with warm water, and a small quantity (on the point of a knife) of rennet powder is added. As soon as the milk is coagulated it is passed through a fine meshed hair sieve.

The liquid which drips through is the whey; the solid part remaining is white cheese or pot cheese.

To clarify the whey the white of an egg is added and well mixed; the whole is then boiled until the white of the egg is coagulated and strained through cheese cloth.

Or the white of an egg may be added and well mixed, and the whole allowed to stand until clear, and then strained. The result is a limpid and clear liquid of a light greenish yellow color having a very agreeable sweet acid taste; the acidity should not be strongly marked. It is a liquid, very difficult to preserve

for it is very easily and rapidly altered, and becomes then strongly acid; hence its preservation and transportation require particular care.

Chemical composition. Whey contains the lacto albumins and the lacto globulins of the original milk less 1 per cent.; it contains lecithins, nearly all of the milk sugar and inorganic salts, with the exception of the earthy phosphates which remain in the coagulum.

Lastly, it contains oxidizing ferments and active hydrolysers. The chemical characteristic of whey is its poverty in fat and casein and its richness in lactose, lactic acid and the inorganic salts.

	Hammarsten cow's whey per cent.	Fleischmann cow's whey per cent.	Lehmann goat's whey per cent.
Water	93.20	93.30	93.77
Albuminoids	0.85	1.05	0.58
Butter	0.23	0.10	0.02
Lactose	4.70	4.40	4.97
Lactic acid	0.33	0.33	0.33
Salts	0.65	0.82	0.66

Method of using. In Germany and Switzerland, whey is given in the natural state or at first mixed with mineral waters; it is afterwards given pure, a glassful at a time until two or three may be taken daily, the best time being when fasting, generally about half-past seven A.M., ten A.M., and three P.M. (For our part we generally employ whey for the preparation of soups in the lacto farinaceous regimens, whenever we see the necessity of diminishing both the casein and fats.)

Physiological action. Whey is frequently difficult to digest in the beginning, so that unless it is given in the form of soup it is always best to mix it with "Vals Saint Jean" water, but tolerance is soon established.

In small doses it has no effect, in larger doses it is diuretic and slightly laxative.

Therapeutic action. Owing to its poverty in albuminoid substances, and to the fact that the one it contains is lacto albumin easily digested and more easily assimilated, whey is

valuable in arthritism and in the treatment of digestive nitrogenous auto-intoxication. The more so as its richness in inorganic salts helps to compensate their great loss in both these conditions.

Its richness in lactose and lactic acid make it also very useful in the treatment of auto-intoxication, because, owing to these two substances it is diuretic and slightly laxative.

Its alimentary value is feeble; 24 calories per 100 grams.

Buttermilk

Buttermilk is the liquid remaining in *fermented milk*, after the churning of the cream.

The composition of buttermilk is therefore different from that of *skimmed milk* or from that of *centrifuged milk*, for in these it is the *fresh milk* which has been deprived of its butter by means of either the cream separator or the centrifugal machine.

	Lactic Acid p. 100	Casein p. 100	Fat p. 100	Lactose p. 100
Centrifuged milk	0.	0.40	0.25	4.75
Skimmed milk	0.	3.11	0.74	4.75
Buttermilk	0.70	2.44	0.45	2.97

Centrifuged milk contains the total quantity of lactose (4.7 per 100) the lacto albumin and the salts but contains hardly any fat (0.20 per 100) or casein (0.40 per 100). In consequence its food value is very small; 100 grams of centrifuged milk representing only 37 calories.

Skimmed milk. Its composition is also very different from that of buttermilk, the only difference between it and ordinary milk being its poverty in fat.

Centrifuged and skimmed milks are therefore poor milks, and it is only for that reason that they are employed in the treatment of intestinal auto-intoxication.

We frequently prescribe them in the place of whole milk for the preparation of farinaceous soups; in enteric cases and in all those who do not tolerate milk well. They exercise no direct disinfectant action in intestinal putrefaction as buttermilk and whey do.

Buttermilk. It is not the same with buttermilk, for it is a milk which has been modified by fermentation, the same as curdled milk and whey.

Buttermilk is a liquid more or less thick, according to its mode of preparation and having a fresh, slightly acid taste.

It is greatly used in the north of France, Belgium and Holland, and in certain cantons in Switzerland, where on account of its cheapness, the poor people employ it in the preparation of farinaceous and rice soups. (I remember having, as a child, taken it many times at the family table and my father, who was physician of the little town of Sarraz, was in the habit of recommending it to all the country people as a most healthy food.)

Mode of preparation. Buttermilk may be prepared from either soured milk or cream.

In infantile dietetics, buttermilk should always be made from the milk of cows fed upon hay or fresh fodder to the exclusion of beets, oil cake, distillery grains, etc.

The fresh milk[1] is allowed to remain for twenty-four hours at a temperature of 20° C. (a room in winter or cellar in summer), it should be kept in a clean and covered vessel, and stirred two or three times during the day as with curdled milk. The acidifying of the milk may be hastened by adding a tablespoonful of the previous day's soured milk.

The milk should then be churned, the longer the better (one to two hours), so as to separate all the butter, as much as possible of the casein, and to obtain a fine division of the remaining curds.

The buttermilk should be consumed as fresh as possible.

Buttermilk from cream.[2] As soon as taken from the cow, the milk should be centrifuged and the separated cream removed.

The cream may also be obtained in a simpler manner by means of a cream separator.

This consists of a flat tin dish containing another within it; the interior one contains the milk, the outer dish cold water for the purpose of cooling the milk. After standing for some hours,

[1] Jacobson: Arch. méd. Enf. 1903. p. 66.
[2] Decherf: Arch. méd. Enf. 1905. p. 517.

the cream rises to the surface; the faucet situated at the bottom of the inner receptacle is opened and the skimmed milk is allowed to flow out, leaving only the cream which may then be removed and poured into a large wooden vessel where it is allowed to sour spontaneously in summer and in winter by adding a little of the previous day's soured cream. The cream sours very slowly; the churning should be done as soon as it begins to thicken.

To the cream should be added from a sixth to a third of boiled water or skimmed milk, cold in winter and warm in summer.

The churning should continue for a long time and as slowly as possible (on an average two hours). The butter is then separated from the buttermilk. In summer this buttermilk does not keep longer than twenty-four hours, and its sourness rapidly increases.

Chemical composition. This varies according to its mode of preparation.

	Buttermilk from milk	Buttermilk from cream	Buttermilk from centrifuged cream
Nitrogenous bodies per 100	2.44	2.16	2.88
Fat, per 100	0.45	0.50	0.36
Lactose, per 100.....	2.97	1.70	2.86
Salts, per 100	0.53	0.54	0.69
Lactic acid, per 100	0.077	0.066	0.078
Acidity in (Na OH) 1st day	0.23	0.24	0.28
Acidity in(Na OH) 2d day	0.24	0.28	0.30
Acidity in (Na OH) 3d day	0.26	0.29	0.31

Of these three kinds of buttermilk, the best is that made from whole milk, for it contains less casein but more lactose, capable of producing lactic acid *in a nascent state*, and this is an energetic intestinal disinfectant.

The other forms of buttermilk, containing more casein, less lactose and more lactic acid are less disinfectant, their lactic acid being immediately absorbed and neutralized.

Decherf employs buttermilk diluted, water 2 parts to buttermilk 3 parts, deducting, however, the water added at time of churning.

Its composition is:

Albuminous bodies	1.84
Fats	0.27
Lactose	1.88
Salts	0.67
Lactic acid	0.064
Acidity 1st day	0.18
Acidity 2d day	0.20
Acidity 3d day	0.22

This diluted buttermilk is distinguished by its feeble acidity and small proportion of fat and casein.

Condensed Buttermilk

Condensed buttermilk of Doctor Graanboom.[1] The originator of this buttermilk prepares it by the following process:

The centrifuged milk is pasteurized, then inoculated with a pure culture of *Bacterium acidi lactis*, and submitted to its action until the acidity attains 0.50 per cent.

The acidified milk is next subjected to cold condensation, until reduced to one-third volume, when sugar in the proportion of 50 grams per liter, and 6 grams of cream per liter are added.

The result is a creamy homogenous mass of very agreeable taste, which is put up in sterilized bottles containing 330 grams each. For use, the contents of a bottle are mixed with 600 grams of a cereal decoction; this gives one liter of buttermilk broth.

Condensed buttermilk of Biedert. *Biedert* and *Selters* have had manufactured by the *Deutsche Milchwerke* of Zwingenberg, a second kind of condensed buttermilk (*Buttermilch Conserve.*) This preserve, which we have used on many occasions with the greatest satisfaction, is most useful, for it is difficult to find everywhere a buttermilk having the same composition; whereas with this preparation we have at our disposal and at all times, a pure buttermilk rich in lacto albumin, poor in lacto casein and fat, and containing a constant proportion of lactic acid; all this in a form easily preserved and transported.

To prepare buttermilk from this *preserve*, mix one part with two of boiled water and there is obtained a buttermilk having the following composition:

Lacto casein	2.19 per 100
Lacto albumin	0.44 per 100

[1] Graanboom: Arch. méd. Enf. 1905. p. 551.

Lactose	2.30 per 100
Cane sugar	6.00 per 100
Lactic acid	0.50 per 100
Fat	0.50 per 100
Salts	0.58 per 100
Lime	0.06 per 100
Phosphoric acid	0.15 per 100

Its caloric value = 50 calories per 100 grams.

Condensed buttermilk soups. *Biedert* and *Selters* have also had manufactured by the same makers, buttermilk flours or condensed buttermilk soups, employing wheat flour (*Buttermilchmehlsuppe*) or barley (*Buttermilchgerstensuppe*). One part of the preserve is mixed with 3 parts of boiled water, and brought to the boiling point.

These buttermilk soups have given us great satisfaction, for children become fond of them.

Method of using. Buttermilk may be taken in its natural state, but it must be fresh from the day's churning and may be diluted with sterilized water.

More frequently it is employed in a cooked state either by itself or with rice or barley flour, or else oatmeal, cornmeal, wheat flour, etc. To one liter of buttermilk, add a large spoonful of flour mixed with a little cold buttermilk, boil slowly over a gentle fire with constant stirring, allow the milk to rise three times, withdraw from the fire and sweeten with about 50 grams of sugar.

The stirring is for the purpose of avoiding the formation of large lumps, and to obtain a finely divided mass.

In our service, in cases of alimentary dyspepsias, we use preferably *dextrinated flour without milk* in the preparation of buttermilk soups, and a *dextrinated and malted flour without milk* in cases of organic dyspepsia; both of these are new flours at present manufactured by the Nestlé Company. We add from 30 to 120 grams of these flours to the liter of buttermilk, according to the digestive capacity of the infant for starches, the dosage being ascertained by examination of the stools.

Buttermilk soup so prepared is ready for consumption. It may be administered through the feeding bottle or else with a spoon. The quantity given should be the same as the milk ordinarily taken; this buttermilk soup is of a homogenous

appearance and has very finely divided masses; it has an agreeable acid taste more or less pronounced, due to the lactic acid fermentation of the milk sugar.

Therapeutic uses. The feeble content of buttermilk in fat and casein, makes it a valuable food in intestinal auto-intoxication; for, as we have seen elsewhere, a strong proportion of these substances favors intestinal putrefaction.

Its content in lactic acid, but especially in lactose, capable of producing lactic acid, *in a nascent state* during its course throughout the intestine, makes it a good disinfectant of the digestive canal and explains its favorable action in the intestinal disorders of nurslings.

Buttermilk was recommended as early as 1875 by two Dutch physicians, *de Jager* and *Teixeira* of Mattos, later by *Salge*, *Caro* and *Baginsky* in Germany, *Jacobson*, *Arago*, *Cardamatis*, *Decherf* in France.

Fermented Sour Milks or Milk Liquors

The milks subjected to lacto alcoholic fermentation are koumys and kephir.

Koumys

Koumys is fermented mare's milk. It is a white, alcoholic and sparkling liquid, with a sharp acid taste and a pronounced sour odor.

It foams on pouring, owing to the large amount of gas it contains; hence it is necessary to keep it in special bottles.

Its use was for a long time confined to the tribes of the Russian steppes, but it is at present prepared with cow's milk at many places in Germany and Switzerland.

Mode of preparation. According to *Gautier*[1] koumys is made by the admixture of ten parts of fresh milk, with one part of already prepared koumys which contains its special ferment. The mixture is placed in an upright barrel and is stirred with a wooden ladle; a rather marked fermentation takes place, at first lactic later alcoholic, the liquid becoming acidulous and alcoholic.

[1] A. Gautier: loc. cit., p. 231.

It is then put into strong bottles, well corked, tied and kept in a cool place.

Chemical composition. This varies according to the age of the koumys.

Koumys	1 day old per cent.	8 days old per cent.	21 days old per cent.
Casein	0.80	0.85	0.79
Albumin	0.15	0.30	0.32
Peptones	1.04	0.59	0.76
Fat	1.17	1.14	1.20
Lactose	0.39	0.09	0.00
Lactic acid	0.96	1.03	1.00
Alcohol	3.19	3.26	3.27
Salts	0.33	0.34	0.35

Koumys has therefore the alcoholic strength of beer.

Its casein is partly changed into albumoses and peptones, while the fat is finely emulsified.

Koumys is used in its pure state and is given between meals in doses of 300 c.c. (or cupful) two or three times daily.

Therapeutic uses. Koumys one day old is an easily assimilated food. Its digestibility is besides considerable and is furthermore increased by the zymases, which have been found in it and are derived from its ferments.

Fresh koumys particularly that of the first day, is appetizing, stimulating, nutritious, and of easy digestion and assimilation; it is, moreover, slightly laxative and diuretic, and lastly, thanks to its feeble content in casein, and to the marked proportions of lactic acid and lactose it contains, it is an intestinal disinfectant and an antiputrefactive food.

But at the side of these advantages, there are some disadvantages which it shares with kephir.

Both of these milk preparations result from alcoholic and lactic fermentation. They contain up to 3 per cent. of alcohol, the daily absorption of which during many long weeks is not desirable for most patients suffering from diseases of the stomach or intestine. Secondly, the yeasts producing these fermentations may become acclimated in the digestive canal (*Metchnikoff*) and exercise a favorable action on some of the pathogenic bacilli. Lastly, the numerous bacteria introduced into the alimentary

canal with the lactic bacilli of the yeast may bring about abnormal fermentations.

Consequently both koumys and kephir are according to *Hayem* absolutely contraindicated in all gastrectases with motor insufficiency, "for, being too long retained, they continue to ferment and they develop besides, accessory butyric and acetic fermentations, which soon aggravate the digestive disorders.

Kephir

This is a foaming alcoholic preparation, very similar to koumys and prepared from cows' milk.

Many kephir cures exist in Germany and Switzerland, principally at Meran, Homberg, Arco, Aussee, etc.

Mode of preparing. The fermentation of the milk is provoked by a special agent called *kephir*; which is sold in the form of small irregular roundish masses, of a yellowish white appearance and about the size of a millet seed.

The ferment is obtained, it is said, from a plant analogous to cauliflower. Microscopic examination shows a special alcoholic yeast the *Saccharomyces mycoderma* and a bacterium, the *Dispora caucasica*, whose action appears to be that of partially peptonizing the casein[1].

To prepare this liquor, the inhabitants of the Caucasus pour the milk from their cows into skin bags, add the kephir powder mixed with a little warm water and allow the milk to remain at a moderate temperature, occasionally stirring it.

At the end of twenty-four hours the preparation is ready for use; if permitted to ferment for two days the fermentative products will be increased. Kephir tablets are manufactured and sold commercially, thus allowing of its preparation at home.

Chemical composition. This in a broad sense resembles that of koumys, but the comparison from an alimentary point of view is in favor of koumys, for the latter is made from mare's milk, the composition of which much resembles asses' and human milk.

From the antiputrefactive standpoint, the advantage lies with kephir.

[1] A Gautier: Loc. cit., p. 232.

	Kephir per cent.	Koumys per cent.
Lacto casein	2.98	0.80
Lacto albumin	0.28	0.30
Peptones	0.05	1.04
Fat	3.50	1.12
Lactose	2.78	0.39
Lactic acid	0.81	0.96
Alcohol	0.70	3.19
Salts	0.79	0.33

Physiological action. From the alimentary point of view, kephir is much richer in casein, but much less so in albumin particularly the peptones than koumys which has besides less fat.

Kephir is therefore less digestible and assimilable; it is also less stimulating than koumys for it contains less alcohol.

Therapeutic action. Both kephir and koumys contain rather marked quantities of lactic acid, but kephir contains more lactose which, insomuch as absorption will permit, gives rise in the intestinal canal to the formation of lactic and succinic acids in *nascent state.*

Consequently, as an antiputrefactive food kephir is superior to koumys.

Rovighi[1] has studied the action by a large number of experiments performed on himself by means of a fixed and always identical diet.

	Sulphoethers	Baumann not reversed
Before Kephir	0.210	10
Before Kephir	0.211	10
Kephir 1,500 grams daily	0.143	18
Kephir 1,500 grams daily	0.170	15
Kephir 1,500 grams daily	0.170	20

As may be seen, the urinary sulphoethers are diminished with kephir, but not as much as with milk.

In kephir as with curdled milk, but to an even greater degree the greater portion of lactose is changed into lactic acid. And yet curdled milk is more disinfecting than milk and the latter more than kephir.

[1] Rovighi: Zeits. f. phys. Chem. XVI., p. 30.

How can this be explained if it is true that lactic acid is the disinfecting substance as is apparently well demonstrated? In order to determine this *Rovighi* studied the antiputrefactive value of lactic acid.

	Sulphoethers
Before any medication	0.212
With 15 grams lactic acid	0.212
With 15 grams lactic acid	0.174
With 15 grams lactic acid	0.168
None	0.189
None	0.198

It appears from this that lactic acid diminishes intestinal putrefaction, but much less than the foods we have examined, less than kephir, less than milk.

The antiputrefactive power seems therefore to depend more on the lactose content than on the lactic acid.

Winternitz sought to confirm this hypothesis by the following experiments:

1st	Before lactose	0.230
	With 100 grams lactose	0.180
2d	Before lactose	0.410
	With 100 grams lactose	0.240

Winternitz, by these two experiments, succeeded in proving the antiputrefactive action of lactose, which greatly exceeds that of lactic acid, while it yet remained much below that of kephir, fresh or curdled milk.

How to explain the antiputrefactive action of these aliments?

Is it due to the combined action of the two associated antiputrefactive elements, lactose and lactive acid?

For, as we have seen, they alone can exert an antiputrefactive action, all the other chemical elements (the salts) being inert or else like the casein and butter frankly putrefactive.

Schmitz[1], by pursuing and repeating these experiments upon another variety of milk food (fresh or pot cheese) succeeded in solving the problem by calling attention to a new phenomena, which had not been sufficiently noticed by investigators: namely,

[1] Schmitz: Zeits. f. phys. Ch. XIX, p. 378.

the greater or lesser facility with which the food opposes the absorption of the antiputrefactive elements, lactose and lactic acid.

Fresh or White Cheeses

(Pot Cheese)

Fresh cheese is the solid part of milk curdled by rennet and deprived of its whey.

Mode of preparation. Fresh or pot cheese. The milk is allowed to stand in a cool place for twenty-four hours until the cream rises, this is partly removed. To the skimmed milk is added either powdered or liquid rennet. The temperature should be about 25° C. to favor the coagulation; when the latter is completed, the whey is allowed to flow off and the coagulated mass is taken up without breaking it and placed in little wooden molds, with trellised bottoms, in which the cheese is allowed to settle and drip off the superfluous liquid; the process may be accelerated by placing little weighted wooden disks on top of the molds.

The remaining dry curd constitutes the so-called *fresh cheese* or *pot cheese*.

2d. Cream cheese. The *whole* milk is curdled at a temperature of about 25° C. by means of rennet; the coagulated mass is taken up and the superfluous fluid allowed to drip off. Then it is placed in a sieve, and mixed with more or less fresh cream so as to form a smooth homogenous mass, which is finally put into willow molds lined with cheesecloth.

At the end of two hours the *cream cheese* is ready for use.

3d. Fresh double cream cheese so-called "Petits Suisses." Add one-sixth volume of good fresh cream to the whole milk, and stir, so as to cause an intimate mixture, then bring about coagulation by adding rennet and keep at a temperature of about 25° C. When completed, the coagulated mass is taken up, placed in a piece of cheese cloth, tied at the four corners and suspended from a nail so as to allow the whey to drip off; pressure or squeezing of the mass will complete the separation.

When this has been accomplished, the mass is kneaded with more cream and lastly is placed in little molds.

These cheeses deteriorate quickly, becoming sour with a rancid odor.

To preserve them they are converted into *demi sel* by adding 2 per cent. of salt.

Chemical composition. Fresh cheese is a food rich in fat, casein and lactose; its alimentary value per 100 c.c. is 182 calories.

	Pot cheese per cent.	Cream cheese per cent.	Double cream cheese per cent.
Casein	20.8	24 to 27	24.00
Albumin	4.10	4.0	4.0
Lactose	3.5	2.5	2.00
Butter	7.3	25 to 30	35.00
Salts	3.40	3.40	3.00
Lactic acid	0.50	0.50	0.60

The salts are alkaline phosphates, the phosphates of lime magnesia and iron.

Physiological action. Fresh cheese, according to whether it is made of milk or with cream, contains more or less nutritive matters. Its casein content makes it an important food, for it furnishes a considerable amount of easily assimilated nitrogenous substances. Fresh cheese has therefore all the advantages of milk, and it is frequently much better tolerated. Undoubtedly fresh cheese often contains bacteria and at times even tubercular bacilli, hence it might be advisable to pasteurize the milk before precipitating the cheese.

Therapeutic action. The experiments of *Schmitz*[1] have enabled us to understand the great value of this aliment as an anti-putrefactive, for its action greatly exceeds that of fresh milk and that of curdled milk which is already considerable.

In animals:	Sulphoethers
Before giving cheese	0.260
With fresh cheese 400 grams daily	0.096
With fresh cheese 750 grams daily	0.049
With fresh cheese 1,000 grams daily	0.077
With fresh cheese 1,500 grams daily	0.022

In man:	Sulphoethers
Before giving fresh cheese	0.552
With 500 grams at one dose	0.332

[1] Schmitz: Zeits. f. phys. Ch. XIX, p. 378.

In man:	Sulphoethers
Before giving fresh cheese	0.240
given in one dose: 500 grams *non sterilized cheese*	0.103
given in one dose: 1,000 grams *non sterilized cheese*	0.071
given in one dose: 2,500 grams *non sterilized cheese*	0.068
Before giving fresh cheese	0.240
1,500 grams *sterilized cheese*	0.059
1,500 grams *sterilized cheese*	0.024

The conclusions from the experiments of *Schmitz* are:

1st. The ingestion of fresh cheese causes a considerable diminution in albuminous putrefaction, both in carnivorous animals and in man.

According to *Baumann* it possesses this function to a higher degree than any other proteid aliment, lactic acid, lactose, kephir, milk and even curdled milk being left far behind.

2d. The antiputrefactive action depends upon the quantity of cheese ingested and increases with it.

3d. *Schmitz* next examined each one of the substances contained in fresh cheese from its antiputrefactive point of view.

The fat exercises but very little influence on putrefaction, only increasing it slightly.

The casein from the same cheese, when given alone, not only does not decrease the sulphoethers, but on the contrary, greatly increases them. This fact is of capital importance, for before making these experiments *Schmitz* and *Baumann* had attributed the antiputrefactive action to the casein.

	Sulphoethers
Before giving casein	0.286
With 250 grams casein	0.286
With 250 grams casein	0.458

Casein therefore, like all proteids, augments nitrogenous putrefaction.

Lactose: Fresh cheese deprived of its lactose, caused an increase in nitrogenous putrefaction, whereas it diminished considerably when present.

Consequently we must attribute the antiputrefactive action of fresh cheese to the sugar of milk which it contains, or rather to the lactic and succinic acids, formed at its expense during its passage through the small intestine[1].

[1] Schmitz & Baumann: Zeits. f. physiol. Ch. XVII, p. 401.

Such being the case, why then does fresh cheese act better than lactose and lactic acid in their natural state?

For lactic acid, the supposition might be that it was because it was not produced in a nascent form, but for lactose?

Fresh cheese acts better than lactose and lactic acid, **because it protects them better from being too rapidly absorbed** ; for their absorption begins in the stomach, and is continued in the small intestine; its retardation enables them to reach the large intestine, and there develop their inhibitive action. The antiputrefactive action of any milk food consequently depends first, upon the quantity of lactose it contains, secondly, upon the protection offered by the physical constitution of the food, against the too rapid absorption of the lactose.

4th. To produce the maximum antiputrefactive effect, it is advisable to administer the cheese in small quantities throughout the day, instead of giving it all at once. This is demonstrated by the following experiment of *Schmitz:*

	Sulphoethers
Before giving cheese	0.240
At one dose—1,500 grams cheese	0.071
In two doses—1,500 grams cheese	0.041
In four doses—1,500 grams cheese	0.022

The experiments of *Schmitz* were repeated and confirmed by *Gussarow*[1] and *Nassarow*[2], both pupils of *Nencki.*

Nassarow was even able to note that large doses of fresh cheese greatly diminished the number of bacteria in the stools.

Antiputrefactive Action of the Milk Foods

From a summary of this first series of experiments, the following conclusions may be drawn:

1st. That milk, owing to the nascent lactic and succinic acids, formed at the expense of its lactose, inhibits the putrefaction of its own casein and that of the other nitrogenous aliments with which it is in contact.

2d. The antiputrefactive action of the milk depends upon the content of the particular milk food in lactose and lactic acid, but especially upon its physical constitution, which protects these substances against too rapid absorption by the intestine.

[1] Gussarow: Diss. St. Petersburg. 1889.
[2] Nassarow: Diss. St. Petersburg. 1891.

3d. The solid derivatives of milk: fresh cheese, and milk curds are, in fact, the most antiputrefactive, because they oppose the too rapid absorption of lactose, and thus enable it to reach the lower portions of the intestine, where both lactic and succinic acids in a *nascent state* are slowly liberated.

4th. The maximum effect is obtained by giving the daily ration in small quantities throughout the day instead of at one time.

We may class the antiputrefactive milk foods into three groups, according to their energy:

First group. In this we place the solid derivatives of milk: fresh cheese and milk curds. These two foods have, it is true, a strong proportion of putrefactive casein, but on the other hand, they have a strong reserve of lactose, which is protected against a too rapid absorption by the casein and fat in a solid state.

They contain a greater or lesser proportion of lactic acid, according to their mode of preparation; this, like the lactose, is incorporated within the protective mass (casein and fat).

Fresh cheese and milk curds constitute therefore the highest and best type of antiputrefactive milk foods.

Second group. In this group we include whey, buttermilk and milk.

These three liquid foods oppose but little resistance to the intestinal absorption of their antiputrefactive elements.

Whey has the great advantage over milk, of presenting a very feeble proportion of putrefactive casein (0.85 instead of 3.50) and a still smaller proportion of ill-digestible putrefactive fat (0.23 instead of 3.69).

And although the amount of lactose is nearly the same in both (4.70 as against 4.88), whey contains besides, a rather large proportion of lactic acid, something which milk does not.

Buttermilk is easily digested, even by dyspeptics on account of the feeble proportion of butter which it contains (0.93 per 100); it holds, however, a greater amount of putrefactive casein than whey (2.5 per 100, *Lam;* 4.06 per 100, *Hammarsten*), according to the milks from which it is prepared.

Per contra, its proportion of lactose is abundant (3.70 per 100),

although less so than whey, while its quantity of lactic acid (0.34) is often greater than that of whey.

From the antiputrefactive point of view, buttermilk and whey are both superior to milk itself, but inferior to fresh cheese or curdled milk.

Third group. In the third group are included the fermented milks: koumys and kephir.

These milk foods, like those of the second group, are liquid, and oppose but slight resistance to the absorption of their antiputrefactive elements.

Koumys contains but a feeble proportion of casein (0.80 per 100) for a notable part (1.04 per 100) has been peptonized and thus escapes putrefaction.

The quantity of lactose is slight (1.50 per 100), but it is replaced in part by a strong proportion of alcohol (3.70 per 100) and lactic acid (0.96 per 100).

Kephir is the least antiputrefactive of the milk foods.

This is due to the considerable amount of casein it contains (2.98 per 100), and to the fact that it is but feebly peptonized (0.05 per 100), therein differing from koumys.

It is furthermore due to its strong proportion of butter (3.5 per 100) and its feeble quantity of lactose (2.70 per 100). On the other hand it contains a marked amount of alcohol (0.78 per 100) and of lactic acid (0.81 per 100), both of which exercise a certain antiputrefactive action without, however, compensating for its defects.

From the antiputrefactive point of view, koumys is therefore greatly superior to kephir. But it may be said that, while the fermented milks are very useful in gastric disorders, they are rather contraindicated in ordinary intestinal auto-intoxication.

The Carbohydrates

It is to *Hirschler* that we owe the first researches upon the influence exercised by the carbohydrates on albuminous putrefaction.

A. Artificial Digestion

Sugar. The addition of sugar in sufficient quantity brings about a complete disappearance of nitrogenous putrefaction.

Glycerin. Does the same.

Dextrin. Inhibits nitrogenous putrefaction, like sugar and glycerin.

Cereals. But it is especially the cereal flours, which, when mixed with proteids and artificially digested in an incubator, prevent all formation of aromatic bodies, even after six days, while the control digestions contain them in large quantities.

B. Normal Digestion

It was by chemical examination of the fæces that *Hirschler*[1] was able to judge the putrefaction. In normal digestion a new factor intervenes, which is not observed in artificial digestion. And that is that the inhibitive substances, if they are soluble, will have been partly absorbed in the stomach and in the upper portion of the small intestine, and partly transformed in their course throughout the intestine.

Consequently only a feeble proportion of the soluble carbohydrates substances will reach the large intestine, and the greater part of the lactic acid which they produced having been absorbed, cannot act upon the contents of the colon.

This is demonstrated by the following experiments:

Cane sugar. Two dogs were fed upon 250 grams of meat; one received in addition 50 grams of sugar.

In the sugar-fed dog but little indol and phenol appeared in the large intestine.

Whereas in the control animal large quantities of indol and phenol were found.

Glycerin. Two dogs were fed upon 250 grams of meat; one receiving in addition 10 grams of glycerin.

In the glycerin-fed dog but little indol and phenol appeared in the large intestine.

Whereas in the control animal large quantities of indol and phenol were found.

Cereal flours. Two dogs were fed upon 250 grams of meat, one receiving 250 grams farinaceous food in addition.

In the cereal-fed dog *no* indol or phenol and *no* skatol.

[1] Hirschler: Zeits. f. phys. Ch. X, p. 306.

Whereas *large* quantities of phenol and indol appeared in the large intestine of the control animal.

Simnitski[1] experimented upon the antiputrefactive action of the different sugars, and he reached the conclusion that the best and most antiputrefactive sugar was lactose, next glucose, then mannite, lastly galactose. With 30 per 100 of lactose there is no production of indol, phenol, ammonia nor sulphureted hydrogen at the expense of albumin.

G. Hoppe-Seyler[2] made a series of experiments in normal man; first, by giving a meat diet only, and next, by giving the same quantity of meat combined with strong proportions of farinaceous aliments.

First experiment:	Sulphoethers
Meat 200 grams	0.280
Meat 200 grams + 50 grams cereals	0.260

Second experiment:	Sulphoethers
Meat 200 grams	0.287
Meat 200 grams + 200 grams cereals	0.150

The addition of a small amount of farinaceous foods has hardly any influence on putrefaction. The addition of half proportions half meat, half farinaceous), markedly decreases the amount of sulphoethers.

Krauss[3], in his experiments, began by allowing a dog to fast for six days.

	Sulphoethers	Indol
After fasting six days	0.041	0.002
Meat 500 grams	0.163	0.050
Meat 500 grams + 500 grams farinaceous	0.084	0.020

Here again the intestinal putrefaction is diminished one half under the influence of the farinaceous aliments.

In a series of experiments instituted by *Combe*, the quantity of meat was given at three separate meals, the dose of farinaceous foods being gradually increased with each one.

[1] Simnitski: Zeits. f. phys. Ch. XXXIX, p. 111.
[2] G. Hoppe-Seyler: Zeits. f. phys. Ch. XII, p. 21.
[3] Krauss: Zeit. f. phys. Ch. XVIII, p. 173.

The following amounts of indol were obtained:

		Indols
1st Series:	200 grams meat + 0 farinaceous food	0.060
2d Series:	200 grams meat + 400 grams farinaceous food	0.035
3d Series:	200 grams meat + 800 grams farinaceous food	0.020
4th Series:	200 grams meat + 1,000 grams farinaceous food	0.005

As may be seen, the maximum effect was obtained, when the proportion of the cooked farinaceous aliments was five times that of the meat.

Ellinger[1] studied the antiputrefactive action of rice:

		Indol
1st Period:	absolute fast	0.267
2d Period:	meat 1kg.	0.479 to 0.664
3d Period:	meat 1kg. + 250 grams rice	0.250 to 0.241

These researches show that *rice exercises the same influence as the alimentary pastes.* Its action is even greater than that of the cereals.

In the midst of this long series of investigations, all of which confirm the antiputrefactive action of the farinaceous foods, two authors, *Biernacki*[2] and *Eisenstaedt*[3], have recently expressed some doubts as to their antiputrefactive action; but *Backmann*[4] has raised such objections against their experiments that no further comment need detain us.

Antiputrefactive Action of the Farinaceous Aliments

We can therefore conclude from this second series of experiments upon the farinaceous foods:

1st. That the carbohydrates must be considered as inhibitive to nitrogenous putrefaction.

2d. That in natural digestion the farinaceous articles (rice, cereal flours and their derivatives, the alimentary pastes) are superior to all other carbohydrates, because they are less easily absorbed, penetrate further in the intestine, while they at the same time gradually furnish both lactic and succinic acids.

3d. That to saturate the intestine with inhibitive farinaceous substances, it is necessary to give them to the maximum amount,

[1] Ellinger: Zeits. f. phys. Ch. XXXVIII, p. 406.
[2] Biernacki D.: Arch. f. kl. Med., LIX., p. 310.
[3] Eisenstaedt: Arch. f. Verdauungskrankheiten, III, p. 1557.
[4] Backmann: Zeitsch. f. kl. Med., XLIV, p. 469.

at each meal of which proteids form part, and that their proportion should be *about five times that of the proteids;* **furthermore the meals should be divided, and their number increased as much as possible.**

General Conclusions

1st. The albumins and the fats represent the putrefactive foods.

2d. The milk and farinaceous foods represent the antiputrefactive aliments.

If we compare the two groups of antiputrefactive foods we have just studied from *the point of view of their application to the treatment of intestinal auto-intoxication*, we shall soon see that the superiority remains with the farinaceous articles.

The Milk Foods

1st. Milk and its derivatives contain a strong proportion of nitrogenous substances, liable to become the prey of the proteolytic bacilli.

2d. Milk and its derivatives contain in varying degrees an antiputrefactive substance of undoubted activity (lactose), but this, according to its protection is more or less rapidly absorbed in its course through the intestine; so that the casein still undigested and deprived of its antiputrefactive element, continues to putrefy the same as any other proteid.

3d. Milk is an excellent culture medium for the proteolytic bacilli, and they are the ones that predominate almost exclusively in the nitrogenous putrefaction of the colon and in enteritis.

4th. Hence in all acute enteric cases, milk and its derivates by themselves (that is not mixed with cereals) should be absolutely prohibited; for they soon decompose with the formation of gases and bloating; they provoke pain by irritating the intestine and greatly increase the muco glairy evacuations and the vomiting.

5th. In chronic enteritis, milk may be harmful from the very beginning of its administration; the patient feels worse; he has diarrheas and complains that the milk does not agree with him; or else the milk appears to be well borne at first, but soon the appetite diminishes, colics occur, the temperature rises and

an acute enteric outbreak results with all its consequences. So that, although milk may be employed with benefit as an antiputrefactive in the ordinary forms of intestinal auto-intoxication, and in albuminuria; the same cannot be said of auto-intoxication resulting from enteritis, for in this form and according to circumstances, *milk per se* should be interdicted, or its use limited.

In all cases of acute enteritis, *milk per se* is absolutely contra-indicated, and it is never tolerated for any length of time in this affection.

So much is this the case that it is almost symptomatic of enteritis, its observation being so frequent.

The Farinaceous Foods

Cereal Flours, Rice, Alimentary Pastes

1st. The farinaceous substances contain only feeble proportions of nitrogen and vegetable nitrogen, and these resist putrefaction much better.

2d. The farinaceous substances themselves constitute the antiputrefactive factor or rather they contain it in germ, for it is only by slow degrees that the lactic and succinic acids are formed during the course of the alimentary mass through the intestinal canal.

In consequence, the inhibitive substance instead of becoming exhausted as happens with the lactose of milk, keeps on forming and reproducing in proportion as the bacterial life of the small intestine becomes more intense.

3d. The farinaceous substances constitute a bad culture medium for the proteolytic bacilli.

4th. They facilitate the gastric functions of secretion and digestion.

5th. Their digestion requires only a limited intestinal activity, the salivary ptyalin compensating for any possible insufficiency of pancreatic amylase.

6th. The farinaceous foods are admirably borne in all affections of the large intestine, which is the pre-eminent site of intestinal nitrogenous putrefaction and the stronghold of enteritis.

In enteric affections, the farinaceous foods therefore constitute the very best antiputrefactive alimentation, the only one capable of favorably modifying the intestinal culture medium.

Hence the lacto farinaceous regimen is the anti-putrefactive regimen.

Influence of the Lacto Farinaceous Regimen upon Intestinal Auto-intoxication

We have already seen in the section on symptomology that the intestinal flora of auto-intoxication was far from being

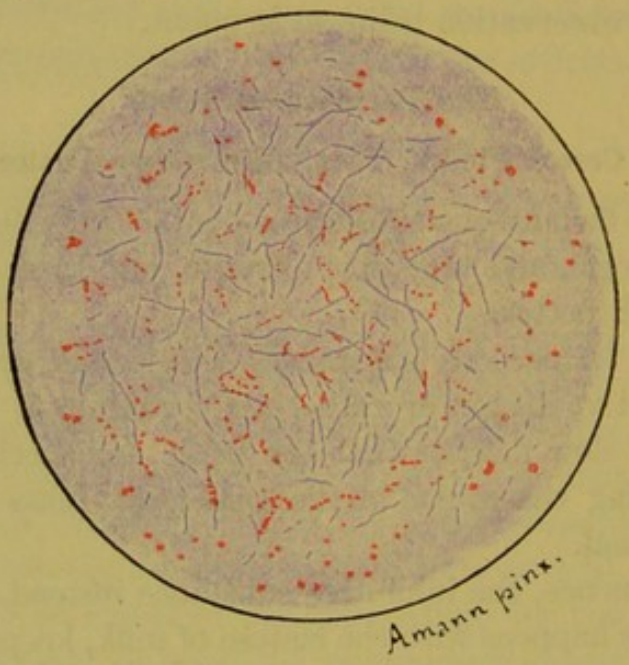

FIG. 6.—ACUTE INFANTILE ENTERITIS (Stools Before Treatment).
Proteus Vulgaris and Bacillus Fluorescens.
(Weigert Escherich Stain.) Specimen Prepared by Dr. Amann.

uniform; it is on the contrary, extremely varied, according to individuals. Nor is it less true that while the bacteria vary greatly, the nature of the flora is very characteristic.

As soon as nitrogenous putrefaction becomes accentuated, a profound modification of the normal flora is noted.

The aerobic bacteria (*"coli and lactis aerogenes"*) greatly diminish and are replaced by a large variety of proteolytic anaerobies, which subsist only in an alkaline medium, and are the organisms of intestinal putrefaction.

We have just seen that the lacto farinaceous regimen modifies the intestinal soil, that it lessens the amount of nitrogenous substances in the intestine, that it brings about the appearance of lactic and succinic acids in a nascent state; all of which are extremely unfavorable to the growth of the anaerobic microbes of putrefaction.

What influence does the antiputrefactive regimen exercise upon the intestinal flora?

We have had occasion to observe it very frequently, and we have always found a great diminution, and at times the com-

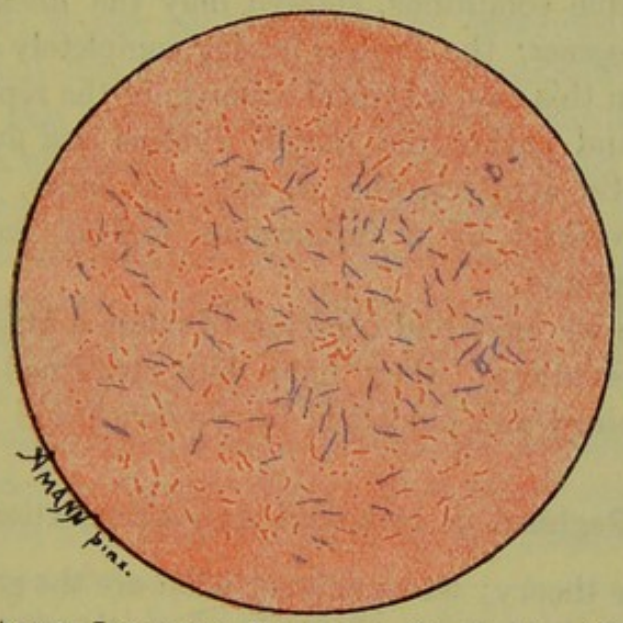

FIG. 7.—ACUTE INFANTILE ENTERITIS (Stools After Six Weeks of Treatment).

Bacillus Bifidus and *Bacillus Coli.* (Weigert-Escherich Stain.) Specimen Prepared by Dr. Amann.

plete disappearance of the anaerobics of putrefaction, and the reappearance of the normal intestinal flora.

A very typical example was observed by *Amann* in his own child.

The child, twenty-six months old, was seized as a result of faulty diet with an outbreak of severe auto-intoxication, beginning with a subacute enteritis, rise of temperature, somnolence, great depression and a rapid loss of strength and weight.

First examination. A culture on peptonized and sweetened gelatin was made by inoculation from the diluted stools, the usual precautions being carefully observed.

Instead of the *colon bacillus* usually found, and whose colonies rapidly invade all the plates, there was found besides several colonies of the *Bacillus fluorescens liquefaciens* of *Flügge*, a quantity of small colonies of a very elongated and extremely motile bacillus that we feel justified in identifying as the *Proteus vulgaris* of *Hauser*.

Second examination. *Fifteen days later.* During this period the child had been placed upon an exclusive farinaceous diet to which was added a daily dose of 20 grams of lactose. The child's condition had greatly improved, and new cultures made under the same conditions, showed only the *Bacillus coli* and the *lactis aerogenes;* the *Proteus* having completely disappeared.

We have in this case a typical example of the replacing of the proteolytic and pathogenic *Bacilli Proteus and fluorescens*, by the amylolytic aerobies, the *B. coli* and *lactis*, through the influence exercised by a farinaceous diet in modifying the intestinal contents.

Since then we have had occasion to make a large number of similar observations; they have but confirmed the results already obtained and published by *Escherich* and his school.

Regimen of Intestinal Auto-intoxication

Such is the theory; let us now see what are the general indications to be derived from this study, from the dietetical standpoint of enteritis, and their application in practice.

A. General Indications

Nitrogenous foods. 1st. To diminish as much as possible the nitrogenous foods, from which the intestinal bacteria obtain their nourishment.

2d. Absolutely prohibit those nitrogenous foods that are favorable media for the development of bacteria and that form veritable culture bouillons.

3d. To choose among them eggs in preference as being less putrefactive in the intestine.

Fatty foods. 1st. Avoid the fats of meat for they increase putrefaction.

2d. To choose fresh butter in preference as a fat, for its action is much less harmful.

Farinaceous foods. 1st. To introduce in the diet as large a proportion of farinaceous substances as possible.

But to obtain a result it is necessary to saturate the intestine with carbohydrates.

We use the word *saturate*, because in fact, it is not sufficient to simply add a few farinaceous substances to the diet. We must, in five or six meals, distributed throughout the day, systematically fill the patient with farinaceous aliments.

He should not be permitted to take his nitrogenous ration (meat or milk) unless accompanied—as experiments demonstrate—by about five times its weight of farinaceous aliments. It is only in this manner that an intestinal antiputrefactive action will be obtained; but we will be rewarded by a real success and often by a marvelous transformation in the patient.

2d. In auto-intoxication from acute enteritis, or in the acute recurrences, an exclusive farinaceous diet must be maintained for several days; for it plays the same part in acute enteritis that a liquid diet does in acute catarrh.

3d. In auto-intoxication due to chronic and subdued enteritis, the antiputrefactive regimen should be a mixed one; at first, lacto farinaceous and later, modified by the addition of very small proportions of eggs and meat.

4th. In ordinary auto-intoxication, milk mixed with farinaceous articles, the latter predominating, is much better borne than milk only, owing to the prevention of the large coagulum formed by cow's milk and to the antiputrefactive action of the farinaceous substances, which is joined to that of the milk lactose, lastly to the fact that the lactose is protected against rapid absorption by the farinaceous substances. A still better result will be obtained by using curdled milk or fresh cheese; both of these are readily taken with alimentary pastes, but particularly so with rice and puddings.

The only difficulty—but it is a great one—is to determine the quantity of milk tolerated by a new case, for this varies with individuals, often in the same individual and according to the stage of the intestinal disorder.

It is well to begin with a rather strong proportion, so as to test the patient's susceptibility.

In case of either gastric or intestinal intolerance, the amount is diminished until all symptoms disappear, which may be ascertained by examination of the stools.

In cases of casein intolerance, the milk should be replaced by whey, where the intolerance is for fats, buttermilk should be used.

We can therefore state that in intestinal auto-intoxication, the lacto farinaceous is the regimen *par excellence*.

This regimen has been employed for many years, by German physicians in similar cases; among others:

Albu, *Gravitz*, *Rosenheim*, *Senator*, *Ewald*, *Schwenninger*, etc. *Rosenheim* has employed it for a long time instead of an exclusive vegetarian diet, "which he deems harmful as being deficient in albumin, and because it diminishes resistance to infections."

The lacto farinaceous regimen (milk, butter, alimentary pastes) with the addition of the yolks of eggs, a food containing but little nitrogen while rich in fats, is according to *Rosenheim*, indicated in the secondary treatment of gastric ulcer and in all affections of the large intestine, from simple membranous colitis to the grave dysenteric lesions.

Senator adopts it in the treatment of muco-membranous colitis, nervous insomnia, and certain skin diseases of intestinal origin.

We make no pretensions whatever to any priority when recommending this method; for in applying it, while systematizing and extending it, we have only made use of dietetic principles, long known, accepted and advised in Germany.

We are very happy to have made it known and adopted in France, where it was not employed.

B. General Rules

1st. Do not drink while eating, nor eat while drinking.

The separation of liquids and solids is one of the great principles established in his regimen by our teacher, *Professor Schwenninger*. Nearly all dyspeptics feel better for it, and, provided nothing at all is drunk with the solid food, one very

soon gets accustomed to it and without any difficulty. *Rovighi*[1] has shown that the separation of liquids and solids greatly diminished nitrogenous putrefaction; for that reason we apply it rigorously in all cases of intestinal auto-intoxication.

	Sulphoethers
Fasting	0.008
3 hours after meal with a *great amount of liquid*	0.031

After a period of four days.

	Sulphoethers
Fasting	0.008
3 hours after meal with *large amount of liquid.*	0.036

On the following day and fasting, the intoxication still continued:

	Sulphoethers
Fasting	0.026
3 hours after a *dry meal*	0.014

Schumann[2] experimented upon himself by taking exactly the same solid ration.

	Average of Sulphoethers
3 days dry meals	0.107
2 days with 1,500 grams water	0.145
6 days with 1,500 grams beer	0.163
10 days with 1,500 grams sprudel water	0.157

We can therefore conclude that nitrogenous putrefaction is markedly diminished with dry meals.

2d. To divide the daily nourishment into several small meals, and always alternate a dry with a liquid meal.

Adrian[3] has demonstrated that the nitrogen ingested in fractional meals is always better digested, is absorbed more easily, more quickly, and is particularly less apt to putrefy.

Period of Ten Days

	Sulphoethers	Urinary Nitrogen	Fixed Nitrogen
1st meat 600 grams at one meal	0.275	19.7	0.36
2d meat 600 grams in four meals	0.217	18.1	0.33
3d meat 600 grams in one meal	0.299	19.7	0.41

[1] Rovighi: Zeit. f. phys. Ch. XVI, p. 30.
[2] Schumann: Wien. klin. Woch. p. 10. 1901.
[3] Adrian: Zeit. f. phys. Ch. XVII, p. 628 and XIX, p. 123.

Wicke and *Weiske*[1] have confirmed these facts in the most complete manner.

Consequently we are in the habit of prescribing three solid meals and three liquid meals per day.

Dry Meals	Liquid Meals
7:30 A.M.	10:00 A.M.
12:30 P.M.	3:30 P.M.
7:30 P.M.	10:00 P.M.

3d. To lie flat on the back, or on the right side for one hour after each solid meal, but without sleeping.

Doctor Schüle, assistant to *Baumler* (of Fribourg), made interesting experiments upon two normal subjects, which consisted in analyzing the gastric contents removed several hours after the experimental meal, this having been followed by repose extended on the back with and without sleep.

He found that sleeping during digestion had the constant effect of weakening the motility of the stomach and of increasing the degree of acidity of the gastric juice, a fact which *Schüle* attributes to the more prolonged sojourn of the gastric contents.

He then observed that simple rest in the horizontal decubitus, but not accompanied by sleep, stimulated the gastric functions without increasing the acidity.

C. Special Rules

1. To withdraw from the alimentation all nitrogenous foods favorable to the vitality of the proteolytic anaerobic bacteria.

1st. Withdraw from the alimentation all foods capable of serving as culture media for the proteolytic bacilli.

Avoid bouillons, meat soups, meat juices, jellies, meat extracts (Liebig's, Brand's, the peptones of Kemmerich, etc.).

Avoid the white of eggs and dishes containing it.

Avoid milk *per se, unless mixed with farinaceous aliments*, for it is a veritable culture bouillon in alimentary auto-intoxication and especially so in auto-intoxication due to acute and chronic enteritis; it should be employed in its pure state only in organic auto-intoxication.

2d. Fatty foods. Avoid meat fats as much as possible. Those from roast or boiled meats, oleomargerine.

[1] Wicke & Weiske: Zeit. f. phys. Ch. XVIII, p. 109.

Use in preference and in moderate quantities, butter and the yolks of eggs, for they are less favorable to nitrogenous putrefaction.

3d. **Meats. Avoid tainted or high meats or those susceptible to rapid decomposition,** or of bad quality, game of all kinds, rare or raw meats. Fish and shellfish, both of which ferment easily should be prohibited, at least in the beginning of treatment.

The toxicity of fish is due to the rapid formation of alkaloids (guanin, neuridin) from the alterations which take place so easily in them, and which may exist, even when the fish retain all the external appearances of freshness.

Springer, in studying urinary toxicity by *Bouchard's* method, found that of all animal foods fish gave the highest toxicity.

For all of these reasons, fish should be interdicted in the antiputrefactive regimen.

In the grave forms of chronic auto-intoxications, meat must be absolutely prohibited.

When its use is again begun, it should be added to the regimen very gradually and progressively. Commencing with cooked ham without fat, then chicken, lastly, thoroughly roasted or broiled meats, the quantities not to exceed 100 to 150 grams per diem.

Furthermore to the meat allowance must always be added farinaceous articles, in the proportion of five volumes of the farinaceous aliments to one of meat and this must be repeated at each meal.

As to the distinction between red and white meats, it is not maintainable from the standpoint of auto-intoxication. For taking only the extractive matters into account, veal and rabbit, typical white meats, contain more kreatin than beef.

From the chemical point of view, the researches of *Rosenqvist* have demonstrated that the difference existing between red and white meats is no greater than that existing between two white meats of different species. Finally *von Noorden* showed clinically that from a digestive point of view the red and white meats differed in nothing.

The meats, rich in nuclein, "the viscera" (the liver, kidneys, sweetbreads, tripe, brains), which favor the formation of uric

acid, shall also be forbidden, owing to the arthritic state of the patients; all the more so because these parts contain extractive and excrementitious matters in abundance.

4th. Casein foods. These we have already considered, but they are too important not to bear repetition.

In all auto-intoxications resulting from acute enteritis, or from acute exacerbations of chronic enteritis and which form an important proportion of all auto-intoxications; milk and its derivatives should never be given.

In the cold or latent stage of enteritis, and in grave cases of alimentary auto-intoxication, milk may be employed but never pure and always mixed with farinaceous articles (purees, puddings).

In preparing the broths, raw milk or pasteurized at the most, should be preferred to boiled milk, but only under the following conditions:

1st. When the milk comes from within a short distance of the consumer, and its transportation is both rapid and clean.

2d. When derived from cows inoculated for tuberculosis and proven free of all taint.

3d. When from cows properly fed on dry and clean fodder. Under these conditions, raw milk is without any danger and presents many advantages from a digestive standpoint, advantages which it shares almost completely with pasteurized milk.

Raw milk and pasteurized milk, containing still their zymases and their lacto albumin intact, are much more easily digested; they are living foods, capable of neutralizing the effects which preserved foods, too long or too exclusively used, might produce.

Such milks may be added to the soups, in variable quantity at time of serving.

When the above mentioned conditions cannot be realized, either boiled or sterilized milk must always be preferred for the preparation of soups. The disadvantages of sterilized milk —a necessary evil in all large cities during the summer—are too well known to require any insistence upon the reasons militating in favor of boiled milk.

If obliged to use sterilized milk for making the soups, it will

be necessary after ten days to add to the diet lemon juice, puree of potatoes or whortleberries to prevent Barlow's disease.

In cases of digestive auto-intoxication from dyspepsia, but without active enteritis, the soups should be prepared with whey (for casein dyspepsia) or with buttermilk (for fat dyspepsia) and the puddings with either diluted or skimmed milk.

In other cases of digestive auto-intoxication of alimentary origin, especially in the second part of the treatment, and also **in all cases of organic origin,** throughout the entire treatment, **milk and its combinations with other foods may be used with advantage.** Milk, buttermilk, and whey may constitute the liquid meals, while the fresh cheese and curdled milk may be combined with the solid meals.

Among the liquid aliments we employ whey preferably, and in these cases it constitutes an important adjuvant to the farinaceous diet. In renal insufficiency, its quantity should be restricted to one liter per diem, in order that the proportion of chlorides ingested be not duly increased. (1.50 gm. per liter.) But it is especially the solid preparations, the fresh cheese and curdled milk which should be employed in these cases, for they are much more disinfecting and more easily taken by patients, who soon tire of the liquid milk preparations.

They should be given either by themselves or combined with the alimentary pastes, but particularly with rice or puddings, these may be sweetened or flavored with cinnamon.

II. TO BRING ABOUT THE PREDOMINATION IN THE DIET OF THE VEGETABLE FOODS WHICH ENHANCE THE VITALITY OF THE AMYLOLYTIC BACTERIA.

1st. Cellulose aliments. Fruits both raw and cooked and also cooked vegetables play a very important role in the alimentation of non-enteric auto-intoxication. It is advisable, at least in the beginning, to give vegetables very thoroughly cooked, mashed, and passed through a sieve; fruits should be prepared in the same manner and if given raw they should be fully ripe and sound.

Whereas, on the contrary, in all cases of spasmodic constipation, acute enteritis or during the first period of the treatment

of its chronic stage, all foods containing a large proportion of cellulose should be forbidden. For they irritate by their contact the already too susceptible mucosa of the colon and markedly increase its spasm. Therefore in these cases vegetables of all kinds, green, fresh, or dry, raw fruits or even cooked, must be avoided.

During this stage, preference shall be given to flours, malted by either steam or roasting, and their thorough cooking must be required.

2d. **Farinaceous aliments. LASTLY, THE CEREAL FLOURS MUST BE GIVEN TO THE MAXIMUM AMOUNT.** The cereal flours and the alimentary pastes constitute as we have seen, the farinaceous alimentation and the disinfecting one; it may be employed in all cases of digestive auto-intoxication, whether of alimentary or organic nature or of enteric or non-enteric origin.

The farinaceous aliments are both liquid and dry.

The liquid farinaceous foods. Coffee Kneipp. This is barley, roasted and flavored by the vapor from Mocha coffee. The barley is first allowed to ferment, then roasted and flavored with the caféon which arises during the roasting of the coffee.

The roasted barley should not be sprinkled with coffee extract.

It is prepared the same as ordinary coffee by allowing a spoonful for each cup and boiling. The boiling liquid is allowed to come to a rise three times, and is then ready.

Cocoa with oats. This is a mixture of oat flour and defatted cocoa.

To prepare it, use two tablets to each cupful of water and boil for ten minutes, allowing liquid to rise four times.

Use either the cocoa and oats prepared by Cassel, that of the *Cheval Blanc* or that of Sprungli of Zurich.

Farinaceous broths. The broths are prepared with malted cereals; those most used being:

1st. *Knorr's creams*; of oats, barley, wheat, corn, and rice.

2d. *Maggi's creams;* oats, barley, rice, etc.

3d. *The American malted foods;* Quaker oats, Hornby's whole wheat, Force, barley food, etc.

4th. Tapioca, sago, arrowroot, rice, semolina.

5th. **The infant foods ;** Nestlé's, Kufeké, Liebe, Benger's food, Keller's Neutralnährung, Neaves' food, Mellin's food, Allenbury's food, etc.

These broths may be prepared with water, milk, buttermilk or whey.

(*a*) **Broths prepared with water.**

The cereal flours are boiled in water for twenty minutes; add some fresh butter on serving.

(*b*) **Broths prepared with milk, buttermilk or whey.**

The broths are prepared as in the preceding; at the last moment add (according to the degree of the affection) from one-fifth to one-half the quantity of hot raw milk.

According to the indications, the raw milk may be replaced by whey (casein dyspepsia) or by buttermilk (dyspepsia of fats).

Later in the treatment the broths may be cooked directly with the different milks.

By boiling two deciliters[1] of milk, whey or buttermilk, adding a little salt; meanwhile stir three spoonfuls of cream of oats, rice, etc., or of malted flour, with one deciliter of cold milk and when well mixed pour it into the two deciliters of boiling milk. Allow the whole to cook on a slow fire for twenty-five minutes, and strain through a fine sieve before serving.

(*c*) **Broths prepared with lactated flours.** Nestlé's, Benger's, Mellin's, Allenbury's, Neaves' and Keller's foods being the most used.

From one to four large spoonfuls of the flour are stirred and mixed with water (300 grams). Boil ten minutes. Milk may be added *after* the broth is cooked.

(*d*) **Broths prepared with buttermilk flours.** *Zwingenberg* of *Hessen* has prepared under the direction of *Biedert* and *Selter*, preserved buttermilk broths.

[1] A deciliter is equivalent to 3.3814 fluid ounces. (tr.)

One is made with wheat flour, the other with barley flour.

To one part of the preserve, are added three parts of water. Mix well and bring to boiling point.

(*e*) **Vegetable bouillon.** The farinaceous broths may be prepared with a vegetable bouillon or stock.

Take of:

Carrots, Potatoes āā grams 65

Turnips, Dry peas or beans āā grams 25

Put these into one liter of water and boil for four hours; when done add five grams of salt for each liter of bouillon obtained.

With this bouillon, the formula of which is due to *Méry*, the various farinaceous soups, rice, barley, oats, malted flours, etc., of which we have spoken, may be prepared and in the same manner.

Broths made with this bouillon are more savory and agreeable than those made with water, but they are also less digestible, and are not suitable in the beginning of the treatment. We allow their use only when the patient tires of the broths made with water.

The Solid Farinaceous Foods

The solid farinaceous foods include the alimentary pastes, puddings and bread.

The alimentary pastes made without eggs (rice, noodles, macaronis, spaghetti, vermicelli, Italian pastes, etc.) are boiled in water (to which salt is added) for twenty-five or thirty minutes according to their nature. When cooked, drain off water and add butter when serving, but never any spices, tomatoes or cheese.

Recipe:

Boil a liter of water to which a little salt has been added; when boiling throw in 100 grams of macaroni, noodles or vermicelli, and cook for twenty-five or thirty minutes; drain off the water and place in the oven for three or five minutes.

These pastes may be prepared as recommended by our eminent colleague, Doctor Roland of Divonne, by cooking in vegetable bouillons (of carrots, parsnips, turnips, etc.), by which means the savor may be greatly varied.

Gniocchi. Boil two decaliters of water slightly salted, add four tablespoonfuls of flour and stir briskly, allow the resulting paste to dry and desiccate at edge of oven for fifteen minutes, until it has become a doughy mass, then remove it from the oven and roll, cut into small pieces the size of a filbert and boil for twenty minutes in two liters of slightly salt water (the water should be boiling when the pastes are put in it), then drain carefully, place in a small dish and put in the oven for twenty-five minutes; serve with salt or sugar.

Gniocchi made with Semolina. Boil two decaliters of slightly salted milk. When the milk boils, sprinkle in three tablespoonfuls of semolina, cook for twenty minutes, then spread the doughy mass with a rolling pin and allow it to become cold. When cold cut into little squares and place in the oven as with the preceding.

Puddings

Puddings cooked with milk (diluted with one-third or one-half water according to the case), sugar and yolk of egg are made with rice, semolina, tapioca, sago, arrowroot, corn meal, and avenalin. It is in this form that milk is best tolerated in difficult cases.

No flavoring is used (lemon, vanilla, etc.).

Recipe:

Boil three decaliters of milk slightly sweetened; when boiling sprinkle in three tablespoonfuls of semolina, rice or tapioca; add the yolks of two eggs, pour into a small dish and place in the oven for twenty or twenty-five minutes, and serve.

Slices of puddings toasted. Puddings may be eaten in the form of toasted or broiled slices. This is a dish greatly used in German Switzerland under the names of Griesspätzli and Reisspätzli; it is prepared as follows:

When the pudding is cold, cut into flat slices, butter slightly and broil or toast. Sprinkle with sugar or a little cinnamon and serve.

Purées

(*a*) **Purée of potatoes** is made with water and fresh butter or with milk.

Baked potatoes are eaten with fresh butter.

Dried vegetable purées (peas, lentils, beans, lima beans, chestnuts). The decorticated vegetables are much more palatable than the vegetable flours (Knorr, Groult), but require much more time to prepare. Recipe.

The vegetable purées are prepared as follows:

The decorticated vegetables are boiled in slightly salted water until cooked, then drained, mashed and passed through a sieve. Mix with milk, or add sugar, butter or salt according to taste, and heat over a slow fire.

Bread

Toasted bread in the form of salted rolls (*longuets*) or sweetened *zwiebacks* is made with wheaten flour and without yeast, the dough rising from the disengaging of carbonic acid gas.

Whortleberries

Since we are speaking of antiputrefactive aliments, we will also mention whortleberries[1]. This mountain fruit greatly used in Germany by the people and recommended by physicians in intestinal disorders and anæmias, has been studied in recent years from the standpoint of its disinfecting and antiputrefactive properties. It is only very recently that *Bernstein*[2] of London called the attention of physicians to the antiseptic and antifermentable properties of whortleberries. *Pouchkine*[3] points out the same fact and praises the action of the tincture of whortleberries in the treatment of infantile gastroenteritis. Unless absolutely contraindicated, we usually include whortleberries in all the alimentary regimens intended to prevent intestinal nitrogenous putrefaction.

They may be eaten fresh, cooked or as a jelly with puddings or else taken in the form of whortleberry wine.

[1] Whortleberries or bilberries, names given to one or two species of *vaccinium*, a genus of plants belonging to the order *vaccinacea* (cranberries), but especially used for the vaccinium myrtillus. Huckleberries are the fruit of the *Gaylussacia*, a genus of *Vaccinacea*. (tr.)

[2] Bernstein: Semaine Med. 1903. p. 68.

[3] Pouchkine: Semaine Med. 1903. p. 156.

Diet lists of intestinal auto-intoxication. We shall mention in the first place the diet intended for the graver forms; the auto-intoxication due to acute or chronic enteritis, and we shall see afterward how it may be modified to meet the indications of the other forms.

A. Dietary of Intestinal Auto-intoxication Due to Enteritis

No. I. Regimen of Broths

This is the regimen of acute and chronic enteritis occurring in infants.

In older children and in adults suffering from enteritis, it is the regimen indicated in the febrile stage and in the acute febrile exacerbations.

Finally, it is the regimen to employ in enterics, attacked by intercurrent febrile diseases (measles, scarlatina, diphtheria, etc.).

Menu :

7:30 A.M., broth.
10:00 A.M., broth and Evian spring water[1].
12:30 P.M., broth.
3:30 P.M., broth and Evian spring water.
7:00 P.M., broth.
10:00 P.M., Evian water.
During night, Evian water.

In the severe forms of acute enteritis and in the acute exacerbations occurring in the chronic form, the broths should be made with some of the already mentioned flours (Knorr creams, Maggi creams or the American creams) *using water only in their preparation.*

Two soups greatly used in Germany may also be employed: Liebig's soup and the *Malzsuppe* of Keller, both of these come already prepared.

Gradually, and as soon as improvement is manifested, whey, buttermilk or milk may be added to the broth, according to the case.

[1] The Evian springs are situated at Evian les Bains, a climatic and watering resort on Lake Geneva.
There are several springs all having about the same composition. The water is faintly mineralized and but very slightly alkaline; it is colorless, so pure and palatable that it is largely used as a table water. (tr)

In the chronic and subdued form of enteritis, the broths or gruels may be prepared with milk from the very beginning of treatment, unless the existence of a dyspepsia should indicate the use of whey or buttermilk in preference to milk.

In this second period the lactated flours may be used with advantage, especially that of Nestlé or the buttermilk flour.

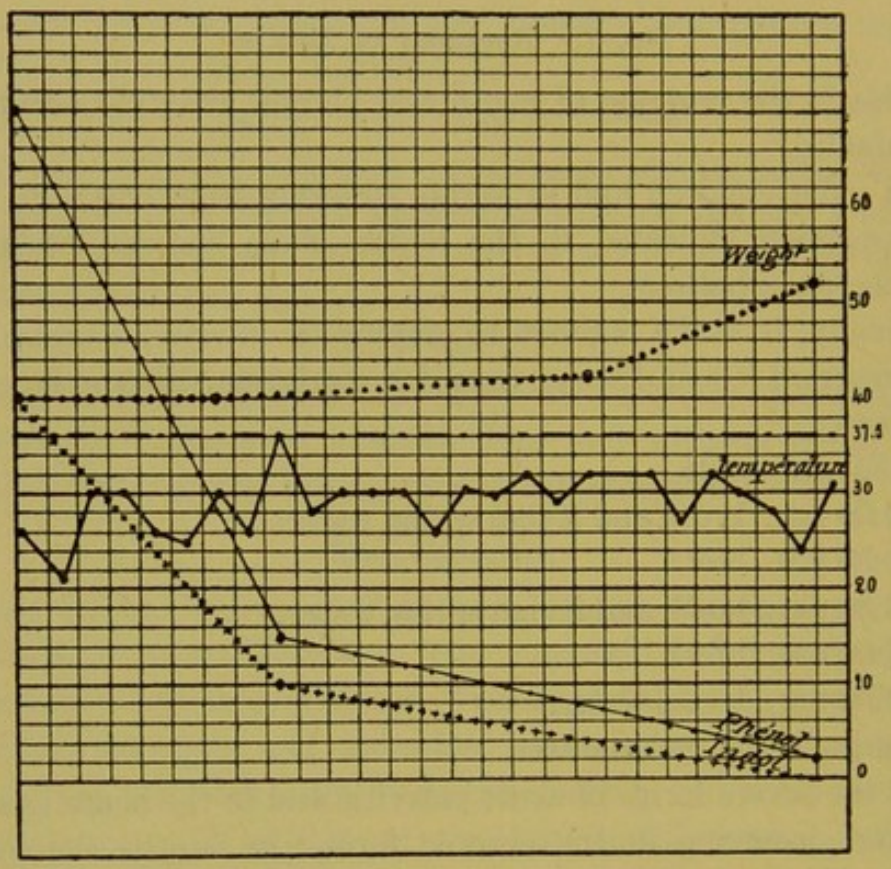

Fig. 8.—N. Huberte, Aged 7½ Years. Auto-Intoxication Due to Nitrogenous Sur Alimentation (Nervousness, *Urticaria*).

Influence of Regimen No. II Upon the Excretion of the Phenols and Indols.

It must be well understood that the diet of broths made with water is a therapeutic regimen and in no sense an alimentary one, for it plays the same part in enteritis that a liquid diet does in intestinal catarrh, we must know how to use it and not abuse it.

As soon as the improvement is maintained we pass to regimen No. II.

If obliged for any special reason to prolong the use of the broths, fresh foods must be added (raw milk or pasteurized),

purée of potatoes, whortleberry juice, or juice of orange or lemon, so as to prevent the development of Barlow's disease.

No. II. Farinaceous Diet without Meat (Fig. 8 and 9)

This diet is employed when a chronic enteritis is not completely subdued, and when it still presents frequent acute exacerbations.

In other words it is the intermediary regimen utilized when passing from regimen No. I to regimen No. III.

Menu :

7:30 A.M. BREAKFAST.

Thick broths made of (Knorr or Maggi creams or lactated flours), and prepared with either water or milk.

Small rolls.

Fresh butter, unless contra-indicated by pyrosis or diarrhea.

From 8:00 to 9:00 A.M. rest, in horizontal decubitus.

10:00 A.M. Lactated flour made with either water or milk, *but no solid food.*

12:30 P.M. LUNCH.

One or two yolks of eggs (raw or soft boiled).

Alimentary pastes (macaroni, vermicelli, etc.), with fresh butter.

Pudding.

Rolls.

Fresh butter.

Nothing to drink.

One to two hours' rest, lying extended without sleeping.

3:30 P.M. LIGHT LUNCH.

Lactated flour made with either water or milk, Evian spring water, *but no solid food.*

7:00 P.M. DINNER.

One or two yolks of eggs.

Alimentary pastes.

Pudding.

Rolls and fresh butter.

Nothing to drink.

8:00 to 9:00 P.M. Rest, lying down without sleeping.

10:00 P.M. Infusion of camomile, peppermint, fennel, anise, or orange flower water, etc.

Glass of Evian spring water.

After eight or ten days of this regimen (No. II) add to the lunch and dinner either purée of potatoes or baked potatoes and either the juice or jelly of whortleberries.

When the liver is involved, leave out the egg yolks; the diet will then remain purely lacto vegetarian.

No. III. Farinaceous Regimen with Meat (Fig. 9)

This regimen is used in membranous enteritis when it has completely subsided, and it must be considered as the therapeutic diet for the first six months of treatment.

Menu :

7:30 A.M. BREAKFAST.

Soup prepared with water or milk.

Lean ham (50 grams).

Rolls or zwiebacks.

Fresh butter.

8:00 to 9:00 A.M. Rest, lying down extended, without sleeping.

10:00 A.M. Oat cocoa or Kneipp coffee with milk (according to case).

No solid food.

12:30 P.M. LUNCH.

Roast or broiled meat without gravy or sauce (50 grams).

One or two egg yolks.

Alimentary pastes or rice.

Potatoes mashed or baked.

Pudding.

Whortleberry juice or jelly.

Rolls.

Fresh butter.

Nothing to drink.

One-and-a-half hour to two-and-a-half hours' repose, lying down without sleeping.

4:00 P.M. REFRESHMENT.

Kneipp coffee, oat cocoa, or Evian water (according to case

No solid food.

7:30 P.M. DINNER.

Roast or broiled meat, hot or cold (50 grams).

Alimentary pastes.

Potatoes mashed or baked.

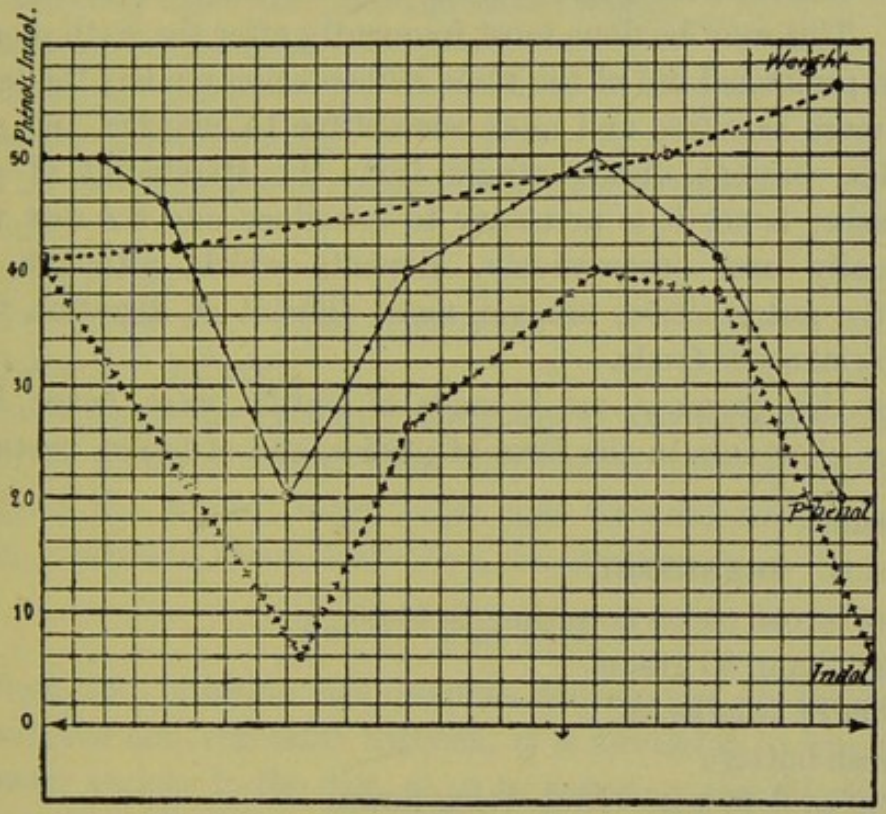

FIG. 9.—JEANNE M., AGED 7 YEARS. DILATATION OF TRANSVERSE COLON. (Anæmia, Nervousness, Pruritus.)

Influence of Regimens No. II and III on the Excretion of Indols and Phenols.

Pudding.

Whortleberry juice.

Rolls.

Fresh butter.

Do not drink and eat less than at lunch.

8:30 to 9:30 P.M. Rest, lying down.

10:00 P.M. Infusion (camomile, anise, peppermint, etc.).

As may be seen (Fig. 9) by the curve of the phenols and indols, the intestinal putrefaction diminished rapidly under

regimen No. II. It increased at first under regimen III, owing to the meat it contains, but it subsided quickly and definitely.

No. IV. Lacto Farinaceous Regimen with Dried Vegetables

When, as a result of the influence exercised by the intensive farinaceous regimen No. III, the intestine has become less sensitive when the colics have ceased and the general condition shows considerable improvement, it is advisable to modify the diet. This may be done most frequently after the sixth month. A too prolonged use of the same alimentation renders the intestine more sensitive and more susceptible to changes, and may besides, present disadvantages from the standpoint of acid dycrasia; hence it is necessary to introduce into the diet very gradually and progressively, aliments which, although but slightly putrefactive, are yet more difficult of digestion than the farinaceous foods.

For this purpose, use is made of lentils, pease, beans, lima beans, chestnuts in the form of purées, and of baked custards.

Menus :

7:30 A.M. BREAKFAST.

Tea or oat cocoa according to taste.
Lean ham, 50 grams.
Rolls or zwiebacks.
Fresh butter .
8:00 to 8:45 A.M. Rest, lying down.
10:00 A.M. Kneipp coffee.
Do not eat.

12:30 P.M. LUNCH.

Roast or broiled meat.
One or two egg yolks.
Alimentary pastes.
Vegetable purée (beans, peas, etc.), or mashed potatoes according to preference.
Pudding.
Cup custard or whortleberry juice or jelly according to taste.
Rolls.
Fresh butter.

Do not drink.

Rest, lying down for one-and-a-half hour to two-and-a-half hours without sleeping.

4:00 P.M. REFRESHMENT.

Kneipp coffee, oat cocoa or weak tea, according to taste.

7:30 P.M. DINNER.

Absolutely fresh fish, boiled in salted water.

Roast or broiled meat.

Alimentary pastes.

Dried vegetable purées.

Whortleberries or cup custard, according to choice.

Rolls.

Do not drink.

8:00 to 9:00 P.M. Rest, lying down.

10:00 P.M. Infusion.

The custards are prepared according to the English method, either in liquid or baked form (cup custard) using egg yolks (without the whites) milk, sugar and flavoring with vanilla, lemon, chocolate, cocoa, tea, coffee, etc., as desired.

No. V. Full Diet

When the intestine has become accustomed to the lacto-facinaceous and vegetable regimen, it is advisable to introduce a greater variety in the diet, so as to accustom the intestine to foods not only less digestible but leaving much larger residues.

To accomplish this, use is made of fresh vegetables and cooked fruits.

These aliments, however, can only be digested when finely divided in purées and strained by passing through a sieve, otherwise the intestine may be irritated and painful spasms provoked.

Purée of Green Vegetables (spinach, chickory, lettuce, watercresses, cooked salads, green peas, artichokes, etc.). These should be finely hashed, strained and prepared with milk or butter; *meat juice, gravy or fat should never be used.*

Fruit Purées (apples, pears, peaches, prunes, plums). *No acid fruits.*

These are cooked in water, mashed, strained and served as purées.

Menu :

7:30 A.M. BREAKFAST.

Tea
Oat cocoa } according to case.
Café au lait Kneipp

Lean ham, 50 grams
Cold meat " " } according to choice.

Rolls or toast.
Fresh butter.
8:00 A.M. to 8:30 A.M. Rest, lying down.
10:00 A.M. Rest, lying down.

12:30 P.M. LUNCH.

Fresh egg yolks
Fish *court bouillon* } according to choice.
Roast or broiled meat

Alimentary pastes
Vegetable purées } according to choice.

Green vegetable purées

Pudding
Custard } according to choice.
Fruit purée

Rolls or toast.
Fresh butter.
Beverage, 50 to 100 grams.
Rest, from one-and-a-half to two hours, lying down.

4:00 P.M. REFRESHMENT.

Either weak tea or café au lait Kneipp.
Dry biscuits or wafers (Marie, Albert, Palmers).

7:30 P.M. DINNER.

Same as at lunch.

Soft boiled eggs or scrambled
Roast or broiled meats } choice of.
Boiled fresh fish, butter sauce

Alimentary pastes
Vegetable purées
Green vegetable purées
} according to choice.

Pudding
Custards
Fruit purées
Fruit jellies
} according to choice.

Toast.
Fresh butter.
Beverage, 50 to 100 grams.
8:30 to 9:00 P.M. Rest, lying down.
10:00 P.M. Infusion.

Fresh fruits. Finally, as soon as the condition of the intestine will permit it, add to the diet *fresh and fully ripe fruit* (grapes, peaches, plums, pears) beginning with the autumnal fruits, much sweeter and more easily digested.

Bananas. We employ these in preference.

The banana should be eaten when fully ripe, for it has then converted into sugar the greater part of the starch with which it is so richly endowed.

It then contains about 5 per cent. of albuminoid substances, 1 per cent. of fatty matters and more than 20 per cent. of carbohydrates.

Nothing is easier of digestion than this excellent fruit. It is the food of choice for all delicate stomachs and is always best eaten raw; although the races whose principal food it constitutes, like it cooked, probably to vary their dietary. The fact remains that cooked bananas offer a most delicate and appetizing food. In America and India, it is often baked in skin like potatoes, care being taken to cut off the ends to allow the escape of gas.

Fruits should be given between the solid meals; at 10:00 A.M. or 4:00 P.M. in order that they should not be taken at the same time as meat, for they greatly retard the digestion of the latter as shown by *Bourget.* Such are the regimens we make use of in enteritis; they are the most severe of all those employed in intestinal auto-intoxication.

Hence it is advisable to closely watch the patients and to

gradually modify their diet as soon as its purpose has been accomplished, so as not to keep them any longer than necessary under a severe regimen, for this would only occasion a waste of time and weaken the intestine. In order not to miss the opportune moment, we have both the analyses of the urine and stools repeated at the end of three or six months according to the case.

B. Menus of the Other Forms of Auto-intoxication

These will vary in their severity, according to whether we are dealing:

1st. With microbic auto-intoxication.

2d. With organic auto-intoxication.

I. Menus of Microbic Auto-intoxication

These menus will differ according to the degree of auto-intoxication.

I. Menus of Grave Digestive Auto-intoxication

Depending upon the gravity of the symptoms, the patient will be given:

(*a*) The strict vegetarian regimen.

(*b*) The mitigated vegetarian regimen.

1st. The Strict Vegetarian Regimen

In the strict vegetarian regimen milk, eggs, meat and fish are entirely left out.

Menu:

7:30 A.M. BREAKFAST.

Farinaceous broths, Knorr, Maggi, etc., cooked in water.
Oat cocoa or Kohler defatted cocoa cooked with water.
Rolls and fresh butter.

8:00 A.M. to 9:00 A.M. Rest, lying down.

10:00 A.M. Fully ripe and sound grapes or fruit in season.

12:30 P.M. LUNCH.

Thick farinaceous soup made with water and fresh butter.

Alimentary pastes made without eggs or else rice
Dried vegetable purées, pease, lentils, beans, potatoes, etc.
Green vegetable purées.
} choice of.

Cocoa pudding without milk.

Rolls. Fresh butter.

Purées of cooked fruits.

Nothing to drink.

1:00 to 2:00 P.M. Rest, lying down without sleeping.

3:30 P.M. REFRESHMENT.

Fruit in season or cocoa made with water.

No solid food.

7:00 P.M. Dinner.

The same as at lunch, *only much less should be eaten and nothing drank.*

8:00 to 9:00 P.M. Rest, lying down without sleeping.

10:00 P.M. Infusion.

2d. The Mitigated Vegetarian Regimen

This menu is mitigated by the addition of milk and the yolks of eggs.

It admits of great variations and these are often necessitated by the state of digestion of the patient.

Menu :

7:30 A.M. BREAKFAST.

Farinaceous soup, Knorr, Maggi, or lactated flour made with milk, whey or buttermilk.

Rolls.

Fresh butter unless contraindicated by pyrosis or diarrhea.

8:00 to 9:00 A.M. Rest, lying down.

10:00 A.M. Whey, 250 grams
Grapes
Fruit in season
} according to choice.

No solid food.

12:30 P.M. LUNCH.

One or two egg yolks, soft boiled, raw or scrambled with milk.
Alimentary pastes with fresh butter.
Vegetable purées
Green vegetable purées } choice of.
Pudding.
Fresh cheese or curdled milk
Whortleberries or cooked fruits } unless contraindicated.
Rolls and fresh butter.
Nothing to drink.
1:00 to 2:00 P.M. Rest, lying down without sleeping.

3:30 P.M. REFRESHMENT.

Lactated flour
Café au lait Kneipp
Fruit in season, spring water } according to choice.
No solid food.

7:00 P.M. DINNER.

One or two egg yolks.
Alimentary pastes with fresh butter
Vegetable purées
Green vegetable purées } according to choice.
Pudding, baked custard
Fresh cheese or curdled milk
Whortleberries or cooked fruits } according to choice.
Rolls and fresh butter.
Nothing to drink.
8:00 to 9:00 P.M. Rest, lying down without sleeping.
10:00 P.M. Infusion or spring water.

It is unnecessary to say that these menus simply enumerate the choice or list of aliments, which may be employed in the diet of the auto-intoxicated.

They must be chosen according to the appetite, the digestive capacity of the patient and the therapeutic indications furnished by his symptomology.

2d. Menus of Digestive Auto-intoxication of Moderate Degree

These menus are the same as the two preceding, except that they are further mitigated by the addition of meat and whole eggs.

They may be subdivided into:

(*a*) The lean or half carno vegetarian regimen.

(*b*) The full carno vegetarian regimen.

1st. *The Lean Carno Vegetarian Diet*

In this regimen a small amount of meat is allowed once a day, at the midday meal preferably. But the patient is advised to do without meat at least one day in the week.

Lean ham, chicken, and, if obtainable, very fresh fish will be recommended. These are easily digested and should be used at first before passing to butcher's meat.

These articles or whole eggs added in moderate proportions to the vegetarian regimen, constitute the midday meal of the lean or half carno vegetarian diet.

The other two meals should be purely vegetarian.

The formula of *Monteuuis* (of Dunkirk) may very well be adopted for this regimen.

Morning—**Fructivorous.**

Noon—**Carnivorous.**

Evening—**Vegetarian.**

Sauerkraut. This disinfecting food greatly used in Germany, is often added to the regimen, to the great satisfaction of the patient.

When well cooked and not too much fermented, sauerkraut constitutes an aliment of not too difficult digestion and is greatly appreciated by those who like it. It is, moreover, a valuable antiputrefactive food, thanks to the strong proportion of lactic acid which it contains.

The white cabbage (*Brassica olerac. capit alba*) is used for the preparation of sauerkraut.

It is sliced very fine, salt is added and it is put into a barrel, where it undergoes spontaneous fermentation.

Chemical Composition

	Cabbage per cent.	Sauerkraut per cent.
Nitrogen	1.8	1.4
Fat	0.2	0.7
Sugar	2.2	1.0
Lactic acid	0.0	1.42
Carbohydrates	2.5	2.8
Cellulose	1.8	0.3
Salt	1.2	1.7
Phosphates	0.12	0.12
Sulphur	0.03	0.03

Therefore in sauerkraut the lactic acid is formed at the expense of the sugar which disappears. There is found besides a little acetic and butyric acids, but only in very feeble quantities. Sauerkraut may be given at the midday meal with ham and instead of vegetables.

2d. *Full Carno Vegetarian Diet*

This regimen is intended for cases of mild auto-intoxication. For its composition add to the vegetarian regimen meat at the midday and evening meals and eggs in the morning. But it must be understood that the meat and eggs shall only be given in moderate quantities and that it will be necessary to neutralize their toxic effects by giving large proportions of farinaceous aliments with them and at the same time.

II. Menus of Organic Auto-intoxication

These menus will differ very greatly according to whether it is a question of:

(*a*) Hepatic insufficiency or

(*b*) Renal insufficiency.

A. Regimen of Digestive Auto-intoxication Due to Hepatic Insufficiency

This form of digestive auto-intoxication is of frequent occurrence. It may be caused by primary hepatic insufficiency

or else by hepatic insufficiency secondary to that of the intestine.

It is manifested by the clinical and urinary signs already described and by an alimentary glycosuria provoked by a too intensive farinaceous diet. From the dietetical point of view, it is necessary in hepatic insufficiency.

1st. **To reduce the farinaceous foods** *below the glycosuric ration;* this ration varies with the particular case and it must be determined each time by the method of *von Noorden.*

2d. **To give a hypo-nitrogenized regimen.** (50 grams of albumin at the maximum) meat and white of egg to be taken with only one meal.

3d. **To avoid meat fats and fried articles.** *Per contra,* use fresh butter and oil, provided the pancreas acts well, which may be determined by analysis of the stools, to ascertain the presence of fat residues.

4th. **To avoid all alcoholic beverages.**

Menus of Hepatic Insufficiency

These should be composed:

1st. Of whole and skimmed milks, whey, buttermilk, or curdled milk and yoghourt (made from skimmed milks).

2d. Rice, potatoes and oatmeal in the form of broths or as vegetables, and in as large quantities as may be taken; these articles favor *alimentary glycosuria* to a lesser degree than the alimentary pastes and cereals.

3d. Cereal flours and alimentary pastes as broths or vegetables, and in the measure permitted by the alimentary glycosuria.

4th. Purées of dry vegetables.

5th. Green vegetables, hashed and strained; non-sweetened cooked fruits and raw fruit.

6th. Aromatic infusions and Evian spring water as beverages.

B. Regimen of Digestive Auto-intoxication Due to Renal Insufficiency

Renal insufficiency is not exceptional. It may be caused by primary renal insufficiency or else occur secondarily to that of

the intestine, as we have demonstrated elsewhere[1], and basing ourselves upon the analysis of the important works of *Widal, Achard, Castaigne, Strauss* and others.

The regimen of renal insufficiency must be both hypo-chlorized and hypo-nitrogenized.

(*a*) *Hypochlorized,* because owing to insufficient elimination of the chlorides, they accumulate in the organism; this necessitates an accumulation of water with chloruræmia, in order to maintain the isotonicity of the sera; the immediate consequences being an increase in the fluid mass, and the blood pressure.

The test for *alimentary chloruria* will determine to what point the dechlorization of the diet should be carried.

(*b*) *Hyponitrogenized,* because both nitrogen and uric acid not being sufficiently eliminated, accumulate in the organism and with them the large albuminous molecules, far more dangerous, and from which results uræmia with all its grave consequences.

Hyponitrogenized lastly, because the ingestion of albumin greatly augments intestinal putrefaction. The test for *alimentary azoturia* (nitrogenous content) will in each case determine to what extent the diet may be deprived of nitrogen.

From the conclusions of our study we see:

That in renal insufficiency with nitrogenous and chloride retention, the diet must be hypochlorized and hyponitrogenous and modified pro rata with the degree of retention of these bodies; this to be determined by the tests for alimentary chloruria and azoturia.

Dietary of Renal Insufficiency

Mauté[2] has given to this study a part of his excellent work, from which we have largely drawn. Until lately the general idea with regard to the diet of albuminuria had been altogether borrowed, from the method adopted in fixing the alimentary hygiene of diabetics.

In diabetes all aliments capable of increasing the sugar were

[1] Combe: Beiträge zur Chlor-und Stickstoffarmen Ernährung bei Morbus Brightii (*Monatschrift für Kinderheilkunde*, IV, 1 and 2).

[2] Mauté: Thèse de Paris. 1903.

left out; likewise, in albuminuria, all aliments capable of increasing the albumin were withdrawn.

To-day we actually know that the connection between the intensity of the lesions and the importance of the albuminuria can no longer be maintained, for we may see fatal cases of nephritis with but little albumin, whereas others presenting no gravity have a considerable amount.

Based upon so uncertain a sign, it is not surprising to find the same uncertainty exist in the dietary of Brightism.

Meat, for example, is forbidden by most authors, and recommended by *von Noorden, Kauffman* and *Mohr.*

Eggs are prohibited by *Claude Bernard* and most physicians; yet *Loewenmayer* gives them as exclusive nourishment to nephritics, while *Potain* and *Teissier* recommend them. Upon one aphorism only do all the authors seem to agree; that:

A milk diet is the specific regimen of albuminuria.

1st. Milk Diet

It was particularly *Chrestien* of Montpellier, who in 1831, called the attention of the medical world to the usefulness of milk in the treatment of albuminuria. Milk, in fact, presents theoretically, at least, all the requisites demanded to constitute a perfect food in albuminuria. It is a complete food containing all the necessary alimentary principles.

	Per 1000		Per 1000
Lacto albumin	5.3	Water	817.7
Lacto casein	30.2	Salts	7.1
Fats	36.0	of which *Chlorides*	1.50
Carbohydrates	48.0		

Its caloric value per liter = 670 calories; 3 liters (= 2,080 calories) suffice for a bedridden adult; 3½ liters (2,680 calories) suffice for a workingman.

It is therefore a sufficient food, for its deficiency in carbohydrates is compensated by its excess of fat.

It is a mild food, rapidly digested in most cases and easily peptonized.

It leaves unimportant intestinal residues, gives rise to but few toxins and diminishes intestinal auto-intoxication, as

Winterntiz and others have demonstrated theoretically and *von Massen* practically.

This investigator showed that by causing the blood of the portal vein to flow directly into the vena cava in a dog exclusively milk-fed, no accidents occurred; whereas, the same experiment performed in a meat-fed animal was followed by a rapid and fatal intoxication. This nearly absolute absence of intestinal poisons is of inestimable value when these poisons must be eliminated by a partly obstructed filter, as in the nephritic.

Lastly, milk is diuretic and generally causes a diminution in the albumin excreted. All of which certainly constitute most precious advantages. But at their side how many serious disadvantages!

Shall we speak of the almost invincible dislike certain patients have for milk, a repugnance which may be conquered, it is true, by will power and habit, or else by concealing the taste with tea, coffee or effervescing waters, or by substituting for the milk, whey, buttermilk or curdled milk; these being often much more useful and better tolerated.

In the second place, milk is not well tolerated by all patients; specially by those suffering from enteritis as well as nephritis. In many it provokes disorders of digestion, constipation, meteorism; in others diarrheas as soon as the quantity taken becomes large.

In consequence the patient is soon obliged to decrease more and more the amount of milk he takes; this falling sometimes below one liter per day, an amount absolutely insufficient for the maintenance of life. Furthermore, after prolonged use even with a dose of 3 liters per day, milk *per se*, is insufficient and debilitating even to a bedridden patient.

It will be still more so to a patient in active life as the nephritic so frequently is; in consequence after a certain time we see his strength diminish, emaciation comes on, anæmia supervenes and with it more or less incapacity for physical or mental effort. (*Mauté.*)

Next, the abundance of liquid forming part of an absolute milk diet, increases the arterial tension and fatigues the heart;

this is always serious but particularly so in the nephritic, who is already a cardiac sufferer. It was *Oertel*, and after him *von Noorden*, who especially called attention to these facts, and they ordered a diminution in the amount of liquids taken by their patients to one liter per day, with best results. In this dose a milk diet is absolutely insufficient.

Last, but not least, if we add the acknowledged fact, verified many times clinically, that an absolute milk diet is sometimes useless, even harmful at times in certain renal insufficiencies, and that in such cases the patient is greatly improved by a cessation of the milk diet, at least by its diminution, we will better understand why, for a number of years past, we have seen many authors oppose the dogma of an exclusive milk diet in the treatment of nephritis.

Among these we may cite *von Noorden*, *Ewald*, *Senator* in Germany; *White*, *Ralph* in England; *Vergely*, *Lecorché* and *Talamon*, *Mabboux*, *Fleissinger*, *Mauté*, etc., in France; *Polidoro*, *Lucci* in Italy.

It is unnecessary to say that while we join with these authors in opposing the dogma of an exclusive milk diet in nephritis, we are far from condemning milk, which—as very many observations attest—**often gives most excellent results in albuminuria.**

These results are due to the properties already studied, and in a greater degree to the poorness of milk in chlorides (1.50 grams per liter). (*Widal.*)

Consequently milk may appear with great advantage alone, or combined with other aliments in the hypochlorized menus of albuminuria; *when the renal insufficiency is but slightly accentuated.*

2d. Hypochlorized Regimen

Whenever the renal insufficiency to chlorides and urea is considerable, milk as the sole food contains much too great a quantity of chlorides and albuminous substances.

	Chlorides	Albumin
2 liters of milk	3.0 grams	70.0 grams
3 liters of milk	4.50 grams	105.0 grams
3½ liters of milk	5.25 grams	112.5 grams

The dose of 2 grams of chlorides is the fixed ration of maintenance for the chlorides. This is the necessary and indispensable ration, which every daily menu must contain to insure the chlorinated metabolism. Any surplus is *ration de luxe,* borne without inconvenience by healthy kidneys, but not so when the kidneys become incompetent. In fact, in renal insufficiency the excessive ration (*ration de luxe*)—that is to say, the one that exceeds the fixed ration—becomes the *ration of tolerance,* and is absolutely individual, in the sense that some insufficient kidneys do not tolerate any excess, while others will bear a more or less great *ration de luxe.* It can now be understood why in certain cases an exclusive milk diet does not give good results.

That is, whenever the dose of salt contained in the milk (3 to 6 grams) exceeds the ration of tolerance of the patient.

It is then necessary to substitute for the milk diet, **the hypochlorized regimen ;** a regimen offering greater variety and much more agreeable to the patient.

The patient may, in fact, associate proteids with one liter of milk; meat, fatty foods, butter, sweetened aliments; fruits, carbohydrates; fresh vegetables, cereals, alimentary pastes, without for all that, exceeding his *dose of tolerance.*

An absolute milk diet, or else combined with the juice of fresh fruit and light cereal soups without salt, will always remain the alimentation of choice in *acute* nephritis, for in these cases all solid food is proscribed.

But in chronic nephritis, in which salt and albumin are in divers degrees dangerous aliments, restriction in one or both of these substances may be necessary, according to the case.

The regimen in such cases will be both hypochlorized and hyponitrogenized.

Here are the aliments which enter into the hypochlorized regimen, and which may be combined in the most diverse manner to attain the quantity of salt contained in the fixed or maintenance ration and the ration of tolerance, while remaining always below the latter.

1kg. of bread without salt contains	0.09 grams
1kg. of cereal flours	0.60 grams
1kg. of alimentary pastes	0.30 grams
1kg. of dry vegetable flours	0.30 grams
1kg. green vegetables	0.30 grams
1kg. of dry vegetables	0.60 grams
1kg. of fresh fruit	0.30 grams
1kg. of butter	0.180 grams
1 liter wine contains	0.02 grams
1 liter soup, rice, barley, oat, contains	0.050 grams
1 liter soup, lentils, pease contains	0.050 grams
1 liter soup, lactated flour contains	0.23 grams
100g. of pudding contains	0.025 grams
100g. of semolina pudding with milk	0.122 grams
100g. of whortleberries	0.008 grams

Hypochlorized dietary. Let us examine more closely the aliments constituting the hypochlorized menus.

Bread. Ordinary bread is the most dangerous aliment in renal insufficiency, for it contains (according to the locality), variable amounts of salt, but always very considerable.

1kg. ordinary bread	2.00 Richet
1kg. ordinary bread	3.50 Toulouse
1kg. ordinary bread	12.50 Stryswoski
1kg. bread without salt	0.22 Stryswoski

Bread made without salt contains only the quantity originally in the flour. Consequently while ordinary bread is contraindicated in the dechlorized regimen, bread without salt (white bread, rye bread, bran bread), rolls and biscuits without yeast and salt (such as we have made in Lausanne for our regimens), may be allowed to the patient.

Alimentary pastes. These, when prepared with water and butter, or with milk or cream, but without adding salt, bouillon or meat juice, meet the requirements of the hypochlorized regimen.

One hundred grams of pastes contain 0.03gm chlorides, that is, the maximum amount which may be consumed at one meal.

We might add that their antiputrefactive action in intestinal albuminous putrefaction furnishes another indication for their use.

Cereal flours. The soups, broths or puddings made of cereal flours or semolinas (barley, oats, wheat, corn) rice, tapioca, sago, arrowroot, are prepared with water and butter or milk, whey and buttermilk, but without the addition of salt.

100 grams of cereal flour contain 0.05 grams chlorides.

100 grams of broths (barley, rice, oats) = 0.005 grams of salt.

100 grams of soup of semolina contain 0.0025 grams salt.

100 grams of pudding contain 0.020 grams salt.

These broths, soups and puddings are therefore indicated in the same manner, and for the same reasons as the alimentary pastes.

Oat cocoa. Each cubic gram of oat cocoa contains 0.152 grams of salt. (*Stryzowski.*)

A cup of oat cocoa = 2 cubic grams = 0.300 grams salt
100 grams of milk = 0.200 grams salt
Total 0.500 grams salt

Consequently it must not be used to excess in the dechlorized regimen.

FRUITS may be given raw or cooked as jellies, jams or purées, or made into tarts, pies, provided the dough is prepared without salt.

Five hundred grams of fruit contain 0.15 grams of chlorides. Fruits are all the more indicated in the hypochlorized regimen of nephritics, because they do not give rise to extractive matters.

Fresh vegetables. Like the fresh fruits, fresh vegetables, especially the green vegetables are all indicated in the dechlorized diet.

They may be prepared with water and fresh butter, or with milk or cream, and *without salt;* meat juice or gravy should never be used.

150 grams of fresh vegetables contain 0.03 grams salt.

50 grams of dry vegetables contain 0.03 grams salt.

The green vegetables (spinach, lettuce, chicory, endives, watercresses, cooked salads), carrots, string beans and fresh peas are all indicated. *Senator* advises—and with reason—avoidance of all vegetables containing essences capable of irritating the kidneys; radishes, onions, parsnips, artichokes, etc.

The same may be said of the cabbage species, which besides, have a tendency to produce intestinal fermentations.

Dry vegetables. The flours or meals of dried vegetables (lentils, pease, beans, lima beans, chestnuts, etc.), may be included in the dechlorized regimen.

One hundred grams of vegetable flours contain 0.03 grams salt.

They may be employed in the form of soups, purées cooked in water with fresh butter or milk, but without addition of salt, or meat juice, gravy, etc. It is advisable, however, not to use them in excess, for they easily produce intestinal fermentation.

Moreover, the dry vegetables contain notable proportions of nitrogen and phosphorus. Since urea is retained in the organism in some cases of renal insufficiency. (*Achard* and *Paisseau*), and phosphorus likewise (*Gouraud*)[1], there may therefore result in such cases an auto-intoxication, slight it is true, but which will be added to that already caused by the kidneys. Consequently it is advisable to abstain from the use of the dry vegetables in all severe cases, and to limit their use to the lighter forms of Bright's disease.

Potatoes. The same may be said of potatoes, which are mostly contraindicated in no matter what form. In fact, it must not be forgotten that their content in potassium is very high and that it is impossible to take a large quantity of potatoes without getting sodium chloride, for the potassium being no longer neutralized by the sodium may manifest its toxic action.

Butter (fresh) **and oil,** containing but few chlorides are permissible foods and among the most useful in dechlorized menus.

Butter is, in fact, of great assistance in carrying out the regimen, for its use permits of more varied seasonings. According to *Professor Stryzowski*, 100 grams of butter contain 0.018 grams salt.

3d. Hyponitrogenized Regimen

For *Widal*, hypochlorized nitrogenous aliments, such as meat and eggs are permissible in large quantities, for they contain but few chlorides. The quantity of albuminous matters contained in a diet, *Widal states:* "has no influence upon the amount of albumin excreted by a nephritic.

"The albuminous substances of milk may be replaced by those of meat without finding any increase in the albuminuria.

[1] Gouraud: (Thèse de Paris. 1903).

"There would therefore be no reason to prohibit the use of meat to nephritics, provided its amount was regulated, according to the indications of dechlorization in regimen No. 1." (*Widal.*)[1]

From the hypochlorized point of view, the nitrogenous foods would consequently be nearly all allowable.

But is that a sufficient reason for permitting their use without restriction as *Widal* suggests?

Evidently not! Because on one side the albumins favor the nitrogenous putrefaction of the intestine and increase the intestinal toxins.

On the other hand, in renal insufficiency—in some cases at least—there is observed, besides the retention of chlorides, a retention of urea and uric acid, as demonstrated by *Achard, von Noorden, Strauss, Ernberg,* etc. **In such cases the nitrogenous retention will consequently necessitate a hyponitrogenized regimen combined with a hypochlorized one, and calculated in view of relieving the renal filter and at the same time maintaining the forces of the organism.**

In the acute forms of nephritis and in the acute exacerbations of chronic nephritis, it is necessary above all to relieve the kidneys. In chronic nephritis, while bearing this in mind, we must also endeavor to keep up the strength of the organism. The investigations of *von Noorden, Wiczkowski* and *Kœster* show that the *quality* or rather the *derivation of the albumin;* milk, eggs, meat, exercises but little influence upon the kidneys, although of all the albumins, that of milk is best tolerated. Much more important than the *quality* is *the quantity of albumin ingested.*

Aufrecht[2] was the first to require a hyponitrogenized regimen in renal insufficiency.

Dujardin-Beaumetz and especially *Leube* insist upon this point. The latter clinician, however, advised that in chronic cases the quantity of albumin given should not be lower than 80 grams, and that in acute cases, it should remain at 50 or 60 grams, and only for a short time.

[1] Widal et Javal: La cure de déchloruration. Paris. 1906. (*Actualités Médicales.*)

[2] Aufrecht: Berlin kl. Woch. 1883. p. 51.

Senator[1] even allows in serious cases and for a short time the lowering of the daily quantity of albumin to 30 or 40 grams. *von Noorden, Sirven, Hoffman* insist upon the important fact that a hyponitrogenous diet, with less than 50 or 60 grams, should not be too prolonged, although the example of vegetarians shows that daily doses of 50 grams are amply sufficient and may be borne for many years, provided the caloric value is replaced by fats and carbohydrates.

Finally, *Ernberg*[2], in his magnificent work, demonstrates that a hyponitrogenized regimen containing 40 grams of albumin compensated by fats and carbohydrates, is indicated in all cases of acute nephritis, or acute exacerbations, for it rests the kidneys and favors the elimination of the retained nitrogen.

Therefore the conclusions drawn from all these works are that in cases of acute nephritis from 40 to 50 grams of albumin and in chronic nephritis from 60 to 70 in the daily ration, are absolutely sufficient, if the diminution of nitrogen is indicated.

Hyponitrogenized menus. Let us now examine separately the aliments constituting the hyponitrogenized menus.

The milk foods. These need not be referred to as they have already been studied.

Milk, curdled milk and better still, buttermilk and whey, are hyponitrogenized aliments permissible in moderate quantities in acute cases and in large quantities in the mild forms of renal insufficiency.

They will render valuable services in nitrogenous retention, for of all the albumins lacto casein and lacto albumin are best tolerated.

Cheese, on the contrary containing as it does, large amounts of salt and casein is prohibited:

100 grams of cheese contain 29.49 grams casein.

100 grams of cheese contain 2.82 grams salt. (*Stryzowski.*)

Fresh cheese, however, in its natural state or with sugar, does not contain any more than the milk and may be used under the same conditions.

Eggs. These are altogether admissible in the dechlorized regimen.

[1] Senator: Erkr. der Niere. p. 280. (Pentzoldt's und Stinzing's Hbd. 1903. XI.)

[2] Ernberg: Loc. cit. p. 69.

An ordinary egg weighs on an average 50 grams.

An egg weighing 50g. contains	0.089 grams salt	Stryzowski
The yolk contains	0.020 grams salt	Stryzowski
The white contains	0.068 grams salt	Stryzowski

Such are the figures which *Professor Stryzowski*, with his usual courtesy, was kind enough to furnish at our request.

The ordinary daily ration in the hyponitrogenized menu, will therefore be 4 yolks containing 0.08 grams salt.

Eggs, however, have for a long time been forbidden in the diet of albuminurics, because of the celebrated observation made by *Claude Bernard*, who, after having taken two underdone eggs, noted a slight amount of albumin in his urine. Most authors have noted the same fact; that non-cooked egg albumin produces alimentary albuminuria. Its cause was demonstrated by *Ascoli*[1].

Whereas the most methodical investigations, now show that eggs cooked without salt and taken in moderate quantity, not only do not engender albuminuria in healthy men, but that they do not increase its output in the nephritic. Such is the opinion of *Dujardin-Beaumetz*, *Potain*, *Teissier* and most of the observers quoted by *Ernberg*.

But the eggs must be absolutely fresh, for even in that condition, they greatly increase the nitrogenous putrefaction of the intestine.

When the renal insufficiency is secondary to that of the intestine, the whites of eggs must be forbidden; the same holds good for primary cases, if nitrogenous retention is added to the retention of chlorides.

Meat. In renal insufficiency, the *uric acid retention* is still more frequent and greater than *the retention of urea*.

Hence all meats rich in nucleins—the mother substance of uric acid—must be prohibited to nephritics.

Liver, kidneys, sweetbreads, tripe, brains, in a word, all the interior or visceral organs, must never form part of the diet in renal insufficiency, because these aliments increase the retention of uric acid.

They, moreover, exaggerate digestive auto-intoxication, because they are rich in excrementitious products.

[1] Ascoli: Münch. Med. Wochen. 1902. p. 10.

Dosage of the urea retention by means of the test for alimentary azoturia, will determine the quantity of meat which may be allowed, or whether the indispensable albumin ration will have to be exclusively drawn from the one liter of milk and the gluten of the cereals, forming part of the severe hypochlorized and hyponitrogenized regimen. If nitrogenous retention does not exist, or if it is but slight, the hypochlorized regimen will be especially indicated, and in such cases, meat may be used with advantage every day and at each meal.

1kg. of meat contains	0.60 grams salt
100 grams roast meat contains	0.37 grams salt
100 grams ham contains	8.75 grams salt

Ham, although recommended by many authors, must be absolutely forbidden.

Red and white meats. Numerous controversies have arisen on the subject of the various kinds of meat. Most authors recommend the sole use of white meats (chicken, veal, rabbit), and interdict the use of the red meats (beef, mutton, game). It is hardly necessary to say—for us at least—that game, stews and highly seasoned sauces of all kinds should be absolutely forbidden.

Per contra, we make no distinction between the different kinds of meats, from the standpoint of their harmfulness.

For in the first place, if only the extractive matters be considered, we shall find that veal and rabbit, both typical white meats, contain more kreatin than beef.

In the second place, from a chemical point of view, the researches of *Rosenqvist* have demonstrated that the differences between red and white meats are no greater than those found between two white meats of different species.

Finally, from the clinical point of view, *Von Noorden* has shown that the quantity of albumin passed by a nephritic, was no greater whether the patient ate chicken or beef.

Kaufmann and *Mohr*[1] studied this same question in five nephritics, to whom besides their fixed non-nitrogenized alimentation, they gave sometimes white meats, at other times red meats.

[1] Kaufmann & Mohr: Zeits. f. kl. Med. 1902.

They came to the conclusion that the nature of the meat had no influence whatever upon the progress of the albuminuria.

These researches confirmed by *Kouchnir*, enable us to conclude that whenever meat is permissible, no distinction need be made between red and white meats.

Fish. If this article of food is considered solely from the standpoint of its content in salts and albumin, fish would be altogether indicated in nephritis, for it contains less of these substances than meat, and for that reason, *Senator* recommends it. Nevertheless it is prohibited by the majority of authors on account of its toxicity. This is the result of the rapid formation of alkaloids (neuridin, guanin) derived from the extremely easy and rapid changes which fish undergo, and which may exist, even when it has preserved all the exterior characters of freshness.

Springer, in studying urinary toxicity by *Bouchard's* method, found that of all meats fish gave the maximum toxicity.

For all these reasons, fish though fresh must be forbidden; such is the advice of *Potain, Teissier, Nollet, Dujardin-Beaumetz*, etc.

Meat juice and bouillon. These aliments contain 8.9 grams of salt per liter; they are absolutely contraindicated in all hypochlorized regimens and the more so because they are very rich in extractive substances.

En résumé, the regimen of renal insufficiency should be hypochlorized and hyponitrogenized, but within variable limits according to the patient and the degree and duration of the disease ; this to be determined by means of the tests for alimentary chloruria and azoturia.

The hypochlorized regimen, to be composed of nitrogenous and non-nitrogenous foods.

The hyponitrogenized regimen, to be strictly milk or lacto-vegetarian or carno vegetarian, these admitting of easy combination with the hypochlorized regimen.

Objections to the Vegetarian and Lacto Vegetarian Regimens

As a number of objections have been made against these regimens, it becomes necessary to carefully examine the objections.

1st Objection. That the Regimen Is Debilitating

A priori, this should not be the case.

The cereals often contain a strong proportion of gluten; certain semolinas made from Russian wheats and used in the manufacture of alimentary pastes contain it up to 19 per cent.

They contain lecithin in relatively large proportion.

Lastly, they contain starch, which is admirably digested, for even with a farinaceous suralimentation hardly more than ten per cent. is found in the stools. (*Rosenheim.*)

Here is the analysis (according to Koenig) of the cereal flours, used in making the broths with either water or milk.

	Nitrogenous Substances per 100	Fat per 100	Carbohydrates per 100	Cellulose per 100	Salt per 100
Wheat	9 to 19.0	2.2	79.75	2.1	1.9
Wheat, Russian	19.0	2.2	79.75	2.1	1.9
Wheat, German	15.0	2.2	79.75	2.1	1.9
Wheat, Hungarian	14.0	2.2	79.75	2.1	1.9
Wheat, French	13.0	2.2	79.75	2.1	1.9
Barley	9.8	1.9	66.2	4.9	2.4
Oats	10.6	4.9	58.3	10.5	3.9
Corn	9.4	4.1	69.3	2.3	1.3
Rice	7.6	2.2	74.7	1.7	4.4
Rye	10.8	1.7	70.2	1.7	2.6

	Salts per 100	Iron per 100	Phosphoric Acid per 100	Chlor. per 100
Wheat	2.0	1.2	47.4	0.32
Barley	2.6	1.2	35.1	1.2
Oats	3.2	1.1	25.6	0.9
Corn	1.4	0.7	45.6	0.9
Rice	4.4	1.84	40.6	0.8
Rye	2.0	1.2	47.7	0.4

Chemical Composition of the Alimentary Pastes

Water	13.00 per 100
Gluten	9.00 per 100
Fat	0.27 per 100
Sugar	1.50 per 100
Dextrin	1.00 per 100
Carbohydrates	73.70 per 100
Salts	0.84 per 100

Hence, **from the chemical point of view,** the cereals and the pastes made from them may be considered as valuable foods.

Finally and especially since the farinaceous foods prevent the putrefaction of the nitrogenous substances, they must save more of the utilizable or assimilable albumin required by the organism.

From the biological point of view and with respect to the proteids, they may therefore be considered as protective and economizing aliments.

Are these altogether theoretical views verified by experiments?

Pettenkofer and *Voit* had already demonstrated the favorable influence, exercised by the addition of sugar and farinaceous elements to a nitrogenous diet. This fact was confirmed by *Rubner*[1] and *Munck*[2], whose conclusions are as follows:

1st. Thanks to the addition of farinaceous elements, there results a nitrogenous saving, a better assimilation and fixation of the albumin, and a diminution in the azoturia.

2d. The farinaceous elements, by attenuating the nitrogenous putrefaction, diminish the urinary sulphoethers and favor the digestion of albumin.

Krauss[3], for a period of six days, gave to a dog 500 grams of meat only, and during the following six days 500 grams of farinaceous substances in addition to the 500 grams of meat.

	NITROGEN		
	Introduced.	Excreted.	Fixed.
First series, *meat only*	102.0	81.5	20.9
Second series, *meat + farinaceous*	160.2	93.9	66.8

It is seen that with the farinaceous elements present, the putrefaction being less pronounced, the amount of albumin digested by the enzymes is greater and the fixed albumin increases from 20.9 grams to 66.8 grams.

Wicke and *Weiske*[4] confirmed these facts by numerous experiments on sheep.

Kumajava[5] took the precaution of making the experiments upon his own person.

[1] Rubner: Zeit. f. Biol. XV, p. 146.
[2] Munck: Arch. Virch. 101.
[3] Krauss: Zeit. f. phys. Ch. XVIII, p. 173.
[4] Wicke & Weiske: Zeit. f. phys. Ch. XXI, p. 42.
[5] Kumajava: Virch. Arch. CXVI, p. 370.

	ALIMENTS INGESTED.		
	Albumin. Grams.	Carbohydrates. Grams.	Fixed Nitrogen Grams.
1st Experiment.....	58	201	Loss ..... 1.50 per diem
2d Experiment.....	50	560	Gain..... 0.50 per diem

From this it is seen that, owing to a sufficiently abundant introduction of farinaceous elements, a better nitrogenous fixation is obtained from a lesser amount of nitrogen; while an increase of albumin in the nourishment, without a parallel increase in the farinaceous elements, does not allow the obtaining of an equivalent increase of nitrogen; all the surplus undergoing putrefaction and being thus lost to absorption.

We may then conclude that the lacto farinaceous regimen is not debilitating; it allows the diminution of the ingested albumin ration without, for that reason, lessening the quantity of nitrogen assimilated, this still remaining three times greater.

2d Objection. That the Regimen Is Too Dry and Is Dangerous from the Standpoint of Urinary Elimination

The regimen is only apparently dry.

The alimentary pastes absorb from seven to eight times their weight of water; the puddings contain 25 per cent.

The so-called dry meal therefore represents from 300 to 400 grams of water.

If to this is added the liquid nourishment given between meals, it will be seen that the quantity of liquid is more than sufficient.

The best proof is found in the urine, which rapidly increases, never falling below 1,100 or 1,200 c.c. in twenty-four hours.

3d Objection. That the Regimen May Conduce to Barlow's Disease

This, in our opinion, is a much more serious objection.

Does not the lacto farinaceous regimen contain too few fresh foods and too many dry and preserved aliments, and may it not in consequence provoke scurvy in the infant (*Barlow's disease*) or anæmia, purpura, or scurvy in the adult?

It is certain that regimen No. 1 containing only dry preserved

foods (cereal flours, lactated flours cooked with water) might deserve such reproach if continued too long.

But in our lectures, in our consultations and with all our patients, we have always insisted upon the fact that this regimen *is a therapeutic and not an alimentary regimen;* that it plays in enteritis the same part that a liquid diet does in intestinal catarrh, and that it is therefore necessary, as soon as possible, as soon as its effect is produced, to add raw or pasteurized milk, potatoes, whortleberry juice, or lemon juice to the diet and thus avoid all danger.

Some time ago, *Professor Hutinel,* in speaking at the Pediatric Society of Paris, mentioned the case of a child suffering from Barlow's disease as the result of treatment which we had prescribed.

Unfortunately, *Professor Hutinel,* to whom we immediately wrote, and who very courteously replied, had not noted the name of the child, so that we were unable to find out what regimen had been followed by the little patient.

At all events, it will be prudent to insist even more than in the past, upon the necessity of discontinuing the **exclusive farinaceous diet,** as soon as the result sought for is obtained.

After the fifteenth day, from ten to fifteen drops of lemon juice may be added, even with infants.

With the regimens No. II and III, the ordinary regimens in enteritis, similar consequences seem to us absolutely impossible, for they contain fresh articles in sufficient quantity (milk, potatoes, berries, meat, etc.).

Furthermore after using these different regimens for more than fifteen years, we have never observed a single case of Barlow's disease.

Undoubtedly it would be otherwise if the patient of his own initiative, were to leave out for one reason or another the potatoes, milk, meat, etc., without apprising his physician, as happened to two of our colleagues last year.

It is therefore absolutely necessary to insist upon the regimen being carried out in its integrity ; lemon juice to be added if the other fresh aliments mentioned are contraindicated.

With these precautions the lacto farinaceous regimen presents no danger whatever.

4th Objection. That the Regimen May Cause Experimental Acid Dycrasia

The aliments we have just studied: curdled milk, whey, buttermilk, kephir, the cereals and alimentary pastes act upon nitrogenous putrefaction, especially by the production of lactic acid.

Under their influence the digestive canal therefore contains this acid more often and in greater amount.

Charrin[1], who has studied the effects of lactic acid describes them as follows:

Injected under the skin, this acid is rather toxic (0.0005 grams per 100 in forty-eight hours); in extremely small doses it alters the field, diminishes diuresis, lowers the intensity of agglutination and the bactericidal power; consequently, in the presence of this acid dycrasia, the evolution of infection takes place more easily.

In the digestive canal, *per contra*, this acid occasions but little harm for quite a number of factors attenuate its toxicity, among which figure the alkaline mucus; difficulty of absorption, the action of the intestinal mucosa and the liver, finally but particularly the presence of the alkaline salts which rapidly neutralize it.

Nevertheless *Charrin* continues, even in this degree, its action remains sufficient to engender good effects, to regulate the bowels, restrain putrefactive fermentations, the more so as lacto farinaceous aliments leave but little residue to nourish the intestinal micro-organisms. But it is better not to exceed certain proportions (0.50 grams per 100), nor make use of it for too long a time.

If these precautions are ignored, a lowering in the alkalinity of the plasmas, and an exaggerated elimination of mineral matters in the urine will be observed, and following this, lesions of the liver and kidneys will be noted.

Charrin and *Leplay* found in such cases that the hepatic cells were reduced to their cell walls with destruction of their nuclei. This explains why chemical urinary analysis indicates in these

[1] Charrin: Acad. des Sc. IV, p. 10. 1905.

same cases, a phosphaturia derived from the destruction of the phosphatic albumins, and an abundant elimination of uric acid derived from the destruction of the nucleins; for the destruction of these elements in the nuclei, is most important as we have noted by administering lactic acid *per se*.

It is thus seen that the noxious action of lactic acid depends upon its mode of entrance ; it produces harmful effects when introduced subcutaneously and is useful when introduced by the intestine and not in excess. These facts teach us prudence, and to act within measure. It is for this reason that we have for many years given up the use of pure lactic acid, and it is for the same reason that the soured milks (curdled, whey, buttermilk, and kephir) we prescribe, must be made from milk having undergone twenty-four hours acidification only; those several days old being harmful.

Finally, it is also for this reason that we prefer to the soured milks the alimentary pastes which contain no preformed lactic acid and which furnish their lactic and succinic acids in a nascent state, in small doses and pro rata with the abundance of the microbic flora, because it is the microbes themselves that cause their production.

Besides which, the urinary analyses made during the course of treatment for the purpose of ascertaining the elimination of uric acid and particularly that of phosphoric acid, at once show the point which should not be exceeded, and with the farinaceous regimen, such as we prescribe we have never noted any phosphaturia.

5th Objection. That This Too Exclusively Farinaceous Diet May Conduce to Diabetes

Without doubt, this regimen is and should be contraindicated in diabetes.

But in the first place this is of very exceptional occurrence, for we have but very rarely observed the coincidence of the two affections.

Secondly, after having dosed according to *von Noorden's* method—the quantity of carbohydrates tolerated by the patient,

without the appearance of sugar in the urine—the regimen may be modified and rendered suitable to the condition.

It is, moreover, unquestionable, that in hepatic insufficiency, the farinaceous regimen serving for experimental glycosuria, may cause alimentary glycosuria; but in all these cases the presence of sugar is sought for every ten days; here again it is easy to recognize it and modify the regimen accordingly.

6th Objection. That the Regimen Is Not Always Accepted

Willingly accepted? Not always, certainly; but if the purpose and the end to be attained are explained to the patient, he will very rarely refuse.

As soon as he will have lost the habit of the more savory foods and have become accustomed to the rather insipid regimen, he will end by finding these tasteless foods agreeable, and will soon take them willingly.

7th Objection. That the Regimen Is Not Always Well Borne

If care is taken to prohibit drinking with the solid farinaceous substances, the regimen is very easily borne after, at the most, eight days discomfort.

There exists, however, two contraindications to the intensive farinaceous diet and these should be well recognized. They are patients who besides an inflammation of the colon have also chronic inflammation of the small intestine. These are easily recognized by the diarrheal form of enteritis from which they suffer.

In them the farinaceous elements ferment in the small intestine with abundant production of lactic and butyric acids, thereby causing acid diarrheas with colics and a very defective assimilation.

Others without having inflammation of the small intestine, have not a normal digestion; they have a dyspepsia of the small intestine.

For one, two or three months the farinaceous diet is tolerated, then without any appreciable cause, the same fermentations and discomforts as in the preceding cases appear in them.

In these two classes of cases, it is necessary to modify the diet and to replace the greater part of the farinaceous elements by the dry vegetable purées, and to substitute yoghourt for the milk.

But these are exceptional cases, and *in a general manner*, it may be stated that these regimens are without disadvantages and without danger, that they are easily accepted and still more easily borne by patients.

B. TO COMBAT INTESTINAL NITROGENOUS PUTREFACTION BY THE INTRODUCTION OF ANTAGONISTIC BACTERIA

Let us remember that the principal characteristic of the intestinal flora in auto-intoxication, is the great diminution in the saccharolytic aerobic bacilli, and the appearance of an enormous number of proteolytic anaerobic bacilli; these are the indefatigable producers of nitrogenous putrefaction. We have seen that the vegetarian and the lacto farinaceous regimens, thanks to the slight quantity of nitrogen which they contain and thanks to the lactic acid which they form, were powerful means for modifying the intestinal culture bouillon, far too favorable to the proteolytic bacteria.

We are able to modify the intestinal culture bouillon in still another manner, by introducing other microbes inoffensive in themselves but capable, either by their presence or through their secretions of proving harmful to the proteolytic anaerobies of putrefaction.

For, in fact, the proteolytic anaerobies find powerful enemies among other microbes, notably as we have seen those which provoke the fermentation of sugars and form lactic acid.

Would it not be possible therefore to acclimate these lactic microbes in the digestive tract in order to combat intestinal putrefaction with their aid.

Of course it is not sufficient to find the inoffensive and antagonistic microbe, for it must also be able to survive in the intestine of man.

Bacteriology teaches us that many microbes ingested in very large quantities and repeatedly, perish in the intestinal canal of man and animals. Thus as *Metchnikoff* pointed out, the comma bacillus, the dreaded cause of Asiatic cholera, has on several occasions been ingested with impunity and by different

individuals. Its destruction was so complete that it was impossible to find any in the fæces.

The same observation has been made with other microbes, that of tetanus for example. Hence this method can only be utilized with some chance of success, when it will be possible:

1st. To recognize the proteolytic flora of the intestine as the cause of the autotoxic disorder.

2d. To find and introduce in the intestine a culture of lactic microbes, antagonistic to the proteolytic anaerobics of putrefaction, but inoffensive to man and capable of living in his intestinal tract.

Many experiments have been made directed against:

(*a*) Certain bacteria causing specific infections.

(*b*) The proteolytic anaerobic bacteria of putrefaction in general.

A. PROTEOLYTIC INTESTINAL INFECTION INDIVIDUALIZED

Tissier, the distinguished bacteriologist, whose studies of the intestinal flora of infancy are authoritative and which complete those of *Escherich*, has made many trials of this method in certain individualized intestinal infections, and with very favorable results.

Tissier has just published a study on the subject[1] of which we shall give a brief résumé, for it not only shows the importance, but also the practical and clinical difficulties of the individualized method.

From the group of acute intestinal infections the etiology of which is still so confused, *Tissier* attempts to separate a form, special in its symptoms, progress and particularly in its bacteriological characteristics.

This refers to an infection caused by a strict anaerobic, the *Bacillus perfringens*, the pathogenic action of which is well established. An habitual guest of the adult intestine, it is not met with in the normal suckling, except in the first days of life and before the expulsion of the meconium and the appearance of the characteristic *golden yellow* stools.

[1] Tissier: Ann. Instit. Pasteur. 1905.

The infection imputable to it is betrayed by a greenish diarrhea abundant and foamy like the froth of beer, with it local and general symptoms of acute catarrh.

Its duration is from one to two months in the suckled infant; it is most serious in the bottle-fed child and may in certain grave cases end fatally in less than a week.

The bacteriological study of the stools shows special results; the *Bacillus bifidus*, which in the normal state forms the base of the intestinal flora in the suckling, has completely disappeared.

Instead, the facultative anaerobies, the cocci, and diplococci which abound in all infantile diarrheas are found in great numbers. Finally, from the large number of abnormal and varied species present, the *Bacillus perfringens* was isolated by *Tissier* in all the cases.

The biological properties of the *Bacillus perfringens*—a microbe of proteolytic function—demand treatment, for the ordinary medication of catarrhal disorders, the liquid diet, calomel and enteroclysis are always powerless.

1st. It is necessary in the first place—as we ourselves advise—to modify the intestinal culture medium by restricting the albuminoids and increasing the carbohydrates (lactose, farinaceous elements).

2d. In the second place, *Tissier* opposes to the *bacillus perfringens*, a bacterium inoffensive in itself, or through its secretions and fermentative products, but which is yet capable, while acting as a saccharolytic ferment of inhibiting the growth of the proteolytic *perfringens*.

For this purpose *Tissier* proposes the *Bacillus acidi paralactici* of *Kosaï*, and he administers it to sucklings in the daily dose of one or two teaspoonfuls of the pure culture, with the greatest benefit.

We have taken pains to quote in detail the interesting observation of *Tissier*, so as to make clear the practical difficulties. In order to individualize an intestinal infection, it is necessary in the first place to be an experienced bacteriologist, but this is not sufficient, for it requires a bacteriologist who is also thoroughly familiar with the normal and pathological intestinal flora.

We also cause both microscopical and bacteriological examinations to be made in all cases of digestive infection, and we realize their difficulty, for in the majority of cases we may esteem ourselves fortunate to know with some degree of certainty whether the predominance of the flora is saccharolytic or proteolytic.

This is sufficient to determine the regimen; it suffices to determine the kind of antagonistic microbes, but only a bacteriologist by profession can individualize the microbe causing the infection, and oppose to it, its antagonistic organism, as proposed by *Tissier* in his first work.

This manner of treating individualized intestinal infections is therefore still a laboratory method, one which cannot be employed in general practice, and which will remain the appanage of a few privileged scientists.

B. MIXED PROTEOLYTIC INTESTINAL INFECTION

Most frequently the intestinal infection is caused by very numerous proteolytic microbes, among which it is impossible to find any predominating or specific species.

Therefore, and in order to combat the nitrogenous putrefaction of the large intestine, *Metchnikoff* advises the acclimation in the intestine of the harmless saccharolytic bacilli, which produce quantities of lactic acid in a nascent state, and are consequently formidable antagonists to the proteolytic bacteria which cause intestinal nitrogenous putrefaction.

This acclimation occurs in the first place and quite naturally with our lacto farinaceous regimen ; for this transforms the intestinal culture bouillon favorable to the proteolytic anaerobics into one favorable to the saccharolytic aerobics.

This acclimation may occur in the second place as a result of the introduction in the digestive tract of the natural lacteal ferments. The natural lacteal ferments are derived either from our own curdled milks or from the oriental curdled milks, transmitted to us by ancestral usage, such as the Egyptian ferment *leben*, the Bulgarian ferment *maya*, the Tartar ferment *kephir*, all of which contain lactic bacteria and even yeasts, as well as many other microbes.

This acclimation may finally take place by introducing in the digestive tract, artificially selected lactic ferments. To accomplish this, use must be made of some of the lactic bacilli, found in the natural ferments; they must be scientifically selected, and made into culture bouillons capable of being introduced into the digestive canal either pure or with milk.

Hence two new methods of diminishing intestinal nitrogenous putrefaction.

1st. By the introduction of natural lactic ferments in the intestine.

2d. By the introduction of selected lactic ferments.

1st. INTRODUCTION OF NATURAL LACTIC FERMENTS IN THE INTESTINE[1]

The oriental natural ferments may be introduced in the digestive canal:

(*a*) In the form of oriental curdled milk.

(*b*) In the form of pure cultures of oriental lactic bacilli.

ORIENTAL CURDLED MILK

The ordinary curdled milk which we have already considered when speaking of the lactic acid foods cannot be compared with the oriental curdled milk, from the standpoint of its action in the intestine, for it is very different.

The occidental or ordinary curdled milk, curdled by the common methods, that is, either by dry or liquid rennet or else spontaneously in the open air through the agency of the *Bacterium acidi lactis*, is as we have seen an excellent aliment to combat nitrogenous putrefactions; but it does not act bacteriologically; it acts simply as a chemical agent through its lactic and succinic acids.

In fact, the *Bacterium lactis* occurring in the spontaneously curdled milk cannot by itself cope against the proteolytic microbes.

It is a very delicate microbe, easily destroyed, and it never traverses the intestine, for it is not found in the stools; it disappears completely before reaching the colon owing to the action of the antagonistic bacteria.

[1] See Appendix.

It is not apt therefore, even when it exists in large quantities in the ingested curdled milk, to struggle against the other bacteria in the intestine.

Oriental curdled milk. It is not the same with the oriental curdled milk, for this is not only an aliment, but a culture bouillon, containing, it is true, lactic and succinic acids, both of which have their own proper antiputrefactive action, but it contains especially a considerable number of various saccharolytes, among them the *bacilli of Massol;* these are extremely active and resisting bacilli which successfully struggle throughout their entire intestinal course against the proteolytic bacteria of the large intestine, for they are found in the stools.

This constitutes the difference and the superiority of the Bulgarian curdled milk, over the ordinary curdled milk.

Historical. The use of oriental curdled milk as a food of the people, goes back to the most remote periods.

The Bible tells us that when Abraham saw three men appear before him, he gave them, to render them honor, milk curds and not meat as an Occidental would have done.

We still see the Jews continue to nourish themselves with curdled milk, vegetables and fruits, with only occasional use of meat.

From those times the custom has been perpetuated in all the oriental countries in which curdled milk forms a large part of the alimentation. In Egypt, the use of this food known under the name of *leben* goes back to the highest antiquity. The bacteriological analysis of the Egyptian *leben* was made by *Rist* and *Khoury*[1]; they found in it five species of microbes, among them lactic bacteria which, as *Tissier* and *Martelly* have demonstrated, are antagonistic to the proteolytes and possess an energetic antiputrefactive action.

In ancient Greece and in Rome curdled milk formed an important part of the peasant's food and was always present on the citizen's table.

Pliny mentions that at the great feasts of the patricians, the offering of curdled milk at the end of the banquet was never omitted; it bore the name of *oxygala*. Furthermore,

[1] Rist & Khoury: Ann. de l'Institut Pasteur. Jan. 23, 1902.

in ancient times, veritable cures of curdled goat milk were made; the curdled milk being called *schiston*.

We thus see that from the remotest times, each oriental nation has made very great use of milks, either curdled, coagulated or prepared by different methods.

The reason being that these peoples, originally pastoral and nomadic, were keen observers, and the observations resulting from the accumulated experience of numerous generations, had taught them the beneficial effects derived from the use of curdled milks.

In consequence, their reputation spread beyond the localities in which they were popularly used, and their reknown was even carried to occidental countries.

History tells us, *Dybowski* states, that the reputation of oriental curdled milk had spread to France during the reign of Francis the First.

On consulting the biography of this monarch, we learn that he was very much debilitated, and reduced to a languid state, which became progressively worse each day. The most vaunted remedies having been tried in vain.

Francis learned that there lived in Constantinople, a Jew who had the reputation of being able to cure such conditions by only requiring the adoption of a certain regimen.

Francis thereupon commanded his ambassador at the Sublime Porte to send this Hebrew doctor to Paris.

The latter consented on condition that he be allowed to make the journey by short stages and that he should be accompanied by several ewes.

Surrounded by four ewes, the Jew arrived in Paris, examined Francis the First, and ordered him to live solely upon the curdled milk made from the milk of his ewes, the recipe for the preparation of which he was never willing to divulge.

The king, however, rapidly regained his strength; the ewes of the Jew having died, the latter continued his cure with asses' milk.

At the present day the use of curdled milk exists throughout Africa. The nomadic tribes of Algeria and Tunis, having a marked predilection for curdled milk or *rayet*.

It is also the principal food of the Arabs.

Most of the negro tribes of Africa also make use of it. All the people inhabiting hot countries instinctively appreciate the disinfecting value of curdled milk as well as that of a meatless diet, which is particularly necessary in hot climates, for the climate itself is prone to exaggerate intestinal putrefaction. The same exists in the oriental countries, where all the nations have religiously preserved the tradition of the beneficial action of curdled milk.

The best known and most studied of all the oriental curdled milks is the Bulgarian.

Bulgarian curdled milk or yoghourt. This is especially used throughout European and Asiatic Turkey, in Greece, Montenegro, Servia and Bulgaria.

It is eaten alone with a little salt or sugar, or mixed with *various other foods;* with rice as in Turkish pilaff or with berries or with such vegetables as squashes and egg plant.

Yoghourt is prepared with a particular ferment called *maya*, possessing special properties. Maya dates from the most remote periods and has been transmitted and preserved by successive inoculations. The orientals in fact, inoculate their day's milk by adding to it a little of the previous day's yoghourt, and in that manner transmit the culture intact.

Chemical composition of yoghourt. Yoghourt is a milk concentrated to half volume and contains according to *Olaf Jensen:*

Casein	7.10 per cent.
Fat	7.20 per cent.
Lactose	8.3 to 9.4 per cent.
Lactic acid	0.80 per cent.
Alcohol	0.02 per cent.

A rather notable quantity of casein, about 38 per cent., has been rendered soluble and transformed into albumoses and peptones (*Fouard*), which shows that in yoghourt, the albuminoid elements are no less prepared for digestion than in kephir.

The phosphate of lime, which constitutes the greater part of the mineralized substances of milk, has likewise been made more soluble during the fermentation (in the proportion of 68 per cent.). All these findings show how valuable and easily digested a food yoghourt is.

Bacteriological composition of maya. The Bulgarian ferment used in the preparation of *yoghourt*, which we term *maya*, is known in Bulgaria as *Podkwassa*.

Grigoroff studied the bacteriology of *maya* in the laboratory of *Professor Massol*[1] of Geneva, and he found besides a multitude of other species, three special lactic bacteria, aerobies and facultative anaerobies.

1st. **The Bulgarian bacillus or bacillus of Massol** is a long rod-shaped organism, apparently non-motile, appearing isolated or disposed in linear series. It is stained by the basic aniline dyes and retains its color with Gram's solution.

It grows actively in sweetened media and causes active fermentation of glucose, lactose, saccharose and mannite.

Sterilized milk inoculated with it is coagulated in twelve hours at a temperature of 37°C. The coagulation is due to the formation of lactic acid, for it does not secrete any ferment.

Forty-five degrees Centigrade appears to be its favorite temperature; it resists to 50° C., but its activity is diminished; 60° C. is fatal to it in a half-hour. This bacillus is the most energetic lactic ferment known.

2d. **A diplococcus.** There are found in soured milk, cocci, appearing isolated, or grouped as diplococci, or else gathered in clumps and endowed with Brownian motion.

They remain colored with Gram's solution and are easily stained by the basic aniline dyes.

This micrococcus develops easily in sweetened media and it is a facultative aerobic, anaerobie. It coagulates milk in twenty-four hours, at a temperature of 37° C. by lactic acid fermentation and does not produce any ferment. It exercises its maximum energy at 45° C.; it resists 50° C., but perishes when exposed for one hour to 60° C.

3d. **A strepto bacillus.** These are short rods, grouped in little chains of from 4 or 5 to 10 elements.

This strepto bacillus is energetically stained by *Gram's* solution and is easily stained by the basic aniline dyes.

This organism develops in sweetened media and coagulates milk in fourteen hours at 37° C. with production of lactic acid;

[1] Massol: Rev. méd. Suisse romande. 1905. p. 716.

and does not secrete any ferment. It is a facultative anaerobie; its greatest activity is at 45° C.; it resists 50° C., but perishes in one hour at 70° C. Like the others, it attacks levulose and saccharose.

These three organisms inoculated into milk, all produce lactic acid, but in different degrees.

In twenty-four hours	The micrococcus	0.07 per cent.
	The bacillus of Massol	0.49 per cent.
	The Strepto bacillus	0.51 per cent.
In four days	The micrococcus	0.16 per cent.
	The Strepto bacillus	0.45 per cent.
	The bacillus of Massol	1.26 per cent.

The bacillus of *Massol* is therefore a very energetic lactic ferment, the most powerful of all the known lactic ferments.

These three organisms form an inactive lactic acid.

Mode of preparing the Bulgarian curdled milk. In Turkey the art of making yoghourt is well known, and its knowledge is handed down from father to son in all families.

Yoghourt, to be good, must be consumed when fresh; therefore it must be prepared at home or near-by, for it does not stand transportation and in the Orient this would have to be done at night and when cool.

This is how it is prepared in the Orient:

The whole milk of cows, goats, or ewes is taken and heated in as large a vessel as possible and over a gentle fire.

It is made to boil *until reduced to half its original volume.*

To hasten evaporation, it is stirred and taken up with a dipper and poured back from some height into the vessel.

The reduction to half having been accomplished, the milk is poured into bowls of varying capacities, according to the needs (generally about 300 grams), and it is allowed to cool down to about 45° C.

It is then inoculated with *maya* or fresh ferment, in the proportion of 2 c.c. to the liter or a teaspoonful (5 grams) per bowl. (Instead of using Maya most families inoculate the milk with two tablespoonfuls of the previous day's yoghourt; this suffices to start the fermentative process. Following this, the bowl or vessel is enveloped in woolen cloths or blanket, so as to maintain the milk at about the same temperature for eight hours.

At the expiration of that time, the milk being curdled, the woolen cloths are removed and it is put in a cool place until completely cold, which requires from three to four hours longer.

Its appearance then is that of a rather firm compact white mass, which does not exude serum when intact.

It is now ready for consumption, *in situ*, for it does not bear transportation, as the shaking and jolting breaks up the mass and liquefies it in such a way as to give it the appearance of sour milk, in which state it is no longer presentable.

Sometimes the curdling is completed in five or six hours, at others times it is not finished at the end of ten hours. It should then be given longer time; this depends upon the season and the temperature.

Commercial preparation. In Europe there has been an endeavor to furnish to the public a fresh and active Bulgarian ferment. For this purpose, the so-called Bulgarian Maya Company was formed in Paris.

This company aims to supply a ferment prepared in the country where it originated, and capable of being preserved and transported anywhere.

"In order to accomplish this and have a ferment of assured origin, a factory was installed in Asiatic Turkey, and it is in the laboratories of this factory that the company manufactures its Bulgarian ferment. It is desiccated and pulverized and may be carried anywhere, while still retaining its activity, and keeping indefinitely.

The preparation of the ferment in Turkey would seem a superfluous precaution, for pure cultures of the *maya* bacilli may be cultivated in any place with the present bacteriological methods.

Be it as it may, the company delivers to the public a *Bulgarian maya* in dry powdered form, put up in small vials containing from 20 to 100 and 200 doses.

To facilitate the preparation of yoghourt at home, the company has devised special incubators in which the constant temperature of 47° C. necessary for its manufacture, may be maintained in the house of the consumer. These incubators

are constructed as boxes in which little braziers are kept lighted, or else as real incubators heated by hot water.

This is the method recommended:

1st. Select good milk and boil down to half volume.

Fill the bowls in the incubator (each containing 300 grams) with the boiled milk and let its temperature descend to about 50° C.

2d. In each vial of the ferment will be found a little spoon serving as measure. Put into each bowl a little spoonful of the ferment which should be distributed by sprinkling, then stir so as to thoroughly mix the powder with the milk.

3d. Fill the boiler of the incubator with *boiling water*, replace it, close the incubator and allow the curdling to take place.

4th. After twelve hours remove the bowls the contents of which should form a uniform mass, and place them in a cool spot. By preparing the milk in the evening and withdrawing the bowls the following morning, it will be ready to use during the day.

In Switzerland the Pury Company at Montreaux prepares the *maya bacilline* in a dry form and the Henneberg Company of Geneva prepares *lacticose* in liquid form.

These two ferments are prepared from Bulgarian maya, and have the same properties and advantages as the one described.

Mode of use. Yoghourt may be taken by itself with salt, sugar or flavored with cinnamon.

It may be taken fasting in the dose of 300 grams or in place of a light breakfast, or else as a refreshment at 4:00 P.M., or before retiring.

It may be taken *at meals* with alimentary pastes but especially with rice in the form of oriental pilaff, or as a dessert with pudding, and in the same dose. Finally, in the more serious cases it may be taken with a light breakfast, at lunch and dinner, each time in the dose of 300 grams, so that about 1 kilogram is consumed during the day, a quantity which it is rarely necessary to exceed.

However, when taken in large doses, its use should not be too prolonged to avoid the ill effects of the acid cachexia already mentioned.

Physiological action of yoghourt. Its great advantage consists in its very agreeable taste, which never offends the patient as milk does so frequently when its prolonged use is required. Like milk, it is a complete food, but being concentrated, it corresponds in lesser volume to a larger quantity of milk; and given in equal quantities, is therefore more nourishing. Owing to its slight acidity, it is easily digested; it contains considerable lactose and lactic acid and thanks to these two substances, it is mildly laxative and diuretic, two precious qualities in the treatment of desintoxication. Should it contain—as it is said—less salt than milk, it would be a most valuable aliment in the treatment of renal insufficiency and epilepsy by means of the hypochlorized regimen.

Therapeutic action of yoghourt. *Dybowski* and *Tubbendjuan* (of Turkey)[1] have shown with what great advantage yoghourt may be substituted for milk in all diseases in which a lacteal diet is indicated.

But its particular action, as pointed out by *Metchnikoff*, is due to its special composition; that is to say, its abundance of lactic ferments, these being the most powerful antagonists of the intestinal microbes. It is therefore a powerful antiseptic of the digestive tract and finds its special indication whenever intestinal intoxication exists.

Herter of New York[2], after having introduced quantities of microbes directly into the intestines of a series of dogs, found that while the *Bacillus proteus* increased the urinary sulphoethers, the introduction of large quantities of *lactic bacilli* markedly diminished the indican and the sulphoethers.

Cohendy, from a personal experience of six months' use of yoghourt, found after determining the proportion of urinary sulphoethers with a mixed regimen, and submitting himself to a meat diet that the urinary sulphoethers were markedly increased, as always happens. He then added one liter of yoghourt; its good effects were soon evident, for the quantity of sulphoethers fell to a minimum.

The examination of his stools demonstrated the constant

[1] Dybowsky & Tubbendjuan: Journ. des sc. méd. d' Angers. Nov., 1904.
[2] Herter: British Med. Journ. 1897. p. 1848.

presence of the same lactic bacilli used in the preparation of yoghourt, these having survived their passage through the intestine.

Furthermore, their influence lasted long after ceasing the use of yoghourt, for notwithstanding a strong meat diet, the quantity of sulphoethers remained very low and only began to increase several months later.

In our city practice, we have made use of the yoghourt prepared from *maya* by the *Laiterie Centrale* of *Lausanne.*

And we can confirm in all points the results obtained by the authors we have just cited.

In intestinal auto-intoxication, yoghourt is a most valuable antiputrefactive aliment.

In the auto-intoxication due to membranous enteritis, yoghourt is harmful, almost as much so as milk, and it must not be employed. Whereas, in the glairy diarrheal form of enteritis, a disease affecting the small intestine and not amenable to the alimentary pastes, yoghourt gives absolutely remarkable results.

Pure Cultures of the Oriental Lactic Ferments

All of the microbic flora of the Bulgarian maya may be administered—without the intermediary of curdled milk—in the form of powder, pills or compressed tablets.

In our hospital service we have begun the study of one of these preparations, the *maya bacilline of Pury,* but the experiments instituted not being terminated, we are as yet unable to give any conclusions.

2d. Introduction in the Intestine of Selected Lactic Ferments

The natural ferments intended for the preparation of soured milks are far from representing pure cultures of lactic bacilli. We have seen that *maya* contains besides the three bacilli described by *Grigoroff*[1], yeasts and a large number of other bacteria.

Rist and *Khoury*[2] found in *leben* three lactic organisms and two alcohol-producing yeasts.

[1] *See* page 422.
[2] Rist & Khoury: Ann. de l'inst. Pasteur. 1902. p. 65.

The soured milks prepared with the natural ferments have therefore this disadvantage, that besides the useful lactic bacilli, they also contain other indifferent or even noxious bacteria. That is why *Metchnikoff* has modified the preparation of yoghourt and instead of introducing all the microbic flora existing in the natural ferments just described, he has proposed inoculation by means of pure cultures of lactic bacilli.

Other authors have followed the same lead and to-day there are actually three lactic culture bouillons:

(*a*) The liquid lacto bacilline of *Metchnikoff*.

(*b*) The biolactyl of *Fournier*.

(*c*) The paralactic bouillon of *Tissier*.

THE LACTO BACILLINE OF METCHNIKOFF

Among the lactic bacilli, there is one to which the attention of *Professor Metchnikoff* was more particularly attracted.

It is the large bacillus isolated from *maya*, by *Professor Massol* (of Geneva) and his pupil, *Grigoroff*, and commonly known as the Bulgarian bacillus, but which it would be better to designate as the *bacillus of Massol*, for it is also found in the Egyptian ferment *leben* and in the Turkish ferment.

According to the researches of *Heupel* and *Grigoroff*[1], this bacillus is much the best producer of lactic acid and as we have seen, it is capable of bringing about the coagulation of milk by itself only.

The bacillus of *Massol* is robust, of large size, 5 to 20 μ. long and very resistant, for ingested by man it is not destroyed in the intestine and reaches the end of the colon in a living state. Its presence was noted in the stools several days after its ingestion through the mouth by *Cohendy*, and we have also found it in the stools whenever sought for.

This bacillus is therefore one that does not normally form part of our intestinal flora, but which may be artificially implanted in it, and which is capable of acting efficiently against intestinal putrefactions. *But this bacillus likewise attacks fats*, and in so doing imparts to the milk a most disagreeable tallow-

[1] Heupel & Grigoroff: Loc. cit.

like taste,[1] which renders it unfit for use. To remedy this disadvantage, it became necessary to associate with *Massol's* bacillus belonging to the oriental lactic flora, another lactic organism belonging to the European flora, and chosen from among those that are harmless to man and even to the most sensitive laboratory animals.

By using milk serum, pure culture bouillons of these two lactic bacteria were secured, with exclusion of all the other microbes, so numerous in *maya* and particularly of the alcoholic ferments.

The great difficulty is to procure the pure culture bouillons; this, however, has been greatly facilitated for the public by the formation of the Ferment Company under the patronage of *Metchnikoff*.

This company prepares by scientific selection pure culture bouillons of lactic bacilli to which it has given the name of *lacto bacilline*.

Mode of using. *Lacto bacilline* is supplied to the public as a liquid ferment and is put up in small vials containing 10 c.c. each.

The bacteria which they contain in pure cultures—and that is the most important guarantee given by the Company—have been studied by *Metchnikoff* and he has established their perfect innocuity by long usage in man and numerous experiments upon animals.

These bacilli thus exercise a very favorable influence on digestion; they regulate the intestinal functions, combat constipation and they particularly and energetically combat the proteolytic bacteria by preventing putrefaction.

The lacto bacilline cultures may be introduced into the intestine either through:

(*a*) The intermediary of yoghourt or

(*b*) By themselves.

Yoghourt Made with Lacto Bacilline

Mode of preparing. Boil sufficient milk for five minutes and allow it to become cold. Wash two or four bowls holding 250 grams each in boiling water, let them drip without wiping them.

[1] Metchnikoff: Remarques sur le lait aigri, p. 26.

Pour into each bowl a quarter liter of milk and one-fourth of the contents of a lacto bacilline vial, mix well and cover. Put them in a warm place or better still in an incubator at a maximum temperature of 35° Centigrade.

At this temperature the coagulation takes place best and in about ten or twelve hours; when the temperature is about 25° the operation takes much longer.

When the coagulation is complete, the milk is allowed to become cold and is then ready to use.

For economy's sake a new portion of milk may be prepared by adding some of the previous day's curdling, but this should not be repeated more than once for the bacilli lose their qualities.

What milk should be employed in the preparation of yoghourt?

Raw milk; from the standpoint of palatability raw milk is the best, for it gives a very agreeable taste to the soured milk.

But raw milk contains many microbes, some of them harmful, those of tuberculosis in particular. These bacteria retain their vitality in the soured milk, the bacilli of cholera and typhoid fever retaining their vitality in it for forty-five days.

Raw milk contains besides fecal dust from the cow, and this is gorged with microbes; the lactic bacilli, while they prevent their multiplication, do not destroy them.

It is better therefore not to introduce all these microbes with the yoghourt, and unless a milk derived from cows tested for tuberculosis and hygienically kept can be procured—which is rarely the case—preference should be given to cooked milk.

Milk pasteurized at 60° C. is not surely rid of tubercular bacilli, nor of the spores of the butyric bacilli.

Sterilized milk at 110 to 120° C. and truly sterile has such a bad taste that it cannot be used.

The better plan is to boil the milk for a few minutes, for all the tubercular bacilli and butyric bacilli are killed by the ebullition excepting a few butyric spores and the spores of the *Bacillus subtilis*, which can only be destroyed by a high and persistent temperature. In this manner there is obtained a curdled milk, inoculated with pure lactic cultures in sufficient quantities to prevent the germination of the spores contained in it and not destroyed by the ebullition (*Metchnikoff*). Since for prolonged

use the consumption of too much casein or fatty matters is not always desirable, the yoghourt may in such cases be prepared from milk simply boiled and not concentrated to half volume, which makes it much heavier and more digestible. In many cases the fats may be still further diminished by using skimmed milk simply boiled.

Lacto bacilline soured milk prepared with whole or skimmed milk, simply boiled and inoculated with pure cultures of lactic bacteria is, as can be readily understood, infinitely superior to

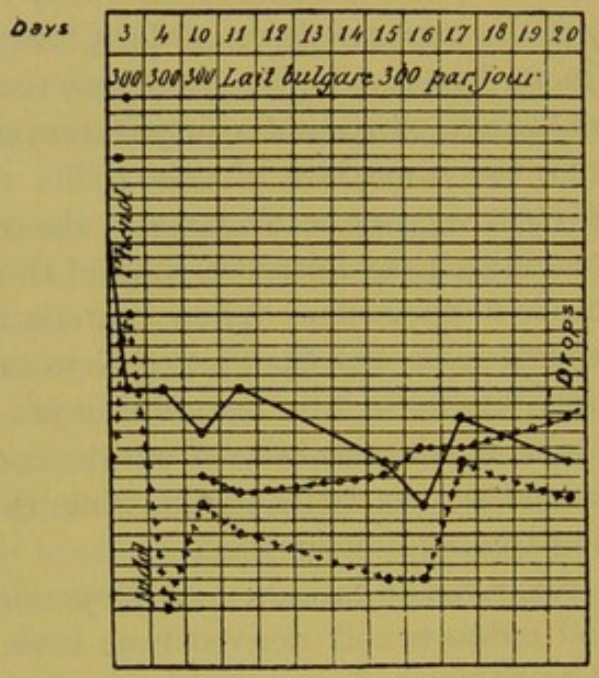

FIG. 10.—CURVE OF INDOL AND PHENOL, WHILE USING YOGHOURT MADE WITH LACTO BACILLINE.

the ordinary yoghourt inoculated with maya; for it is a constant product, perfectly harmless and which nevertheless—from the antiputrefactive standpoint—exercises upon the proteolytic microbes the same inhibiting effects as yoghourt.

Mode of use. The lacto bacilline yoghourt is consumed in the same manner as the ordinary yoghourt, 300 c.c. or a bowlful two or three times daily.

It may be taken on arising, fasting or during the morning; as refreshment in the afternoon or at bedtime; it may be taken at meals with the alimentary pastes or with puddings, else sweetened with sugar or flavored with cinnamon.

Therapeutic action. *Metchnikoff* who has for seven years made use of it in his diet, declares himself most satisfied with the results obtained, and we agree with him that so long an experience, coming as it does from a scientist whose judgment is as enlightened as it is conservative, is sufficient to justify this favorable opinion. Our most worthy interne, *Doctor Pochon*, who undertook to experiment upon himself with yoghourt prepared with lacto bacilline, obtained absolute results from the viewpoint of intestinal auto-intoxication.

As may be seen from the curves in Fig. 10, both indol and phenol diminished considerably under its use, and the action continued even after ceasing the yoghourt.

The action of yoghourt is—as might have been theoretically supposed—much less powerful than that of pure lacto bacilline *per se.*

In one case of enteritis, we were even obliged to stop the employment of the lacto bacilline yoghourt as it was not well borne.

Pure Cultures of Lacto Bacilline

We know—abstraction made of the rather large number of persons who do not like it—that there is quite a category of auto-intoxicated individuals who cannot tolerate milk; they are the ones suffering from chronic enteritis.

These may make use of the Bulgarian bacilli in pure culture.

But as these bacilli need sugar to produce lactic acid, it is necessary when taking them to consume also some sweetened foods, sweetened water, candy, preserves, for as *Grigoroff* showed, the bacillus of *Massol* decomposes glucose and saccharose as well as lactose. Lacto bacilline may be taken in several manners.

1st. Liquid lacto bacilline. This is a pure culture in milk serum of the bacillus of *Massol* belonging to the oriental flora associated with the European bacillus lactis in determined proportions. The hermetically sealed vials in which it comes contain 10 c.c. each.

The contents of a vial are given in two doses, either when

fasting at 10:00 A.M. and 4:00 P.M. and in sweetened water or else at the end of the two principal meals with a little honey, preserves or sweetened water.

2d. Lacto bacilline in powder. This is the pure culture filtered and desiccated under such conditions as to insure its absolute cleanliness.

The powder is supplied in sealed and paraffined glass tubes,

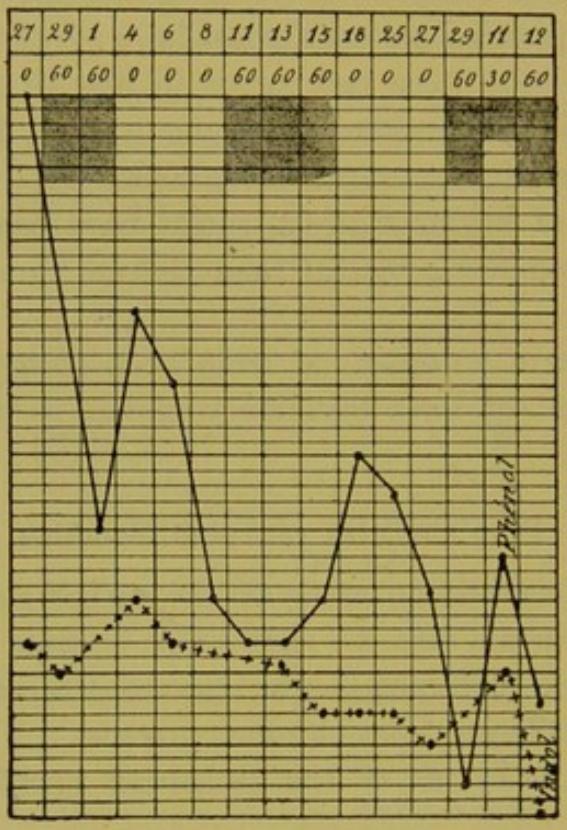

FIG. 11.—CURVES OF PHENOL AND INDOL WHILE USING LIQUID LACTO-BACILLINE. (Rene C., Aged Six Years.)

its preservation and purity being guaranteed. Each tube contains 5 grams of the ferment and will last five days.

The dose of 0.5 grams is taken twice daily fasting or at the end of the principal meals, with a little sweetened water, honey or preserves.

In taking it a tenth part of the tube may be judged, for there is no harm done if the dose should be exceeded.

3d. Lacto bacilline in glutenized globules. Theoretically this is the best manner of administering the ferment.

The glutenized globule passes through the stomach intact,

and the ferment is liberated only when it reaches the intestine, the very part in which its action takes place.

The globules keep almost indefinitely, and thanks to their protective coating are proof against humidity.

Should the ferment undergo no deterioration in their preparation, or suffer alteration by reason of time, these globules of lacto bacilline would be of the greatest value in the treatment of intestinal auto-intoxication.

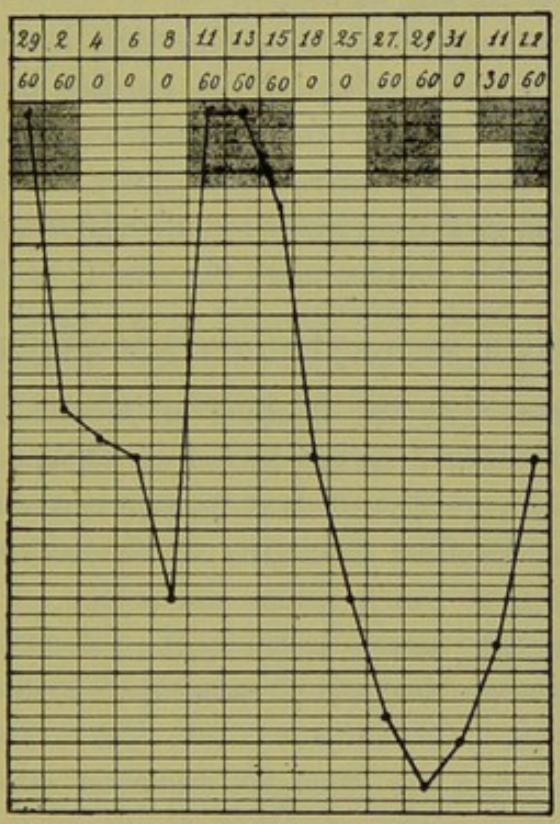

FIG. 12.—CURVES OF INDOL AND PHENOL WHILE USING LIQUID LACTO-BACILLINE. (Alice G——.)

Therapeutic results. The Lacto Bacilline Company of Paris, and the Zyma Company of Montreux having requested us to institute scientific and clinical experiments upon the antiputrefactive action of their products, we have confided this study to two of our pupils who will carry on their work, comparing it with that of two other pupils, who are studying the antiputrefactive action of two other preparations; namely, the selected brewer's yeast from zyma and the selected grape ferment of *Jacquemin* of Nancy.

These studies were begun four months ago and are to cover a period of six; in consequence we cannot yet speak definitely upon the action of these substances, but we shall at some future time.

What we can actually state is that as the two curves (in Figs. 11 and 12) resulting from the studies of our pupil, *Mlle. Tchoumakoff*, demonstrate that **lacto bacilline in a liquid form is a most energetic antiputrefactive agent; its action being prolonged for a long time after ceasing its use.**

This seems to clearly demonstrate that its antiputrefactive action is due to the vitality of the bacillus of *Massol*, which fights energetically against the proteolytic anaerobic microbes. The lacto bacilline in powdered form gives less brilliant results.

The glutenized globules give no results whatever, their preparation having probably compromised the vitality of the lactic bacilli.

THE BIOLACTYL OF FOURNIER

We have seen that the bacillus of *Massol* in pure culture attacks the fats as well as the carbohydrates, so that to confine its action to the carbohydrates only, it is necessary to associate with it another bacillus belonging to the occidental flora, the inhibiting action of which limits the action of the bacillus of *Massol* to what may prove useful to the patient.

For that reason *Metchnikoff* combined with it *the Bacillus acidi lactis.*

That is also what the Biolactyl *Fournier* seeks to do. It is the result of the studies of *Albert Fournier*, formerly demonstrator at the Sorbonne.

Biolactyl is a symbiosis in definite proportions and as constant as possible of the *bacillus of Massol* and another coccus belonging also to the oriental flora. These two organisms are furnished by *Fournier* in pure and particularly rich cultures, so as to present the active elements in a concentrated form.

We have just begun a series of experiments with this product and we shall reserve judgment on the results obtained until some future time when we can form a better opinion.

We may state that at the present time its use has been satisfactory.

The Paralactic Bouillon of Tissier

Tissier, in the paper we have already quoted, apparently desired to limit the use of his paralactic bouillon to certain specific intestinal infections.

But in a more recent paper[1] he has applied his method to combat intestinal putrefaction in general.

Consequently, and in order to be complete, we shall include a synopsis of his work in our general study of the treatment of *intestinal auto-intoxication.*

Tissier recommends in the first place:

1st. **A strict vegetarian regimen**—absolutely similar to ours[2] for the purpose of diminishing the nitrogenous elements in the waste products of digestion, and to increase the proportion of carbohydrates.

2d. **The introduction in the digestive canal of pure cultures of lactic ferments,** so that the flora shall be composed only of *mixed ferments* (acid ferments of the carbohydrates).

To accomplish this, it was necessary to avoid choosing from among the non-pathogenic bacteria, those that form gases, alcohol, indol, phenol, or irritating acids like certain fatty volatile acids.

To obtain this result, *Tissier* made use of pure cultures of the *Bacillus paralactici of Kosaï* and later of a combination of the *Bacillus paralactici* with the *Bacillus acidi bifidus of Tissier.*

The bacillus acidi paralactici described by Kosaï[3] is a facultative anaerobic and is habitually found in milk. It occurs in the form of a small bacillus, sometimes grouped in pairs or as a series of short elements forming little chains. It stains with Gram's, is non motile, does not form spores; and grows at 37°. It is an active ferment of sugars, particularly those giving dextro lactic acid and is non-pathogenic.

The Bacillus Bifidus described by Tissier in his thesis,[4] is a strict anaerobic forming by itself almost all of the intestinal flora of the suckling. It occurs in the form of a diplobacillus some-

[1] Tissier: Tribune med. 1906. p. 117.
[2] See p. 381.
[3] Kosaï: Zeits. f. Hygiene. 1902.
[4] Tissier: Thèse de Paris. 1900.

times bifurcated and is stained by Gram's solution; it is non-motile and does not form spores. It is a very active acid ferment of sugars; and produces inactive lactic acid and acetic acid. Like the bacillus paralactici, it only attacks already hydrated albuminoids.

Finally, like all the anaerobics, it grows in an aerated medium already inoculated with some facultative anaerobic species.

Mode of administration. The cultures are made in peptonated water according to the following formula:

Salt	5.0
Peptone	10.0
Lactose	20.0
Water	1000.0

The culture must be given fresh, for the vitality of the bacilli diminishes after three weeks or a month.

Due to the growth of these bacilli, the culture medium becomes non-putrefactive, for no putrefactive or pathogenic species can develop in it and multiply.

Only certain molds can develop in it and slowly destroy the inhibiting acidity, but this only takes place at the end of several months.

From one to two wine glasses of the paralactic bouillon may be given before breakfast and before lunch—pure or with water sweetened with milk sugar.

Therapeutic results. During the first few days of treatment —as with our lacto farinaceous régime—certain discomforts are noted, gastric disorders, colics, bloating, gases, etc.

"But soon," *Tissier* states, "the constipation ceases, the colics diminish, the breath becomes sweet, the stools lose their fetid odor and on bacteriological examination there is found a reappearance and a progressive increase in the microbes constituting the normal flora. The urine becomes clear and abundant with decrease in the sulphoethers.

The disorders of auto-intoxication, the cardio vascular, nervous, pulmonary and other symptoms next disappear, but more slowly.

"But in order that these good results may persist and become

lasting," *Tissier* adds, "it is necessary to prolong the treatment at least for two and a half months on the average, until the intestinal flora is markedly changed."

It is only at the end of that period that the administration of the cultures may cease, and that a less severe regimen containing a little meat and fish at the principal meals may be permitted.

But the basis of the alimentation must always be constituted by the alimentary pastes, vegetables and fruits.

Cohendy[1], in a very recent work, demonstrates:

1st. That a rational hyponitrogenized regimen is sufficient to obtain the disinfecting action of the lactic bouillon.

2d. That the abstention from meat exacted by *Tissier* is altogether unnecessary.

3d. That the disinfection is apparently not greater with the ingestion of sugars, even in high doses.

4th. That the disinfection is prolonged after the last dose of the lactic ferment for as long a time as the acclimation lasts; that is for at least fifteen days.

We have no personal experience with the paralactic bouillons, but *Tissier* is too good an observer for us to doubt even for a moment, the beautiful results he points out.

At all events, and we speak from experience, the introduction of pure cultures of lactic bacilli in the digestive canal, is an excellent means of rendering it antiseptic and in all the grave and acute forms of auto-intoxication it is an excellent adjuvant to the lacto farinaceous regimen.

[1] Cohendy, C. R.: Soc. de biologie. 1906. p. 633.

C. INTRODUCTION OF MICROBICIDAL YEASTS IN THE INTESTINAL CULTURE BOUILLON

The therapeutic use of brewer's yeast is of ancient date. It has long been known in those countries in which many breweries exist, that the ingestion of beer yeast was an excellent remedy for furunculosis, and its employment was empirically handed down from father to son.

But it was not until 1852 that *Mosse*, an English physician, made the first scientific experiments, and we must come down to the year 1894 before finding a serious exposition of the action of yeasts in a study due to the pen of *Debouzy*. Since then there have appeared each year works of more or less importance on the subject, but which it is impossible to examine here.

Among the most remarkable we shall cite the publications of *de Backer* in France, whose works on ferments are authoritative. From the chemical standpoint we shall cite those of *Buchner* in Germany, and *Manders* in England; from the therapeutic standpoint the works of *Brocq*, *Thiercelin* and *Cheney*, *Pierre Marie* and *Faisans;* from the bacteriological standpoint those of *Nobécourt* in France and *Geret* in Germany; works which elucidate in all its aspects, the question of yeasts and their action.

Classification of Yeasts

The blastomycetes (the group in which the yeasts are classed), and the molds or *hypomycetes* belong as well as the microbes or *schizomycetes* to the lower order of fungi.

The *saccharomyces*—properly called leavens—form a rather numerous group of the order of *blastomycetes*, an order very closely allied by its morphology but particularly by its biology with the schizomycetes or microbes.

This clearly explains both their analogy and antagonism. Among the leavens there are two of more than usual importance, namely:

The *saccharomyces cerevisiæ* or beer yeast.

The *saccharomyces ellipsoideus* or grape yeast. (Fig. 13.)

MORPHOLOGY OF YEASTS

A. Saccharomyces Cerevisiæ or Brewer's Yeast

The saccharomyces cerevisiæ has been particularly studied by *Hansen* of Copenhagen. Under the microscope it presents

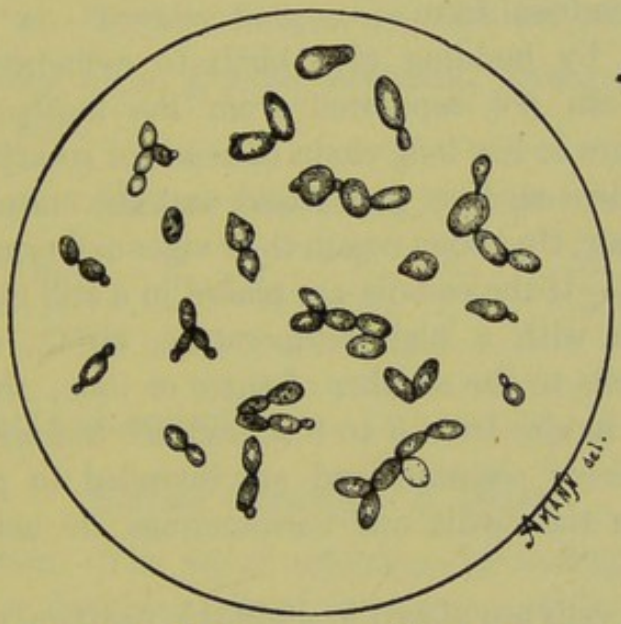

FIG. 13.—SACCHAROMYCES CEREVISIÆ AND SACCHAROMYCES ELLIPSOIDEUS.

different aspects, according to its state of activity and according to the medium in which it was developed.

It occurs in the form of:

Conidia.

Chain of beads or rosaries.

Ascospores.

Conidia. When in its greatest activity, brewer's yeast appears only as round or slightly oval cells attaining from 8 to 9 μ. in their greatest diameter.

These cells absolutely resemble the spores of the higher fungi or *conidia*, hence the name given to them.

The conidia are surrounded by a thin membranous cell wall,

the protoplasm being colorless and homogenous, often showing one or more vacuoles. The cells frequently present little protuberances at either pole; these are the beginning of daughter cells produced by gemmation and soon to become separated from the parent cell to form independent cells.

Conidia constitute the most vigorous and active form of yeast; the one which develops when air sheltered.

It is the only form which should be employed therapeutically.

Chain of beads. When yeast is exposed to the air, the independent round and oval cells are not as numerous. The majority of the cells become much longer in their principal axis and assume a cylindrical form.

They also by budding give birth to cylindrical daughter cells, which are not separated from the mother cells, thus forming a more or less long chain of beads or rosary.

If the nutrient medium is changed and the culture is not exposed to the air, they soon regain their vigor and primitive shape.

Ascospores. If the conidia are placed in a still more unfavorable medium with a high temperature, 30° C., spores form within the cells to the number of three or four; these increase considerably in size from 3 to 6 μ. and are termed ascospores.

They are very resistant and are intended to preserve the species, when the media and surroundings are unfavorable to them.

When such cells are placed in a suitable medium, they rupture owing to the greater increase in size of the enclosed spores; these being liberated, can proceed to form true *conidia*, and like them, propagate by gemmation.

B. "Saccharomyces Ellipsoideus" or Grape Ferment

The saccharomyces ellipsoideus has been specially studied by *Jacquemin* (of Nancy), who differentiated several varieties, a certain number of which correspond to the different vintages of France, and contribute to the formation of the bouquet so characteristic of these wines. The cells are of ellipsoidal shape and their greatest diameter is on an average 6 μ. It is the special ferment of grape juice, so much so that if inoculated in beerwort, it gives to the product a pronounced vinous odor.

Chemical Composition of Yeasts

The chemical composition of the cell wall is that of a mucilaginous cellulose. The protoplasm is of a complex nature.

It is composed as demonstrated by *Zellner*[1] of:

1st. Nitrogenous Substances, 48.4 per 100

Insoluble albumins (leucin, xanthin, tyrosin)	0.12 per cent.
Nucleins and peptones (nucleic acid, lecithin)	45.2 per cent.
Albumoses	1.6 per cent.
Ammonia compounds	1.43 per cent.

2d. Ternary Substances, 11.8 per 100

Fatty bodies, olein, glucose, invertine, glycogen, cholesterin and succinic acid.

3d. Mineral Substances, 13.8 per 100

Phosphoric acid	51.1 per cent.
Potassium	38.6 per cent.
Magnesia	4.1 per cent.
Calcium	1.9 per cent.
Sulphates of soda and silica	4.0 per cent.

Normal Physiology of Yeasts

Reproduction. The yeasts reproduce by budding (or *gemmation*), forming daughter cells at the expense of the mother cells; beginning as simple buds which gradually become detached from the parent cell.

They do not form rosaries or chains of beads and especially ascospores, unless the nutrient medium is unfavorable to their development.

Respiration. Yeast, like all living plants, breathes; but it is facultative, for it may live in contact with oxygen and is then aerobic; and it can also exist without free oxygen; it is then anaerobic. But it does not act in the same manner in both cases.

If it is in contact with air the yeast proliferates by utilizing the oxygen of the air.

[1] Zellner: Zeits. f. Hygiene, XLII, p. 3.

If there is no free oxygen, the yeast attacks the sugar of the nutrient medium in which it finds itself to rob it of the oxygen indispensable to it and in so doing produces a true chemical decomposition of the sugar.

Nutrition. It is seen in the last case that yeast, like all living matter, assimilates, loads itself with the substances it needs and eliminates others noxious to it, but in doing so, it brings about important changes in the sugared medium, and these have received the name of *fermentations*.

The ability of yeast to produce fermentation in sugar containing solutions, is due to the soluble ferments or *enzymes* which it contains and which were discovered by *Buchner* in 1898. This investigator was able to isolate these ferments by crushing and rupturing the cell walls under a pressure of 800 atmospheres. The soluble ferments are found in the filtered water from the crushed cells and they can produce the fermentation of sugar outside of any vital action of the cells.

The saccharolytic enzymes. There are two. One being sucrase (identical with the invertine of *Duclaux*) isolated from brewer's yeast by *Berthelot*.

Its name was changed to sucrase in order that all the ferments of this group should have the same termination in *ase*. Sucrase changes cane sugar into glucose.

The second is *alcoholase* (the zymase of *Buchner*) which splits glucose into alcohol and carbon dioxide, while at the same time its cells take up oxygen and stores of glycogen.

Proteolytic enzyme. Yeast contains besides, a proteolytic enzyme *endotryptase* capable of acting upon the albuminoids or in default upon the yeast itself by digesting its own proper substance through *autolysis*. The soluble ferments of which the ultimate composition remains completely unknown, present common properties; they are soluble in water but they do not form true solutions but only colloidal solutions; that is, a suspension of granules measuring about 1-100,000 millimeter and ultra microscopically visible. These ferments are precipitated from their aqueous solution by alcohol, and are completely destroyed by a temperature exceeding 75° C.

Finally, an important fact is that the quantity of these bodies

is extremely small compared to the mass of the substances which they transform; by that they enter the group of actions termed catalytic.

The term catalytic action introduced into science by *Berzelius*, presents as fundamental character, the considerable disproportion between the catalysor and the mass of the bodies upon which it acts.

What are the conditions upon which the activity of the zymases of yeasts depend?

1st. Influence of the concentration of the body to be transformed upon the rapidity of conversion.

Duclaux has shown that the rapidity is proportional to the concentration.

2d. Influence of the concentration of the ferment. The rapidity of conversion is proportional to the quantity of ferment.

3d. Influence induced by the products of the fermentative reaction. Their concentration retards the reaction proportionally with their accumulation; this may even become sufficiently great to arrest the action of the ferment.

4th. Influence of foreign bodies on the fermentative reaction. *Gromow*[1] shows that all the substances (saccharose, glucose, lactose, glycerin) which favor the action of alcoholase, inhibit that of endotryptase and that on the contrary, all the bodies favorable to tryptase retard the action of alcoholase.

Excretions of yeasts. The excretions vary with the nature of the ferment.

1st. Endotryptase. The end products of the autolytic digestion of yeast have been most carefully studied by *Kutscher*[2].

These products are sensibly the same as those derived from the autolysis of the pancreas. This fact is brought into relief by the two tables at the bottom of the following page.

It is seen from this that the nucleinic acid is destroyed in the autolysis of yeast in the same manner that it is in the pancreas.

II. Sucrase and Alcoholase

One thousand grams of saccharose after undergoing fermentation give 1,036 grams of new products, namely:

[1] Gromow: Zeits. f. Phys., XLII, p. 299.
[2] Kutscher: Zeits. f. phys. Ch. XXXIX, p. 313.

Alcohol	506.15
Carbonic acid	492.95
Glycerin	28.3
Succinic acid	4.5
Other bodies (the higher alcohols, ethers, acetic acid)	4.1

Idransky demonstrated that glycerin is formed at the end of the fermentation, when the cells are nearing exhaustion. He admits that the glycerin is the result of the decomposition of the fatty bodies contained in the yeast.

Buchner[1] shows that besides *succinic acid*, *lactic acid* is also formed by the influence of an antizymase.

The succinic acid occurring under the same conditions, being probably derived from butyric oxidation.

Acetic acid is also found 0.01 to 0.33 per cent. All of these substances, the excretory products of yeasts are toxic to microbes, but also to the yeasts themselves.

For that reason we have long insisted upon the important antiputrefactive action of lactic and succinic acids.

According to *Hueppe* and *Loew*[2], all of the yeast cells do not possess the biological faculty of causing fermentation.

Only a few are active (diplasmatic), but on the other hand, they are capable of decomposing a large quantity of matter in a

Products of the Autolysis of the pancreas by its trypsin:	Products of the Autolysis of yeast by its tryptase:
Guanin (in large quantity)	Guanin (in large quantity)
Adenin	Adenin
Xanthin (a little only)	Xanthin (traces)
Hypoxanthin	Hypoxanthin
Lysin	Lysin
Arginin	Arginin
Histidin	Histidin
Leucin	Leucin
Tyrosin	Tyrosin
Aspartic Acid	Aspartic Acid
Glutamic Acid	Glutamic Acid
Ammonia (a little)	Ammonia (a little)

[1] Buchner: Chem. Ber. XXXVIII, p. 620.
[2] Hueppe & Loew: Centralbl. f. Bakt., IV, p. 792.

short time (a pinch of active yeast sufficing to transform one kilogram of sugar).

In order that they may develop in large numbers, these cells require a particular medium and a special temperature, pressure and aeration.

It is therefore important to know that according to the way it is prepared, yeast differing greatly in action will be obtained.

For instance, by varying the conditions of their culture, a simple proliferation of the cells, or a simple production of alcohol may be obtained, or else both at the same time.

Thus, if the yeast is exposed to a current of air, an abundant cell proliferation will take place; if both a cell proliferation and the production of alcohol are desired at the same time, the medium should be aerated *before* introducing the yeast.

Finally, to obtain active and vigorous yeasts, they must be collected when the fermentation is in full activity, and great care must be taken to do so before the nutrient medium is exhausted of its sugar, albumin and mineral substances; for otherwise only worn out and vigorless yeasts will be found. It is easy to understand that yeast collected under favorable conditions, when it is well oxygenated by the oxygen it has taken from the sugar, when it is replete with stores of glycogen, nitrogenous and mineral substances, when it is filled with zymases; in a word, when it is in full vigor, that under those conditions it will also be able to endure and combat, thanks to its rich reserves, even when placed in surroundings less favorable to its vitality, such as the alimentary canal of man.

Such are the yeasts actually supplied under the name of **active and selected yeast** by the manufactories.

Secretions of yeasts. Do yeasts secrete toxins like microbes? *Jacquemin*[1] appears to admit it, but he furnishes no proof.

Pathological Physiology of Yeasts

Recently the employment of yeasts in diseases of the digestive canal has been greatly advocated, but in an empirical manner and without seeking scientifically, if their use was justified.

Hence before advising their administration in intestinal

[1] Jacquemin: Comm. à l'Acad. des Sciences. Nov. 18, 1902.

auto-intoxication, it is well to carefully consider the two following questions:

1st. What becomes of the yeasts introduced into the digestive tract?

2d. What is their action upon the intestinal microbes and their products?

The first of these two questions was examined by *Nobécourt* in an important paper,[1] from which we borrow largely.

I. Influence of the Intestine upon Yeasts

What becomes of the yeasts introduced in the intestine?

The yeasts are subjected to many influences in their course through the mouth, stomach and intestine. These influences may modify their vitality, inhibit their growth, if it does not cause their death. (*Nobécourt.*)

These influences are:

1st. The temperature of the body.
2d. The digestive juices.
3d. The composition of the media and the absence of oxygen.
4th. The symbiosis with the microbes.

Let us examine each one of these factors.

A first influence comes into play, that of the body temperature much insisted upon by the partisans of grape yeast.

This influence, however, is slight. *Kayser*[2] has shown that yeasts placed in liquid media perished only after fifty minutes, when the liquid was heated to between 50° and 60°. *Blanc*, *Renhorn* and *Moritz* found fermentation still active at 45°, while *Buchner* and *Rapp* demonstrated that its maximum action occurred slightly under the body temperature, 36°. (96.8° F.) The temperature of the body does not therefore exercise the harmful effect which *Jacquemin* (of Nancy) insists upon.

2d. Influence of the digestive juices upon yeasts. Their action is more difficult to establish; it has been the subject of several works, of *Falk*[3], *Simanowsky*[4] and particularly *Neumayer*[5].

[1] Nobécourt: Semaine Méd. 1901. p. 9.
[2] Kayser: Les levures. 1889.
[3] Falk: Arch. f. Physiol. 1882. p. 187.
[4] Simanowsky: Arch. f. Hygiene, IV. 1886. p. 1.
[5] Neumayer: Thèse de Munich. 1890.

Saliva. This has no influence whatever upon yeasts. (*Falk.*)

Gastric juice. Hydrochloric acid in a concentration of 0.5 to 1.5 per cent. favors the action of yeast. Now as the normal acidity of gastric juice does not exceed 2 per 100, it certainly cannot exercise any harmful effect. Without doubt, the gastric juice can, after prolonged contact, diminish the number of yeast cells, but it never prevents the fermentation from taking place, as *Neumayer* and particularly *Beylot*[1] demonstrated by their experiments upon a dog with a gastric fistula.

Moreover, it must not be forgotten that in normal conditions, the gastric juice is diluted by the ingested liquids and that when fasting—the time at which yeast is administered—the gastric acidity is almost nil.

Nor should it be forgotten finally, that part of the yeast rapidly passes into the duodenum.

The harmful action of the stomach is consequently reduced to very little.

Intestinal juices. The reaction of the surrounding medium changes in the intestine and becomes alkaline, but the alkalinity is of no consequence to yeasts, for, according to *Beylot*, 4 per cent. solutions of sodium bicarbonate, the alkalinity of which approximate that of the intestine, have no effect whatever upon the fermentation.

Bile retards fermentation but does not prevent it.

Pancreatic juice has no harmful effect upon yeasts.

The intestinal juices exercise no action whatever upon them.

En résumé, while the alimentary juices may diminish the number of yeast cells, they never prevent fermentation from taking place when in the presence of a 10 per cent. solution of sugar.

3d. Influence of the composition of the intestinal contents upon yeasts.

The digestive juices are not the only factors capable of exercising action upon the yeasts, for the intestine contains also the products and residues of digestion; furthermore there are microbes.

[1] Beylot: Thèse de Bordeaux. 1896.

A. Influence of the Intestinal Surroundings upon Yeasts

The lack of oxygen, which is the rule in the intestine, necessarily exercises a deleterious effect upon yeasts, for in an anaerobic medium, they develop with difficulty and end by dying. In consequence they can only exist in it by borrowing the oxygen they need from the surrounding media. It is therefore necessary for them to find in it a suitable nutrient medium.

The nutrient medium. Yeasts require carbohydrated and nitrogenous matters, also mineral salts.

Among the nitrogenous bodies, egg albumin, casein and fibrin cannot be utilized by the yeasts, but they can assimilate the ammoniacal salts found in the intestine (*Duclaux*). Among the carbohydrates, starch and dextrin cannot be assimilated by yeasts. They can only assimilate directly certain sugars.

Beylot has demonstrated *in vitro* that yeasts destroy the sugar formed by the saccharification of starch, through the action of ptyalin.

Experiments show besides that glucose is likewise destroyed in the digestive canal, through the same influence of yeasts. *Beylot* introduced into the stomach of a rabbit 60 grams of glucose dissolved in water; two hours later the rabbit was glycosuric, but if with the glucose, 10 grams of yeast are introduced at the same time, the glycosuria does not occur.

Beylot noted the same result with dogs.

Thus, brewer's yeast diminishes alimentary glycosuria and the proportion of the urinary sugar is in inverse ratio to the quantity of yeast absorbed.

B. Influence of the digestive products upon yeasts. This is a difficult study, which is far from being completed at present date; and it is the more difficult because these products augment considerably in the pathological conditions for which yeasts are indicated. All that is known is that yeasts appear less active after a sojourn in hydrogen (*Dumas*); that carbon dioxide inhibits fermentation and that formic, acetic, propionic, butyric acids, in proportions of from 0.2 per 100 to 1 per 100 arrest it.

Lactic acid even in the proportion of 2 per cent. has no harmful effect upon yeast.

It must be added, however, that these experiments *in vitro* prove very little and in no manner demonstrate the real and complex influence of the digestive products.

In summary, it can be said that in any case yeasts may survive in the digestive canal and like many other authors we have always found them in the stools of the patients to whom they had been administered.

4th. Influence upon the yeasts of their association with microbes. The action of microbes upon yeasts has not been completely studied.

Nevertheless, the experiments of *Nobécourt*[1], *d'Arsonval* and *Charrin*[2] appear to show that while the *streptococcus* and the *bacillus coli* do not in any way inhibit the fermentation caused by the *saccharomyces cerevisiæ;* that, on the contrary, the *Proteus* and the *pyocyanic bacillus* appear to prevent it completely.

But in no case is the vitality of the yeasts diminished by their contact with bacteria.

But here again it is well to make some reservations on these experiments made *in vitro*, for without other experiments, they cannot be applied to what takes place in the human organism.

En résumé, **the yeasts can live in the alimentary canal of man with a suitable nutrition ; they can destroy in it the sugar substances by causing them to ferment with the production of carbonic dioxide and alcohol.**

But their life is limited and under normal conditions the fermentations cannot exceed a certain degree.

II. Influence of Yeasts upon the Intestine

What is the action of yeasts upon the intestinal contents? The yeasts reaching the intestine may exercise their action upon:

1st. The digestive juices.
2d. Upon the alimentary matters and digestive residues.
3d. Upon the microbes.
4th. Upon their secretory products: the toxins.
5th. Upon the peristaltic movements of the intestine.
6th. Upon the defenses of the intestinal mucosa.

[1] Nobécourt: C. R. Soc. biol. 1900.
[2] D'Arsonval & Charrin: C. R. Soc. biol. 1893.

1st. Action of yeasts upon the digestive juices. This has been greatly discussed.

While *Simanowsky* states that yeasts disturb gastric digestion, *Neumayer* and after him, *Haan*[1], experimenting with high and low yeast or baker's yeast, showed that the unfavorable action of yeasts upon gastric digestion is almost nil if any, but that in reality they did not favor it.

The same contradictory statements exist, from the standpoint of their action upon the different intestinal juices.

2d. Action of yeasts upon the intestinal contents. We have already mentioned their influence upon the sugars when speaking of the yeasts and alimentation.

The simultaneous ingestion of yeasts and a solution of sugar prevents alimentary glycosuria (*Beylot*); on the other hand, it is possible by prescribing yeast to permit a carbohydrated diet to diabetics without increasing the glycosuria. (*Nobécourt.*)

3d. Action of yeasts upon microbes. The *bacillus coli*, the *streptococcus*, *Proteus* and *pyocyaneus* inoculated in yeast cultures from two to six days old develop badly or not at all. (*Nobécourt.*) These experiments were followed up by *Quincke*[2] and by *Landau*, 1889; they employed fresh yeasts.

Albert[3] and later *Geret*[4] continued these experiments using *dry and sterilized yeasts*.

Dry yeast is a brewer's yeast killed, dehydrated and sterilized with alcohol and ether. The sterilization only causes a destruction of the germinative power of the yeast, *while preserving intact the power* of fermentation due to its zymase as well as the proteolytic and reducing properties belonging to the proteolytic enzymes which it contains.

Albert succeeded in showing that yeast possessed an evident bactericidal action, but without being able to specify whether this action was due to the products of fermentation by its zymase, alcohol and carbon dioxide or whether it was due to the action of its proteolytic enzyme.

Buchner and *Geret* sought through numerous experiments

[1] Haan: C. R. Soc. biol. 1896.
[2] Quincke: Congr. f. inn. Med. 1898.
[3] Albert: Centralbl. f. Gyn. 1901. p. 17.
[4] Géret: Münch. med. Woch. 1901. p. 1836.

carried on at the Institute of Hygiene in Munich, to determine this action and they were able to demonstrate **that the bactericidal action was not due to the proteolytic enzymes but to the fermentation products of the yeasts.**

Here are their conclusions:

1st. The bactericidal action only occurs when the yeast is active, when it contains zymase and produces active fermentation.

2d. The action requires the presence of a solution containing sugar.

The products of yeast fermentation are: lactic acid, succinic acid in slight quantities (0.4 to 0.7 per 100), glycerin, but particularly alcohol and carbonic dioxide.

Géret then, pursuing his researches upon the *Bacillus acidi lacti aerogenes*, the *bacterium coli* and the *staphylococcus* was able to confirm the bactericidal power of dry brewer's yeast upon these bacteria, and he demonstrated that this action must be attributed in the **first place to the alcohol** *in nascent state* **next to the progressive acidification of the intestinal contents, which destroys the proteolytic microbes.**

Abraham[1], *Ledermann* and *Klopstock*[2], *Strauss* and *Hessman*[3] confirmed these results.

We may therefore conclude that in the first place it is through their excretory products that the yeasts combat the microbes. Hence it happens quite naturally that in the struggle of the yeast against the microbes, the most vigorous, those having the greatest vital activity will be the ones to conquer.

And this was demonstrated by *d'Arsonval* and *Charrin*.

The *bacilli pyocyaneus* introduced with the presence of brewer's yeast in a bouillon to which was added a sugar solution, arrested the alcoholic fermentation when the temperature was 37°. This being a temperature unfavorable to yeast but favorable to the *pyocyanus*.

Whereas the fermentation is not hindered if the temperature is 10°, one favorable to yeast. These experiments show how

[1] Abraham: Monats. f. Geburtsh. u. Gynæk., XVI.
[2] Ledermann & Klopstock: IV, Naturf. Versamml. zu Karlsbad.
[3] Strauss & Hessmann: Senator's Festschrift, p. 167.

vigorous and active yeasts may in cases of dilated hypochlorydric stomachs, arrest the lactic, butyric and acetic fermentations so common to them.

Summary. Yeasts exercise a primary microbicidal action, thanks to their excretory products which are alcohol, lactic and succinic acids "in a nascent state."

Do the yeasts exercise a secondary microbicidal action through the toxins they secrete as *Jacquemin* maintains? Of this there is no actual proof.

Are the yeasts endowed like the white cells with phagocytic power with respect to the microbes?

In other words, can the yeast cells incorporate and digest the microbes by themselves?

Yeast cells, as we have seen, are from their beginning, surrounded and enclosed by a more or less thick cell wall of cellulose, which limits the movements of the enclosed protoplasm. There can therefore be no question for them of amœboid movements, these being a property of the phagocytic white cells, the protoplasm of which being extremely motile and deprived of enveloping membrane, seize and absorb the microbes they come in contact with.

Hence the yeasts are not active phagocytes. But many authors nevertheless admit that if the microbes should penetrate the yeast cells these would be capable of destroying and digesting them.

Yeasts would then be endowed with a passive phagocytic power.

This passive phagocytic power was discovered accidentally by *Brechat* (of Paris) in the following manner:

Some wine of figs had been sent to this chemist to be examined and to determine the character of the ferment; one of the bottles was accidentally opened during the voyage and arrived in full state of fermentation.

On examination it was found to contain as the other bottles did, the *saccharomyces Pastorianus*, but in addition, large numbers of the *Bacilli aceti*.

A large number of the *Bacilli aceti* were enclosed within the yeast cells; some were intact, but most of them were reduced, destroyed and partly digested, and they did not stain at all or

else badly. The yeast cell can therefore act like a phagocyte with respect to microbes; with this difference, that it can only do so when the microbe penetrates it itself, for the yeast cell has not the power of absorbing it *per se*. **Yeast is consequently a passive phagocyte.**

This accidental discovery gave rise to extended studies, followed up by *Backer* and *Brechat* in France, *Manders* in England, and which showed that it was not merely a question of accidental discovery, but of a general property developed in the active yeast cells, when in the presence of microbes and in a common medium.

This passive phagocytic power, moreover, is not restricted to the saccharomycetes, but is also found in the hyphomycetes.

These experiments demonstrated that when the yeasts are in full activity, they are capable *in vitro*, provided the nutrient medium is favorable to them, of absolutely preventing microbic fermentations whether they be acid: acetic, lactic, butyric fermentations or putrid, like nitrogenous putrefaction.

But for this, two conditions are essential; the greatest degree of activity of the yeasts (we shall see further on how this may be obtained), and the chemical nature of the nutrient media, conditions we shall take up later.

The first experiments in the struggle of yeasts against the microbes were made with the *saccharomyces cerevisiæ* and *Pastorianus*.

Jacquemin, of Nancy, completed them by his investigations of the *saccharomyces ellipsoideus;* he succeeded in demonstrating that the quality of wine depended in great part upon the struggle between the yeasts and microbes.

Grapes, when harvested, not only give shelter to yeasts but to various microbes deposited on them through the air and by flies falling in the must.

In consequence, the natural fermentation is subject to many risks and diseases, which are chiefly due to the predominance of the microbes over the yeasts.

Per contra, if the natural yeasts are in full vigor even if the wine is already under the influence of the *Bacillus aceti*, by adding a small quantity of pure, selected, cultivated and exalted

yeast, the evolution of the pathogenic fermentation will be arrested and the disorder will be immediately stopped.

All these experiments led these authors to examine the phagocytic influence of yeasts upon other bacteria and they were able to demonstrate that the action was exercised, not only upon a large number of saprophytic organisms (*Bacillus aceti, Bacillus termo*, etc.), but also upon a large number of pathogenic bacteria (coli, streptococci, staphylococci) and even upon specific pathogenic microbes (*baccillus of Loeffler, bacillus of Koch*).

Experiments upon animals. Besides the experiments *in vitro* these investigators made a large number of experiments, first on animals, next on man, by employing subcutaneous and intravenous injections of pure and sterilized yeasts.

In the first place they were able to show the innocuity of this method of treatment, and next, that the yeasts entering the circulation were capable of existing in it and even of exercising a microbicidal action upon the microbes contained in the cavities of the body (nose, throat, intestine, vagina), and even in the internal organs (lungs, glands). In cases of tuberculosis treated by subcutaneous and intravenous injections, *Manders*[1] states, having found the same phagocytic power and to have recognized[1] in the sputum of his patients, yeast cells which contained tubercular bacilli in evident state of digestion.

While these last facts do not appear to have been confirmed up to now, **the passive microbicidal and phagocytic action of yeasts is beyond question.**

We may conclude from these experiments that when microbes and active yeast cells find themselves in a common medium, there results an antagonism between these two species of fungi.

Yeast possesses the same chemico-toxic power over the microbes that the latter themselves exercise toward the leucocytes.

The bacteria attack the yeast cells and penetrate their protoplasm; there the two adversaries strive against each other, by means of their respective proteolytic enzymes; these as we

[1] Manders: La thérapeutique par les levures, p. 178.

know, have been isolated from both the yeast cells and the microbes.

In the majority of cases, as the results of experiments show, the enzymes of active yeast cells being more vigorous usually carry off the victory and the bacilli gradually disappear, completely digested.

Meanwhile, the yeast continues to produce its alcoholic fermentation, thanks to its zymases, and the production of alcohol and succinic acid certainly contribute in part toward paralyzing the defense of the microbes.

But if the quantitative and qualitative superiority of the yeast cells does not exist, if the media do not permit them to form the alcohol and succinic acid which contribute to their victory, the microbes will carry off the day and the microbic fermentations and putrefactions, temporarily arrested, will again resume their course.

4th. Action of yeasts upon toxins. Do the yeasts exercise any action upon the toxins secreted by the microbes?

Hallin[1], in a very interesting work, has studied the action of yeasts *in vitro* upon diphtheria toxins; the activity of which he found was diminished considerably. These experiments were again taken up and extended by *Nobécourt*, the same results being obtained. It is therefore permissible to conclude that this weakening action extends also to the toxins of intestinal microbes, although we have no absolute proof at present.

It seems that the attenuating action of the yeast upon the toxins is due to the progressive acidification of the surroundings and we know that by their activity the yeasts maintain a continuous acidity of the intestinal contents (*Nobécourt*).

5th. Action of yeasts upon intestinal peristalsis. A certain number of authors, *Strauss* and *Hessmann* among others[2], have demonstrated the stimulating action of yeasts upon the peristaltic movements of the intestine.

This explains the diarrhea which often accompanies their use in the beginning of treatment; it also explains their favorable action in intestinal stasis and constipation.

[1] Hallin: Soc. biol. 1899.
[2] Strauss & Hessmann: Loc. cit., p. 187.

This stimulant action upon intestinal peristalsis likewise explains in part its beneficial action in intestinal auto-intoxication.

6th. Action of yeasts upon leucocytosis. Yeast—and that is not the least of its properties—when ingested or injected into the organism, increases the number of polynuclear leucocytes in the blood. These are the phagocytes of *Metchnikoff*. It is very probably owing to the nuclein which the yeasts contain in great abundance, that the increase in the number of leucocytes is due and the stimulation of their phagocytic function as well, thereby constituting a veritable defense of the organism against the microbes.

The term nucleins is applied to the albuminoid substances characterized by their abundance in organic phosphorus, the leucocytes and their nuclei being principally constituted by them; they are also abundantly found in the thymus, spermine, etc.

The active principle of nuclein is nucleinic acid ($C^{40}\,H^{54}\,N^{14}\,Ph^{4}\,O^{27}$). It is the organic body richest in organic phosphorus.

It is known that organic phosphorus, when used internally, is much superior to the phosphates because it is not recovered in the stools; it is superior to the glycerophosphates, because it is not found in the urine; superior to the lecithins, because in its decomposition, it does not give rise to toxic products. (*Cholin*).

Thanks to this substance, yeast augments the number of the leucocytes and stimulates their phagocytic function; for we know from the experiments of *Faucher* and *Barbier*, that the leucocytes receive from the nucleinic acid the dynamic energy necessary for the phagocytic struggle.

This leucocytosis, this stimulation of the organic defenses by the yeasts, is another possible and plausible explanation of their action on microbes, on those of the digestive canal in particular.

Summary. The yeasts are microbicidal ; they attenuate the toxins, augment the number of phagocytes and favor intestinal peristalsis. Qualities which must render them useful and valuable in exaggerated intestinal putrefactions, and consequently in digestive auto-intoxication.

DISADVANTAGES OF YEASTS

Yeasts, as we have seen, require some fermentable substance in the intestine in order to act.

The simultaneous presence of these two substances in the intestine may lead to some disadvantages.

Strauss[1] observed some morbid symptoms following the drinking of fresh beer still in a fermenting state (diarrhea, vomiting, transient coma) and attributable to the continuation of the fermentation in the digestive canal.

Intestinal irritation, even gastroenteritis, have been mentioned as caused by yeast. *Lesage* found yeasts fifty-three times in 473 cases of infantile enteritis. This is a first possible disadvantage; a second is due to the chemical composition of yeast.

The extracts of brewer's yeast contain, as *Micko, Zellner* and others affirm, xanthic bases in considerable amount; hence they may prove dangerous to arthritics, for these bodies greatly increase the formation and excretion of uric acid. This hypothesis was examined by *Laqueur* (under the direction of *Professor Brieger*), by means of very conclusive analyses, bearing upon the food, the urine and stools of the persons examined.

Before the administration of yeast	Urine	Nitrogen	10.3
		Phosphoric acid	2.6
		Uric acid	0.47
	Fæces	Nitrogen	1.2
		Phosphoric acid	1.2
After the administration of yeast	Urine	Nitrogen	10.3
		Phosphoric acid	3.0
		Uric acid	0.89
	Fæces	Nitrogen	1.3
		Phosphoric acid	2.2

This shows that brewer's yeast (like the thymus, pancreas, etc.)[2], more than doubles the excretion of uric acid.

The proportion of uric acid increases parallelly with the quantity of yeast, and the augmentation lasts a few days after

[1] Strauss: Arch. f. path. Anat. XXX, p. 601.
[2] Laqueur: Zeits. f. kl. Med. XXXIX, p. 5.

ceasing its use. Hence, we may conclude that the prolonged use of yeast is absolutely contraindicated in arthritism.

Pharmacology of Yeasts

What yeast should we employ? The choice may lie between the two principal forms:

1. Brewer's yeast.
2. The yeast of grapes.

A. Brewer's Yeast

Commercially, brewer's yeast is supplied, fresh or dry or in the form of an extract termed *levurine*.

Fresh Yeasts

Brewer's yeast. Its appearance is that of a creamy substance with a *café au lait* color and emitting a slight odor recalling that of beer.

The commercial yeast is a rather complex mixture, which is never formed of pure yeasts as *Jörgensen* of Copenhagen showed[1].

Microbes occur in it, oftentimes several species of yeasts and the yeast cells frequently contain bacteria.

This impure yeast varies greatly according to the brewery and it is often different in the brews of the same brewery; consequently its effects are variable.

Moreover, it does not keep and must be thrown aside as soon as it becomes slightly sour. During the heated term, it is necessary for it to be fresh and renewed daily, which is impossible in many localities.

Baker's yeast. This is more easily obtained and is supplied in the form of small cubes or homogenous pastes of a grayish white color when fresh, and having a characteristic odor; it easily dissolves in water to which it gives a milky aspect.

Dry Yeasts

The yeast is first selected, and when all but the *saccharomyces cerevisiæ* have been excluded, it is cultivated at 25° C. in a sugared nutrient medium, containing also the nitrogenous and

[1] Jörgensen: Traité des micro-organismes de la fermentation. Paris. 1905.

mineral elements (yeast ashes) indispensable to its growth, and for the development of its full activity.

When it has reached its greatest development—always identical in yeasts—it is rapidly desiccated.

This dry and sterile yeast retains all its peptic enzymes and zymases as may be established by dissolving it in the following mixture:

Water, 60 grams = 4 tablespoonfuls.

Yeast, 6 grams = 2 teaspoonfuls.

Sugar, 4 grams = ½ lump.

Albert of Berlin was the first chemist in Germany to prepare a dry, sterile, but active yeast. There are actually three brands that have acquired a certain reputation. The Wuk, Ovos and Siris, the analyses of which were made by *Zellner*[1].

Humidity	25.8 per cent.
Dry residue	74.1 per cent.
Nitrogenous elements	48.4 per cent.
Non-nitrogenous elements	11.8 per cent.
Mineral elements	13.8 per cent.
Phosphoric acid	6.1 per cent.

In *France*, several preparations are used; the *Debouzy yeast* being one of the best known.

In Switzerland, *Pury*, the chemist, prepares *furunculine*, a dry, sterile, and active brewer's yeast, in the form of unchangeable white powder having the odor of yeast and a taste recalling that of cheese. The name of *furunculine*—which is badly chosen since it specializes the action of the preparation for one condition only—is derived from the disease in which yeast was first used.

For the *gastrointestinal* affections, *Prury* prepares a special yeast termed *zymaline* or bicarbonated yeast, 10 per cent.

Levurine

Levurine extract obtained by *Couturieux* and presented to the Academy of Medicine by *Lancereaux*, is a dried yeast juice, possessing all the therapeutic properties of the type of yeast from which it is extracted.

[1] Zellner: Zeits. f. Hygiene, Bd., XLII, p. 3.

It is a powder of a chestnut color, having the odor of peptone of slightly bitter taste, recalling that of beer and hops and is soluble in water.

Levurine is equivalent to thirty-five times its weight of fresh yeast and six times its weight of dry yeast. It contains all the soluble elements of the yeast protoplasm; the *zymase of Buchner, sucrase, maltase, various diastases,* peptones, albumoses and glycogens.

It is administered in the form of compressed tablets (0.20 grams each), of which *from two to eight may be given daily,* before or after meals.

The best known levurines are those of *Coirre* and *Couturieux.*

Mode of Administering Brewer's Yeast

1st. Subcutaneous and intravenous injections. *Doyen* and *de Backer* in France, and *Manders* in England, prepare sterile yeast in little containers, which, by means of a special syringe, permit the making of sterile subcutaneous injections.

Such injections are, of course, not required in intestinal auto-intoxication.

2d. Local applications. Applications of dry pulverized yeast have been employed in torpid, varicose and cancerous ulcers, with very satisfactory results.

The ulcer is carefully cleaned once daily and is sprinkled with the powder, or else it may be dusted over a *warm* compress or poultice.

Insufflations in the nose and throat have also been used in nasal and pharyngeal diphtheria.

Injections. This method of using, limited to genito urinary diseases, was proposed by *Landau* for simple and gonorrheal vaginitis. Yeast diluted to a syrupy consistence in either water or sweetened water is employed. The results appear to be satisfactory.

Clysters. Used as disinfectants in cancer of the rectum; yeast clysters were also proposed by *Thiercelin* for cases of infantile gastroenteritis.

Dose for a child, a teaspoonful of dry yeast in 60 grams of boiled water is used.

For an adult a tablespoonful in 150 grams of boiled water. Clysters to be repeated two or three times daily.

3d. Internal use. This is the most habitual method of use, in the digestive auto-intoxications. The yeast may be given mixed with a liquid, plain, alkaline or sweetened water, else with beer or honey; it may be given in cachets, but always with sweetened water.

The ordinary dose. For children, a half teaspoonful, two or three times daily a short time before meals.

For adults. A teaspoonful two or three times daily shortly before meals.

Therapeutic Use of Brewer's Yeast in Digestive Auto-intoxication

Cutaneous Manifestations of Auto-intoxication

It is in the cutaneous manifestations of the intestinal affections that the yeasts have given the best results, as is shown by the studies of *Brocq* in Paris, *Lassar* in Berlin, *Presta* and *Tarnella* in Italy, *Oltramare* in Geneva.

Acne, even *acne rosacea*, and *staphylococcus folliculites*, have been very favorably influenced by the ingestion of yeast.

In furunculosis, its curative action is manifest, but not as constantly as in acne (according to our experience at least). Its action is most satisfactory in some cases, but nil in others, and this without any assignable reason.

It is known that in the north of France, beer yeast is a popular remedy for furunculosis, and its admission in medical practice was advocated by *Mosse* (1852) and particularly by *Debouzy*, 1894[1].

Since then it has been used everywhere, but especially by *de Backer* (in 1895) and by *Brocq*[2], who employed yeast in his own case and that of his patients with the most complete success.

Du Bois[3] says, under the influence of treatment, there is perceived an arrest in the evolution of the furuncles in process of formation; the aborted furuncle does not reach the period of suppuration; it resolves and disappears in a few days.

[1] Mosse & Debouzy: Journ. méd. prat. 1894. p. 176.
[2] Brocq: Présse. méd. 1899. p. 8.
[3] Du Bois: Rev. méd. Suisse. Rom. 1901. p. 13.

In the older furuncles already in full evolution, there is a decrease in the necrotic process and in the suppuration, and at the same time an almost complete disappearance of pain and swelling. Consequently, owing to the influence of yeast, there is an evident attenuation of virulence.

The yeast exercises first a preventive action upon the formation of furuncles, this being very generally and constantly so; it next, although not as constantly, exercises an action on the furuncles in evolution; finally, but much more rarely, upon the adult and developed furuncles by diminishing the inflammation and limiting the necrosis.

The pruriginous affections are very favorably influenced by yeasts.

Urticaria. The very favorable effects of yeast, first upon the pruritus, next upon the eruption, is a good demonstration of its disinfecting action upon the stomach and intestine. We have also obtained very good results in the prurigo and strophulus of children.

Finally, *Du Bois*, in *cases of acute and chronic eczemas*, has seen the rapid disappearance of the pruritus, under its favorable influence, the tendency of the eczema to get well, was likewise much greater than in those who did not take yeast.

Gastrointestinal Affections

Stomach. Brewer's yeast has been used with success in all gastric dilatations with exaggerated fermentations, **but only in those not accompanied by motor insufficiency and prolonged retention.**

In such cases our opinion is that thioform and menthol are the most useful therapeutic means we can employ.

It is necessary in this condition, to give yeast when fasting and between meals, to diminish the quantity of sugar with the meals and to abstain from using sweetened solutions with the yeast.

Du Bois (already quoted) mentions the case of a woman with dilated stomach, who, after following several regimens without benefit, was able after a few week's use of yeast, to eat and digest aliments of which she had been deprived for years.

The only contraindication to yeasts is gastric ptosis associated with motor insufficiency; in such cases the yeast remains too long in the stomach and produces secondary fermentations that are very uncomfortable to the patient.

Small intestine. It is to *Thiercelin* and *Cheney* that we owe the first studies on this question. *Blancher* has embodied the results of their observations in his thesis.

Acute intestinal catarrh. These authors administered yeast in *acute infantile intestinal catarrh*, both internally and through clysters, giving one to two teaspoonfuls of yeast by mouth and from one to three clysters daily, each containing a teaspoonful of yeast.

Most of the little patients had been treated with lactic acid and liquid diet, but without results. Under the influence of yeasts these authors saw the temperature fall and the green stools become modified.

Our own experience in the affections of the small intestine is not as favorable, for having tried the use of yeast in these conditions, we have given it up completely. A liquid diet, calomel and lavage of the stomach and intestine appear to us to give very much better results.

Chronic catarrh. In the chronic catarrh of the small intestine, specially in the constipated periods, the results seem to us very much more favorable and combined with a suitable diet the yeasts give good results, **but much inferior to those obtained by the use of the Bulgarian yoghourt and the lactic bouillons.**

In our opinion, the indication for the use of yeast in the treatment, exists more particularly in the fermentations of the non-nitrogenous elements (fats and carbohydrates), which take place in the small intestine.

Large Intestine

In glairy and membranous enteritis, the results do not appear very convincing to us.

Is the albuminous putrefaction which takes place in the large intestine, specially diminished by yeast?

Without doubt, the constipation is ameliorated in many cases, but not in all by any means.

The question is not yet solved; the results published by different authors varying greatly, according to the cases.

Strauss and *Hessmann*[1] found variable results; *Roziczkowski*[2] likewise.

In a case of gastric carcinoma in which slight melanœmia frequently occurred (demonstrated by the aloin test), *Strauss* found:

	Urine	Indican
Before treatment with yeast	1000	98mg.
	1200	100mg.
	910	224mg.
After administering yeast 4 times daily in doses of ½ teaspoonful	980	112mg.
	1400	102mg.
	1390	140mg.
	1600	75mg.
	1800	143mg.
	1380	153mg.

It is seen that the quantity of urine increases, but with the exception of one day the indican also increased; hence we must consider the result absolutely negative.

This case, we admit, is not conclusive because the putrefaction itself was very variable each day, owing to the varying quantity of blood undergoing decomposition. The question requires further study.

At the request of the **Zyma Company of Montreux:**

We have confided to one of our pupils (*Czernikowski*) the task of studying the influence which pure and selected brewer's yeast exercises upon the nitrogenous putrefaction in the intestine.

We have made use of the bicarbonated yeast in all our experiments.

The investigations are not yet finished, but as the curves in figures 14 and 15 demonstrate:

Brewer's yeast in large doses is an energetic antiputrefactive medicine, but contrarily to that of the lactic bacilli, its action is very transient.

As a matter of fact, we find that the curves of indol and phenol rise immediately on ceasing the use of yeast, *and they even go higher than before its administration*, as if yeast favored the absorption of the aromatic bodies.

[1] Hessmann: Senator's Festschrift, pp. 27 and 167.
[2] Roziczkowski: Med. klin. Berlin. 1900.

B. Grape Yeast

Wine ferment may be given to patients in the form of:

1st. Grape ferment.

2d. Grape cure.

Grape Ferment

Jacquemin, of Nancy, is of the opinion that the failure of treatment by brewer's yeast is due:

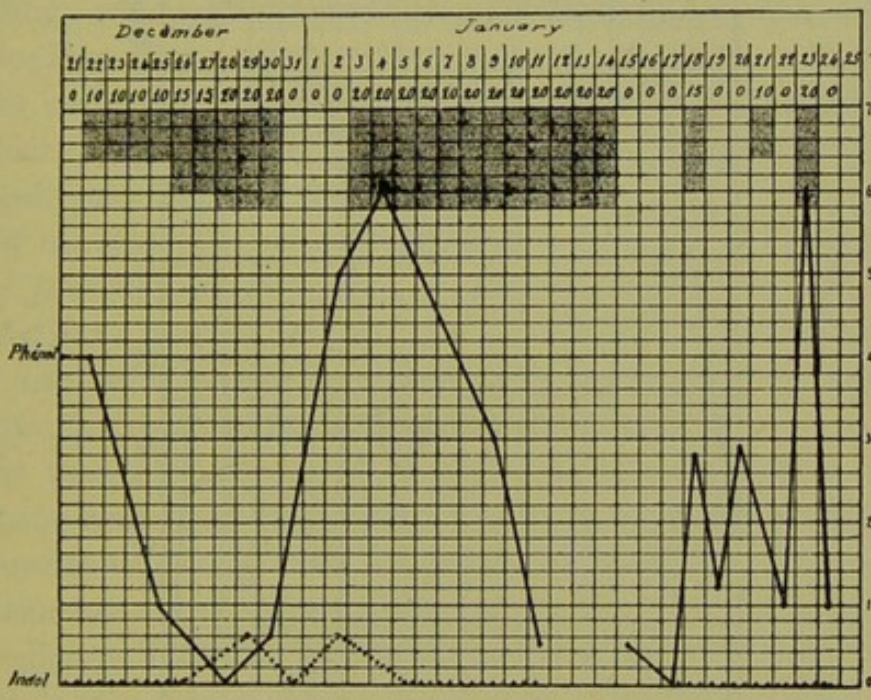

FIG. 14.—CURVES OF INDOL AND PHENOL WHILE USING BREWERS' YEAST. The Days During which the Yeast was Taken and the Doses Given are Represented by the Shaded Portions of the Chart.

1st. To the fact that it is not always pure and selected and solely composed of *saccharomyces cerevisiæ*.

2d. That the yeast is not always collected at the time of its greatest activity.

3d. That brewer's yeast is a ferment which develops in an almost neutral culture medium (beer wort), and at a generally low temperature; that on reaching the stomach, it encounters an acid reaction, a high temperature and unfavorable surroundings; hence it cannot act or only badly and incompletely.

It cannot therefore develop its microbicidal and antitoxic action as it should.

For all of these reasons, *Professor Jacquemin* has thought that the **ferment of grapes** might be substituted with advantage for brewer's yeast, and that a much more intense and constant result would be obtained by choosing the *saccharomyces ellipsoideus*, originating from the grapes of warm countries and accustomed to exist in temperatures averaging 37°.

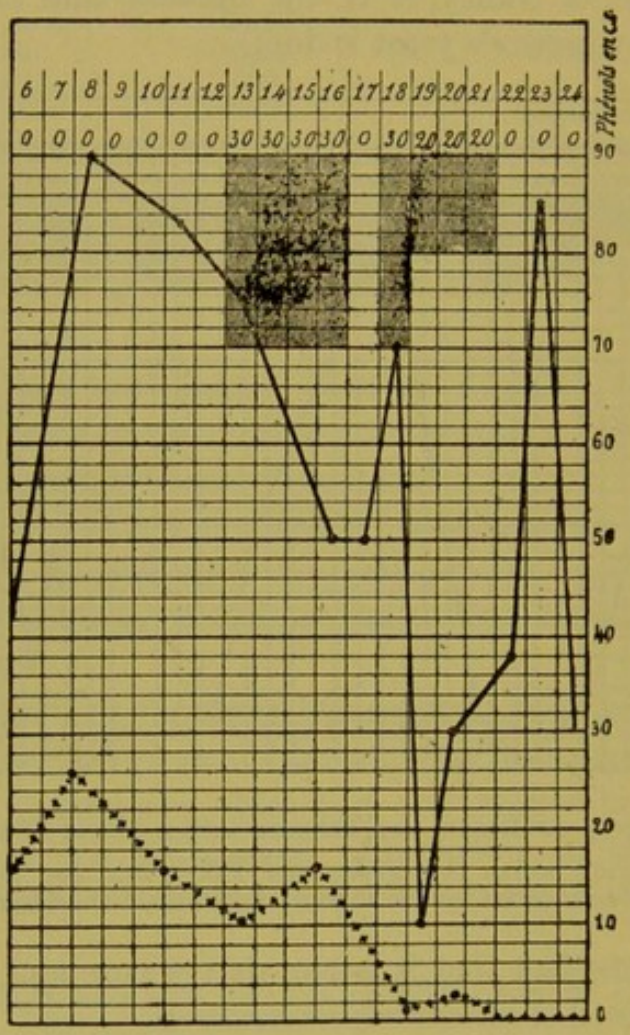

Fig. 15.—Curves of Indol and Phenol while Using Brewers' Yeast.

In the second place, instead of cultivating it in neutral media, *Jacquemin* gradually acclimates it to a rather high acidity, so that when it reaches the stomach it is already accustomed to act in an acid medium like the gastric juice.

Finally, by not desiccating it like brewer's yeast, the grape ferment may be left in its culture medium, thus retaining all the nutritive elements necessary to its evolution. As a last pre-

caution, *Jacquemin* advises taking the 25 c.c. of grape ferment in a wineglass of *water sweetened with a half lump of sugar*.

The grape ferment is prepared in such manner that it is absolutely pure and free of microbes or foreign elements.

We can readily understand that a grape ferment prepared with all these precautions, taken in the form of a culture in full evolution with sweetened water and eminently fermentable, should continue to live in the stomach and its cells keep on budding; while at the same time exercising its microbicidal and antitoxic action.

But unfortunately the active ferment has only an ephemeral existence, at the end of two or three weeks the number of cells diminish and become very restricted.

The microscopic examinations of several vials of *Jacquemin's grape ferment* procured from several pharmacies in *Lausanne* showed how sparse the cells had become and how little action they displayed, for they were incapable of causing the fermentation of the experimental sugar solution.

The reason of its complete failure in the treatment of our patients was thus explained. Consequently, when *Professor Jacquemin* requested that we should undertake some scientific experiments on the antiputrefactive action of his ferment, we immediately accepted and confided the task to a fourth pupil, *M. Mola*, as a study intended to form the subject of his inaugural dissertation.

The vials received at our clinic were two in number; one was the large vial which we knew to be very poor in *saccharomyces ellipsoideus;* the other a small vial containing 25 c.c. and filled with active ferment.

The instructions accompanying them directed that the larger vial should be inoculated with the contents of the smaller, according to an indicated method and that the culture should be left at an average temperature for three days.

The microscopic examination of the contents of the larger vial, made at the indicated time, showed that it contained a pure and extremely rich culture of *saccharomyces ellipsoideus* in full activity.

This process of preparing grape ferment is therefore the only

one to make use of in practice. It is the only sure means of always having an active ferment, and the only one to be recommended.

Mode of using. The pure ferment made from grapes grown in warm countries is very agreeable to take; it has the odor of must and the taste of new wine, and is of a slightly yellowish and cloudy appearance.

Before using, the bottle should be shaken so as to intimately mix the liquid with the sediment, as this contains most of the ferment and this should be done the more energetically as the bottle nears the end.

Remove the stopper and quickly pour out a *small liquor glassful* (15 grams or tablespoonful), care being taken to replace the stopper at once.

The ferment is mixed with 60 grams (four tablespoonfuls) of water sweetened with a half lump of sugar.

This small quantity of sugar is very useful to increase the efficacy of the ferment but would be harmful if the amount were increased.

Dose of the ferment. Our experiments have shown that the doses recommended by *Jacquemin* are insufficient and that to produce an effect on intestinal putrefaction, it is necessary to take from 60 to 80 grams daily (4 to 6 tablespoonfuls). For children, a tablespoonful twice daily will be enough, for adults the dose may be doubled or tripled whenever a more rapid effect is desired.

Finally, the dose may be added to some sweetened water in a small bottle and carried until time to take it, if it should be inconvenient to return home for that purpose.

The ferment cure may be carried out at any time of the year, or at any place, which is not the case with the ordinary grape cure.

2d. Grape Cure

The grape cure, the good effects of which are much better understood than heretofore, is founded on good reasons, for it is much more agreeable than the ferment cure; it necessitates a change of air, a change in the more or less faulty hygienic habits of the patient as well as cessation from work.

Moreover, it has a certain importance from the alimentary standpoint, as the following analysis proves:

Chemical Composition of Grapes

Water	78.17 per cent.
Albumin	0.59 per cent.
Glucose	14.36 per cent.
Free acids (malic and tartaric)	0.50 to 1.40 per cent.

Finally there is a considerable quantity of ferments, *saccharomyces* the *ellipsoideus* specially, and the *Pastorianus* in small proportions.

The grape cure has therefore a certain alimentary value to which is added its antiputrefactive action on the intestine and its diuretic and laxative actions; both of which are not to be neglected in the cure of digestive auto-intoxication.

The grape cure lasts from three to six weeks.

The ferment cure has the great advantage over the grape cure, in that it is possible to carry it out at home, and at seasons when fresh grapes are not to be had.

Therapeutic Indications for the Use of Grape Ferments and the Grape Cure

The indications are the same as for brewer's yeast.

1st. **Cutaneous manifestations of auto-intoxication:** furunculosis, common acne and acne rosacea, folliculitis; the pruriginous affections, strophulus, prurigo, urticaria, certain pruriginous eczemas of intestinal origin, as the eczematous impetigo of children.

2d. **Gastrointestinal affections.** Stomach. Many dyspeptics with dilatation and anorexia are benefited; the bloating, eructations, and sometimes the gastralgias are favorably influenced by grape ferments.

Intestinal stasis and atonic constipation are generally ameliorated.

Nitrogenous intestinal putrefaction. As with brewer's yeast the results published by different authors vary greatly.

As before mentioned, we have confided to one of our pupils, *Mr. Mola*, the task of studying the action of grape ferment upon

intestinal putrefaction, by the examination of the curves of indol and phenol.

The study is not yet completed but the curves in figure 16 show:

1st. That grape ferment like brewer's yeast has a most energetic antiputrefactive action.

2d. That to obtain an antiputrefactive action, large doses of grape ferments (60 to 80 c.c. per day) are necessary.

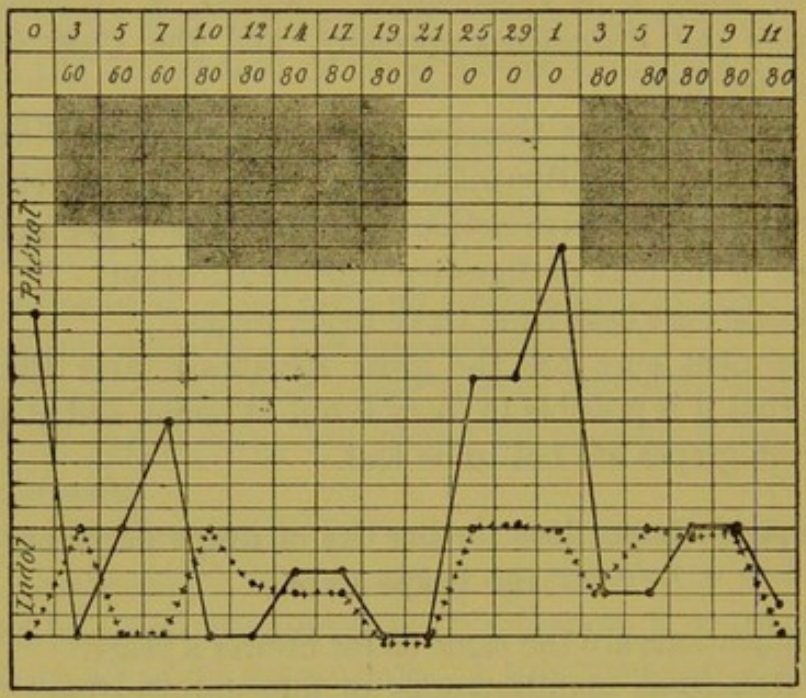

Fig. 16.—Curves of Indol and Phenol while Using Grape Ferment.

3d. That like brewer's yeast, the action of grape ferment is very transient.

For on the day following the cessation of the ferment, the putrefaction starts anew and with greater energy, which would seem to show that the action of the yeasts was more specially due to their zymases than to their bactericidal action. Lastly, it has been possible to note in some other curves that when the use of grape ferment is interrupted, the curves *ascend above normal* for several days as observed with brewer's yeast.

C. Tropical Ferments

When all the yeasts are studied experimentally (brewer's yeast, grape yeast of local grapes or from those grown in warm

latitudes), it is observed that at a certain temperature their functional vitality decreases; at 30° their activity is already lessened but only slightly. This functional debility is accentuated according to the temperature, but it is well to add that at the temperature of the human body it is not marked.

It is only in febrile conditions when the temperature rises to 39° (102.20 F.), 40° (104 F.), even 41° C. (105.80 F.), that the activity of the yeasts really suffers, and it is only then that an

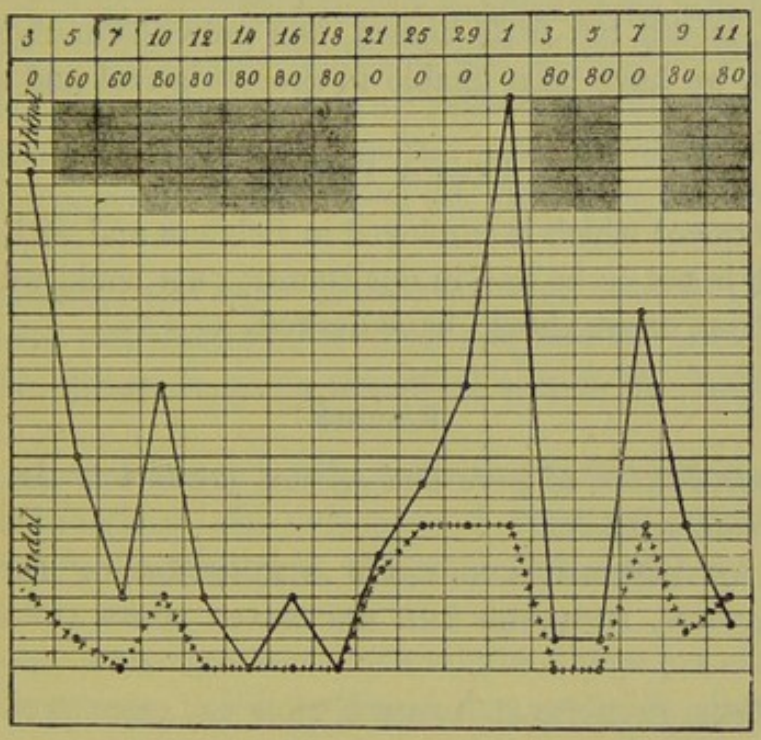

FIG. 17.—CURVES OF INDOL AND PHENOL WHILE USING GRAPE FERMENT.

uncertain and inconstant action is noted. It is for these theoretical reasons that an attempt has been made to substitute for the ordinary yeasts, those derived from tropical countries and accustomed to live, multiply and secrete their zymases in temperatures ordinarily higher.

Jacquemin had already taken one step, by making his ferment from grapes grown in warm latitudes, but without completely fulfilling the desired result. Since then, two other products have been introduced commercially.

One being the ferment of **Phenix dactylifera ;** the other the ferment of bananas.

Ferment of Phenix Dactylifera

This ferment of hot countries, also called *medicinal ferment*, was discovered by a chemist, *L. Van den Hoff*, in a plant of tropical Africa, the *Phenix dactylifera*.

It resists a temperature of 40° to 42° C, retains in it all its fermenting faculties intact, and accomplishes all the physiological actions performed by yeasts at lower temperatures.

This *medicinal ferment*, which is prepared and employed in Belgium, is still but little known, and notwithstanding all our attempts, we have been unable to procure a real and scientific analysis.

Banana Ferment

This ferment which is employed in Belgium and with success, it is said, is not to be had in our country, nor could we procure any for trial, as we should have desired.

Résumé

The introduction of pure and selected yeasts into the digestive canal of man produces:

1st. An evident and rapid diminution of intestinal putrefaction, provided the necessary doses are administered.

2d. This intestinal disinfection is absolutely transient and only lasts during the administration of the yeast.

3d. Disinfection by yeast appears therefore to be indicated only in acute and transient intestinal auto-intoxication.

II. TO DIMINISH THE VITALITY OF THE PROTEOLYTIC MICROBES BY MEANS OF DISINFECTING MEDICAMENTS

The lacto farinaceous regimen by modifying the intestinal culture bouillon, exercises a remarkable antiputrefactive action; for by causing the penetration into all parts of the intestine even the most remote of lactic and succinic acids in *nascent state;* it produces a paralyzing effect upon the vitality of the proteolytic bacilli.

But although the lacto farinaceous diet notably diminishes nitrogenous putrefactions, it does not abolish them, and it cannot be spoken of as an intestinal asepsis produced by the regimen.

As a matter of fact the antiputrefactive action is not complete.

The sulphoethers—the evidences of intestinal putrefaction—are markedly diminished in the urine but they have not disappeared.

Moreover, if the curves of the aromatic bodies are established by daily analyses, it will be found that under the influence of the regimen, the curves descend and approach normal, sometimes going even below. But soon, most usually after ten days, whether because the microbes have become accustomed to their new habitat or for some other reason, the curves will be observed to slowly rise again as if the poisons were accumulating.

If matters are allowed to go on, the appetite will first diminish, the borders of the tongue will become red, the breath will have a strong odor, the intestinal spasms, which had diminished, will again become accentuated; the constipation is again stubborn and the patient complains of headache specially in the evening; he has slight chilly sensations and the temperature rises to 37.8 or 37.9 (100.–100.2° F.). If we do not intervene, the organism is finally compelled to eliminate the intestinal poisons

itself, or else destroy them by some acute crisis, which may be a simple fever or an intestinal seizure (vomiting, diarrhea), or a cutaneous manifestation (pruriginous eruptions with or without fever) or a nervous crisis (migraines meningism, etc.).

After the crisis has subsided, the curves of the aromatic substances descend to near normal. Here is therefore presented a clinical fact which appears to us beyond question that in spite of a well-directed antiputrefactive regimen, the intestinal poisons gradually accumulate and that it is their accumulation which determines the crisis or acute outbreak.

The crisis has for effect the ridding of the organism of the excess of enterotoxins. The appreciation of this fact has a great clinical and therapeutic importance.

For according to the patient, and according to the regimen the accumulation will be more or less rapid; it can be easily foreseen by dosing three or four times weekly, the aromatic bodies contained in the total twenty-four hour urine.

The crises can therefore be foreseen clinically, and therapeutic intervention may prevent them. To accomplish this we dispose of two means:

1st. By abstaining from meat.

2d. By intestinal disinfection.

When the case is serious, the discomfort very great, when the crises recur frequently recourse may be had to both means at the same time.

1st. Low Diet

In all serious cases of intestinal auto-intoxication, the patient must abstain from meat and eggs.

The diet must be (according to case) vegetarian, lacto farinaceous, or purely farinaceous, for a period of one or two weeks or longer.

If the diet must remain purely farinaceous for a long time, add to it either purée of potatoes, whortleberry juice, or lemon juice, so as to avoid Barlow's disease.

2d. Intestinal Disinfection

Of course the word disinfection must not be taken in its bacteriological sense, for so understood, the disinfection of the

intestine and its contents is physiologically impossible. All authors or nearly all, are unanimous in recognizing this fact.

In France, following a report of *Bardet*[1], a warm discussion arose upon the question of intestinal antisepsis, most of the authors denying the possibility of antisepsis of the digestive canal. In Germany the very conclusive experiments of *Fürbringer*[2] had settled the question long ago. The administration of massive doses of intestinal antiseptics scarcely diminished the number of microbes, and the minimum which he observed was always so considerable that he was unable to draw any conclusions as to the disinfecting action in the bacteriological sense.

It can then be supposed that disinfection of the intestine by means of the intestinal antiseptics is impossible.

While admitting the impossibility of disinfecting the intestine with medicines, **we can nevertheless exercise an important antimicrobic action by temporarily diminishing the intestinal microbes and paralyzing their virulence.**

Consequently it is possible to exercise a certain degree of disinfecting action upon the intestine (*Fürbringer*, *Strauss*) by means of medications.

We shall examine the subject first from the theoretical standpoint, next from the clinical:

1st. Disinfecting medicines.

2d. Intestinal disinfection.

Disinfecting Medicines

We shall not stop to examine all of the therapeutic substances utilized as disinfectants of the stomach and intestine, nor to discuss their value.

We shall only speak of those which appear to us to be the best, and to have given the most satisfactory results.

In order to realize intestinal disinfection, recourse may be had to two kinds of medication, both of which we more often combine.

(*a*) *The antiseptic medicines*, which introduce antiseptic substances into the intestine, for the purpose of destroying and

[1] Bardet: C. R. de la Soc. ther. 1895.
[2] Fürbringer: Deuts. med. Woch. 1887. p. 11.

arresting the development of the intestinal microbes, or at least rendering them less harmful.

(*b*) *Evacuating medicines*, those like purgatives, intended for the expulsion of the germs contained in the intestine.

A. Antiseptic Medicines

We shall divide the antiseptic medicines into:

1st. Gastric antiseptics.

2d. Intestinal antiseptics.

I. Gastric Antiseptics

We have seen the great influence that gastric fermentations exercise upon nitrogenous putrefaction.

The gastric antiseptics must therefore be discussed and we shall subdivide them into:

1st. The specific antiseptics: hydrochloric or muriatic acid.

2d. Occasional antiseptics, menthol, thioform and ichthyol.

Hydrochloric Acid

It has long been known that the free hydrochloric acid of the stomach exercises an antiseptic action upon the processes of gastric fermentation. But it is only lately that the question has arisen as to whether it did not also have an antiseptic action upon the intestine.

The question having been discussed before the therapeutic society of Paris[1], *Bardet* declared that the antiseptic action of hydrochloric acid upon the intestine could not be counted on, because it became neutralized and saturated by the alkaline intestinal juices.

It is always well in medicine to refrain from making dogmatic statements, which only carefully made experiments can sustain; else they fall of themselves. *Kast*[2] was the first who sought to solve this question. He found that by neutralizing the acid with sodium bicarbonate, or carbonate of lime the proportion of sulphoethers increased considerably.

Stadelmann[3] arrived at the same result.

[1] Bardet: C. R. de la Soc. therap. Dec. 28, 1892.
[2] Kast: Festschrift. Hamburg. 1889.
[3] Stadelmann: Diss. Stuttgard. 1880.

Wasbutzki[1], in his investigations on hypochlorhydria, constantly found a very notable increase in the sulphoethers.

Biernacki[2], in making comparative analyses of gastric juice and urine, was able to demonstrate that there is found parallelly with the diminution of hydrochloric acid in the stomach, an increase in the urinary sulphoethers.

He finally noted—an important fact from the therapeutic standpoint—that the administration of hydrochloric acid, proportionally diminished the quantity of sulphoethers.

Cahn has proved that by taking away all the salt from the alimentation, the elimination of chlorine is not only diminished in the food but in all the secretions as well, notably in the gastric juice and that hypochlorization is a means as simple as it is easy of diminishing the gastric hydrochloric acid.

Mester[3] has shown that an alimentation deprived of salt, augments the proportion of sulphoethers, which diminish rapidly when salt is again added to the food.

Schmitz[4] found in a case of intense auto-intoxication:

	Sulphoethers
Before administration of Hydrochloric Acid	0.597
With gtt x of 1-14 solution Hydrochloric Acid 3 times daily	0.293

We can therefore conclude that the administration of dilute muriatic acid diminishes nitrogenous putrefaction by nearly one half in doses of from gtt xl to 1 per day.

Menthol

Macdonald[5] declares that a one per cent. solution of menthol is as powerful an antiseptic as corrosive sublimate in 1 to 500.

Freund[6] recommends menthol as an excellent stomach and intestinal antiseptic.

Strauss declares it to be the best antiseptic of the stomach.

Riegner[7], in his experiments upon gastric fermentations, states

[1] Wasbutzki: Arch. f. exper. Pathol., XXVI.
[2] Biernacki: Deuts. Arch. f. kl. Med. XLIX, p. 12.
[3] Mester: Diss. Breslau. 1893.
[4] Schmitz: Zeits. f. phys. Ch. XIX, p. 401.
[5] Macdonald: Edinb. Journ., LXXX.
[6] Freund: Wien. kl. Woch., XCIV, p. 3.
[7] Riegner: Deuts. Med. Woch. 1898. p. 391.

that menthol in alcoholic solution in the strength of 0.50 to 1.0 per 100 arrests all fermentations.

The infusion of peppermint is much less antiseptic.

The antiseptic action of menthol is even manifested in the intestine as shown by *Rovighi*[1]:

		Sulphoethers
Man	Before taking menthol	0.189
	2 grams menthol daily	0.064

Consequently, we can conclude that **menthol in small** doses (0.15 to 0.20 gm.) and the essence of peppermint in strong doses are excellent stomach antiseptics, and that menthol in large doses exercises an antiputrefactive action upon the intestine itself.

Thioform and Ichthyol

Besides the yeasts of which we have already spoken, let us mention two medicines, which render great service in the abnormal fermentations of the stomach, *thioform* (0.50 gm. two or three times daily) and *ichthyol* (0.10 to 0.20 gm.) in pills two or three times daily.

2d. Intestinal Antiseptics

It was at the Congress of Copenhagen in 1884, that *Bouchard* laid down for the first time the rules to be followed in the choice of intestinal antiseptics.

They must be but slightly soluble so that they may not be decomposed and absorbed in the stomach and in the upper portions of the intestine and that they may arrive to the parts in which the putrefaction takes place, that is, in the most inferior portions of the small intestine, and in the large intestine.

They must be reduced to an impalpable powder, so that they may become intimately mixed with the fecal matters.

They must be given in fractional doses, for otherwise, a single dose follows the digestive current and nine-tenths of the intestinal tract are deprived of it when it reaches the intestinal extremity; by giving the quantity in from two to four doses daily, the contact is more prolonged and the action more marked.

The intestinal antiseptics may be divided into:

[1] Rovighi: Zeits. f. phys. Ch. XVII, p. 33.

1st. Specific antiseptic: Calomel.

2d. Occasional antiseptics: Salacetol and Ichthoform.

1st. Calomel

Morax[1] was the first to make scientific experiments with this substance, both in man and animals.

	Sulphoethers
1st day before taking calomel	0.163
2d day with 0.15 gm. calomel	0.150
3d day with 0.15 gm. calomel	0.030

Wassilieff[2] found that artificial digestion was in no manner disturbed by calomel, but that the microbic putrefaction was completely arrested.

He concluded, from his experiments, that calomel prevents the development of microbes in the digestive liquids and diminished the vitality of those already developed, without for that, modifying the digestive secretions.

It is consequently at the same time an aseptic and antiseptic medicine. In fact, calomel stools contain leucin, tyrosin, but no indol.

Hoppe-Seyler[3] has demonstrated that the green color of calomel stools is due to the bile. Normally, biliverdin is transformed by the microbes into hydrobilirubin from which is derived the brown coloration of normal stools.

Owing to the calomel, the paralyzed bacteria allow the biliverdin to pass out unchanged. This is also due to the exaggerated intestinal peristalsis.

Lavarsky[4] showed that in an alkaline medium, calomel is transformed into an oxide of mercury; this occurs in infinitesimal proportions, but sufficient to produce an antiseptic effect.

Bartoschewitsch[5] has made a great number of experiments with calomel which he considers the best of all antiseptics.

		Sulphoethers
In man	Before using calomel	0.551
	Before using calomel	0.601
	With 0.50 calomel	0.548
	With 0.50 calomel	0.131
		0.108

[1] Morax: Zeits. f. phys. Ch. X, p. 318.
[2] Wassilieff: Jeshenedielnaja. klin. gaz. 1882. No. 12.
[3] Hoppe-Seyler: Zeits. f. phys. Ch. X, p. 130.
[4] Lavarsky: Owliani Kalomala Wratsch. 1887. No. 16.
[5] Bartoschewitsch: Zeits. f. phys. Ch. XVII, p. 46.

		Sulphoethers
In man	Before using calomel	0.154
	With 0.50 calomel	0.121
	With 0.50 calomel	0.150
		0.104
Average in 7 cases	Before using calomel	0.282
	With 0.50 calomel	0.134

We can therefore conclude that calomel is an excellent intestinal antiseptic and that it greatly diminishes intestinal putrefaction, more so than any other antiseptic.

2d. Secondary Antiseptics

These may be divided into four classes, according to whether they have a creosote or salycilic acid base or a naphthol and ichthyol base.

1. Creosotated antiseptic medicines.
2. Salycilated antiseptic medicines.
3. Naphtholated antiseptic medicines.
4. Ichthyolated antiseptic medicines.

A. Creosotated Antiseptics

Beechwood creosote is an excellent antiseptic as *Morax* has shown, but it is somewhat irritating, even in oily solution. Nevertheless, we have had very good results from it in serious and persistent intestinal auto-intoxication, but only when the intestine was not inflamed, and by giving *creosote and cod liver oil* (1 in 100) in doses of from half to full teaspoonfuls twice daily for a period of ten or fifteen days according to the case.

B. Salycilated Antiseptics

A long series of antiseptic medicines are derived from *salycilic acid*. This salt according to *Kuhne*[1] arrests fermentations in the dose of 0.035 per 1,000, but it is irritating to the stomach and rapidly diminishes the appetite.

The salycilate of soda in the proportion of 10 per 1,000 might be considered an excellent antiseptic, but being rapidly absorbed, it cannot serve to disinfect the large intestine.

Salol (*phenol salycilate*).

Betol (*naphthol salycilate*).

[1] Kuhne: Deuts. med. Woch. 1892. p. 50.

Eucalyptol (*salycilic acid with essence of eucalyptus.*)

These three may be administered as intestinal disinfectants in doses of 1 to 2 grams daily or else divided into fractional doses, 0.15 to 0.25 gm. every two hours.

We have, however, completely given up their use in intestinal auto-intoxication, for these medicines have one disadvantage; they contain or else produce bodies that are irritating to the intestinal mucosa and they are slightly toxic in children. In consequence, we give preference to the following three substances:

Salacetol (*acetol salycilate*). This is a valuable medicine, occurring in the form of an insoluble powder which decomposes in the intestine into salycilic acid and acetol.

It is less irritating than the other salycilated salts and is non toxic even in doses of 2 to 3 grams daily.

Its antiseptic action is real and most useful, but not to be compared with that of calomel.

In the Child

	Indol	Phenol
1st day before using salacetol	0.035	0.030
2d day with 0.50 gm. salacetol	0.030	0.025
3d day with 0.50 gm. salacetol	0.020	0.025
4th day with 0.50 gm. salacetol	0.010	0.020
5th day with 0.50 gm. salacetol	0.015	0.005

This example, taken from hundreds of similar ones, demonstrates the very favorable influence exercised by salacetol in intestinal auto-intoxication. The comparisons between the proportions of indol and phenol may be looked upon as a true measure of the influence of salacetol, for *Baumann* has shown that salycilic acid has no influence whatever upon the production of the aromatic bodies.

Salacetol may therefore be regarded as an excellent intestinal antiseptic.

It may be administered with the meals and does not necessitate an absolute diet as calomel does.

It is neither constipating nor laxative.

We usually give it at 10:00 A.M., and 4:00 P.M. in the dose of

0.50 to 1 gram, or else it may be taken with the dinner and at 10:00 P.M.; it is advisable to avoid the use of meat at dinner for the salacetol interferes with its digestion.

Bismuth salycilate, praised by *Vulpian*, is less active than salacetol; it decomposes in the intestine into salycilic acid and bismuth oxide.

As a result of the experiments of *Riegner*[1], this salt may be considered as an excellent intestinal disinfectant.

Legendre, on the contrary, considers it but slightly antiseptic.

It is particularly indicated in the diarrheal form of intestinal auto-intoxication—a rare form as we have seen—in doses of 0.50 gm. two to four times daily.

Magnesia salycilate is used in constipated cases, and in the same doses.

C. Naphtholated Antiseptics

Bouchard greatly praised the action of beta Naphthol, given three times daily in doses of 0.50 gm. each.

He proved that by means of this substance, odorless stools and less toxic urines could be obtained.

It does not produce any vesical or cutaneous disorders, which naphthalin—a substance that notably diminishes the sulpho-ethers—frequently does.

The great disadvantage of naphthol is that it is irritating to the stomach, that it provokes heat in the epigastrium and eructations.

Hayem even accuses it of exhausting the secretion of hydrochloric acid.

At the present time, it is very little used.

Benzonaphthol

Benzonaphthol occurs as a white powder nearly insoluble in water; it passes through the stomach without change and splits in the intestine into benzoic acid and naphthol. Theoretically, it should be an ideal antiseptic, for the naphthol disinfects the intestine and the benzoic acid the kidneys. According to *Gilbert* and *Legendre*, it has the advantage over beta Naphthol, of not

[1] Riegner: Deuts. Med. Woch. 1898. p. 391.

irritating the gastric mucosa and of not interfering with the composition of the gastric juice.

Gilbert and *Galbrun* have studied the antiseptic power of benzonaphthol by counting the number of microbes in the fæces.

Under the influence of 3 to 4 grams daily, they found the number of microbes per milligram of fæces fall from 47.212 to 28.280, later to 13.485, which represents a decrease of 55 per cent. on an average. *Ewald* recommends it, although attributing to it, colics and diarrheas which rapidly disappeared when its use was stopped. *Riegner*, in his experiments (already cited), does not credit it with any antiseptic value and many authors look upon it as a deodorizer rather than a microbicide.

Unfortunately as *Baumann*[1] has demonstrated, the benzoic acid increases the sulphoethers and the naphthol does likewise; hence use cannot be made of the dosage of the sulphoethers to determine its antiseptic power.

Although still greatly employed in France, it is now scarcely used, if at all, in Germany and Switzerland in the treatment of intestinal auto-intoxication.

Our experience is not favorable to its use, and we have never seen any good effects from it.

We have therefore completely abandoned it, making use of salacetol or ichthoform instead.

Benzonaphthol is given in the dose of 0.50 gm. five to ten times daily.

D. Ichthyolated Antiseptics

Ichthyol is obtained from the distillation of bituminous rocks found at Creefeld in the Tyrol.

Innumerable remains of fossil fish are found in the strata of these bituminous rocks, the conclusion being that the oil extracted from them is derived from these remains, hence the name ichthyol. The formula given by *Baumann* and *Schotten* $C^{28}\,H^{36}\,S\,(SO^2\,OH^2)$ shows that its content in sulphur is considerable.

The disinfecting action of ichthyol, is probably due to this element, which exists in it in an unstable form and may thus act with considerable energy in its *nascent state*.

[1] Baumann: Zeits. f. phys. Ch. III, p. 45.

It is solely in the form of ichthyolated salts (of soda, ammonium and lithium) that the crude oil is employed.

They constitute salts of ichthyosulphuric acid.

Ichthyol or *ammonium ichthyosulphate* is most commonly employed for intestinal antisepsis.

It is a syrupy, brownish red liquid which in the form of an aqueous solution is particularly used for intestinal lavage. *To a liter of water add* 5 *to* 15 *grams of a* 1 *per cent. solution of ichthyol.*

As our valued friend, *Professor Bourget*, has demonstrated it is a valuable antiseptic owing to the sulphur liberated, to which is added a most energetic vaso constrictor action.

It therefore exercises a local depletive action on the inflamed intestinal mucosa and a sedative one on the pain.

Unfortunately it is rapidly irritating in children, who can only bear it in very slight doses. Internally we prescribe it combined with *thioform* (bismuth dithio salycilate), a closely related sulphur compound, in the dose of 0.10 grams in pills or capsules, and with great advantage in the abnormal fermentations of the stomach.

Ichthalbin. This is a combination of ichthyol and albumin, occurring as a grayish brown powder, tasteless, odorless and containing 40 per cent. of ichthyosulphuric acid.

Owing to the fact that it is insoluble in acid media, it passes through the stomach unaltered and unabsorbed, and is very well borne. It is slowly and gradually decomposed in the alkaline fluids of the intestine into albumin and nascent ichthyol, and it can develop both its disinfecting and vaso-constrictor effects in the lower intestinal portions.

Rolly, under the direction of *Vierodt*, studied its action more closely and he found:

	Sulphoethers		Sulphoethers
Before ichthalbin.....	0.347	Before ichthalbin.....	0.163
With 3.0 gm. ichthalbin..	0.168	With 3.0 gm. ichthalbin..	0.168
With 3.0 gm. ichthalbin..	0.096	With 3.0 gm. ichthalbin..	0.095
With 3.0 gm. ichthalbin..	0.079	With 3.0 gm. ichthalbin..	0.050

This shows that the sulphoethers decrease rapidly to one-third and one-fourth of the usual amounts, but the medication must be kept up for a long time.

It is administered in the dose of 0.30 grams to 0.50 grams for

a child, and 0.50 grams to 1 gram for adults, three times daily.

Ichthargan. This is a combination of silver and ichthyol, containing 30 per cent. silver and is used for intestinal lavage in the strength of 0.20 grams to 0.50 grams per cent.

We have no personal experience with it.

Ichthoform. This is produced by the action of formaldehyde upon ichthyol; it is a brownish-black powder, with scarcely any odor, tasteless and insoluble. It is a powerful antiseptic as the important labors of *Aufrecht* and our colleagues, *Rabow* and *Galli-Valerio*[1] and *Schefer*[2] have demonstrated.

Their results have been particularly interesting in intestinal affections. After its use, *Galli-Valerio* and more specially *Polacco*[3], found in the stools a great diminution in the colonies of bacilli coli and that their development was slower and delayed; the symptoms showed a decrease in the temperature and of the intestinal fermentations, while indol disappeared from the urine.

Polacco, in febrile cases, frequently adds ichthyolated baths to the treatment; 50 to 60 grams of ichthyol to each bath at 35° C. With the exception of acute cases of enteritis in which ichthoform appears to always irritate the mucosa and favor the spasms and colics; this preparation has always given us excellent results in intestinal auto-intoxication.

It is given to children in the dose of 0.50 grams three times daily and to adults in 1 gram doses three times daily.

Résumé

Whenever a prolonged disinfection of the digestive tract is necessary, and

When the stomach is the primary cause, *we can employ with advantage, hydrochloric acid, menthol or thioform, according to the case.*

When the intestine is the primary cause, *salacetol, ichthoform or cod liver oil with creosote, according to indications.*

[1] Rabow & Galli-Valerio: Ther. Monatsch. 1900. p. 125.
[2] Schefer: Deuts. Med. Woch. 1900. p. 12.
[3] Polacco: Wien Med. Presse. 1901. p. 24.

If a rapid and energetic disinfection of all the digestive tract is indicated, *calomel should be used.*

B. Evacuating Medicines

The evacuants most frequently used in intestinal auto-intoxication are:

1. Castor oil.
2. The saline purgatives.

Castor Oil

It is again *Morax*, who took up the question[1] of scientifically determining the influence of castor oil upon intestinal auto-intoxication; his results are as follows:

	Sulphoethers
1st day before using castor oil	0.200
2d day with 15 grams castor oil	0.380
3d day with 15 grams castor oil	0.340

Bartoschewitsch[2] continued the experiments and found as follows:

	Sulphoethers
Before using castor oil	0.243
Before using castor oil	0.235
With 15 grams castor oil	0.258
Before using castor oil	0.258
With 15 grams castor oil	0.452
With none	0.120

From this, it appears that the observations of *Morax* and *Bartoschewitsch* both show that *the administration of castor oil increases the phenomena of auto-intoxication.*

This is a general fact applying to all purgatives, as shown by the researches of *Rovighi* on the saline cathartics, and our own personal experiments with castor oil and calomel.

They are constant results as may be seen by examining the curves in figure 18.

And we always observe them after *liquid disinfections* (*i.e.*, administration of calomel 0.20 grams in the evening followed by 15 grams of castor oil on the following morning).

[1] Morax: Zeits. f. phys. Ch. X, p. 318
[2] Bartoschewitsch: Zeits. f. phys Ch. XVII, p. 46

Saline Purgatives

Rovighi[1] examined the influence of saline purgatives upon intestinal auto-intoxication. These are the results:

	Sulphoethers
Before using Marienbad water	0.264
With Marienbad water	0.272
With Marienbad water	0.138
Before using Carlsbad water	0.193
With Carlsbad water	0.286
With Carlsbad water	0.210
With Carlsbad water	0.163

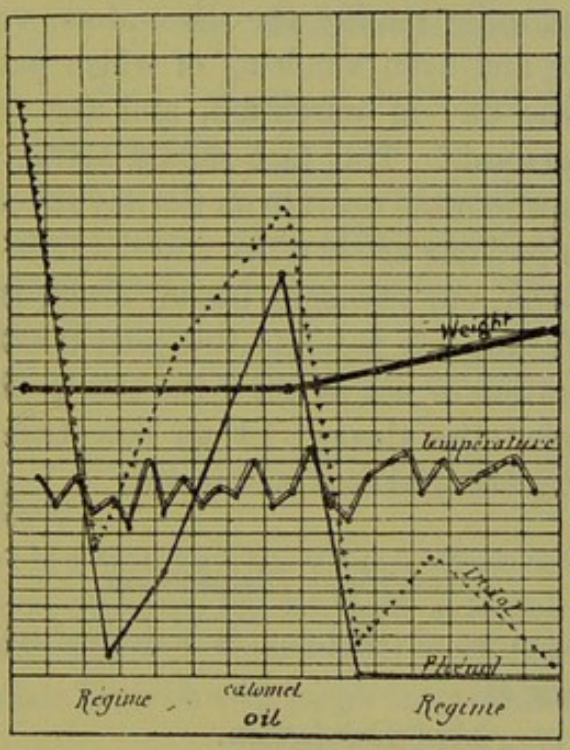

FIG. 18.—CURVES OF PHENOL AND INDOL WITH CATHARTIC DISINFECTIONS.

Gilbert and *Dominici* arrived at similar findings by counting the microbes:

1st day	before using soda sulphate	67,000
2d day	with 15 grams soda sulphate with 15 grams magnesia sulphate	272,000
3d day	none	55,000
4th day	none	1,350

Catharsis therefore brings about a considerable liberation of germs. Their number diminishes on the following day, but it is not until a day later that the action of the purgative becomes

[1] Rovighi: Zeits. f. phys. Ch. XVII, p. 33.

manifest, and that there is found a very marked decrease in the quantity of microbes, which lasts for several days at least.

From all these facts, easily verified, we can conclude that all purgatives (oils or salines) for a short time greatly increase the auto-intoxication by stirring up the intestinal matters, displacing materials adhering to the intestine and setting free the contained microbes. If, however, the examination of the sulphoethers is continued from the following day, their quantity will be seen to diminish considerably, for several days afterwards and then slowly rise again.

This explains quite readily the discomfort, vertigo, nausea, loss of appetite and even vomiting of which patients so often complain on the day of purgation, and the well-being they experience afterwards. This fact should attract the attention of the surgeons who often operate on the day following catharsis, at a time when patients are in a bad state of resistance.

For that reason, our excellent friend, *Roux*, has been in the habit of disinfecting his patients (by cathartics), several days before the operation or not at all, if the case is urgent.

Having studied the theory, let us now take up intestinal disinfection from the practical standpoint.

Intestinal Disinfection

When in the course of treatment it is desired to prevent crises, use may be made of:

1st. *Acute or critical disinfection.*

2d. *Chronic disinfection.*

1st. Acute or Critical Disinfections

We apply the term *critical disinfections* to those made at regular intervals and intended to prevent the accumulation of enterotoxins and thus avoid crises of elimination.

They are divided into:

(*a*) Liquid disinfections.

(*b*) Dry disinfections.

A. Liquid Disinfection

This disinfection comprises:

1st. An antiseptic medicine given at evening.

2d. An evacuating medicine given the following morning.

The antiseptic medicine of choice is:

Calomel given in two doses two hours apart.

Infancy	1 to 2 centigrams at one time.
Childhood	2 to 5 centigrams at one time.
Adolescence	5 to 10 centigrams at one time.
Adults	10 to 15 centigrams at one time.

The first dose is given fasting, at least four hours after the last liquid meal and preferably at 8:00 P.M.

The second dose is given at least two hours later, or about 10:00 P.M. As an excipient some boiled water or infusion.

When the patient cannot tolerate calomel, because of discomfort, cold sweats, vomiting, etc., or if it is contraindicated by gastric dilatation or ptosis, we substitute salacetol or ichthoform for it.

Salacetol may be given dry on the tongue in a tablespoonful of soup or in a cachet.

The first dose is given with the dinner which should consist of alimentary pastes, pudding, but *no meat;* a liquid diet not being necessary as with calomel.

The second dose is given two hours later with some aromatic infusion.

	Each dose
For infants the dose is	10 centigrams
For children the dose is	25 centigrams
For adolescents the dose is	25 to 50 centigrams
For adults the dose is	75 to 100 centigrams

Evacuating medicines: on the following morning give castor oil in the dose of 5 to 15 grams according to age; it may be mixed with plain gum syrup or black currant syrup, half and half.

Castor oil, and

Syr. black currants, āā 10 grams.

This mixture gives an emulsion of pleasant appearance and

agreeable taste, which children take without hesitancy, when added to a weak cup of tea.

Two hours later give a light oatmeal broth or gruel.

To mask the taste and odor of castor oil, a Russian physician, *Obrastzov* (of Kalouga), has recourse to the tincture of iodine and menthol, which besides, have the advantage of being intestinal antiseptics; his formula is:

Castor oil, 30 grams.

Menthol, 20 centigrams.

Tinct. iodine, X drops.

Before giving this mixture, it is advisable to warm it so as to bring about the disappearance of the viscidity that contributes toward making the castor oil so difficult of acceptance. The dose of menthol may appear rather large, but it should be remembered that it is dissolved by the oil and is in great part eliminated with the intestinal contents.

Children of over two years appear to tolerate this mixture very well. Nevertheless, it is better to prescribe a teaspoonful only, of a mixture containing 0.01 menthol and one drop of tinct. iodine to 5 grams of castor oil.

This liquid disinfection should generally be repeated after ten days, then at longer intervals, of fifteen, twenty, twenty-five days, etc., in order to gradually disaccustom the intestine from this artificial aid.

If the auto-intoxication is severe (indicated by the curves of the aromatic substances), *the fixed period added to each interval* should be shorter (two, three, or four days instead of five); in the first case the disinfections would take place at intervals of twelve, fourteen, sixteen, etc., days; in the last case fourteen, eighteen, etc., days. *Whereas if the auto-intoxication is slight, the fixed period added would be much greater*, six, eight, ten, etc., days.

B. Dry Disinfections

This method of disinfection comprises disinfecting medication but without purgatives. These are its indications:

When the curves of indol and phenol remain high, in spite of repeated liquid disinfections, we administer dry disinfectants during the intervals and for more or less long periods.

We do the same when liquid disinfections are contraindicated, as in (gastro enteroptosis), and motor insufficiency of the stomach.

In the constipated forms : powders of *Salacetol* or Ichthoform should be given in the dose of 0.25 grams, one to four times daily with meals.

In the diarrheal forms : we sometimes substitute for salacetol; *The Salycilate of Bismuth* in the same doses; or

Cod liver oil with creosote (1 per 100); this, in the dose of a teaspoonful two or three times daily, gives remarkable results when it is well borne.

2d. Chronic Disinfection

Chronic disinfection is a dry disinfection extending over a long period of time.

These are its indications:

When, in spite of the regimen, the curves of indol and phenol remain high.

When, notwithstanding critical disinfections, the symptoms of intoxication persist, most often because absorption is at fault or else because the antitoxic organs are insufficient. In such cases it becomes necessary to give to the patients besides the critical disinfections at fixed periods, a chronic disinfection which shall be administered once, twice or three times daily, according to the case. For this purpose use may be made of one of the numerous preparations mentioned in the preceding chapter.

When the stomach is at fault *hydrochloric acid, thioform or menthol* should be prescribed.

When intestinal symptoms predominate, Salacetol, or Icthoform should be given two to three times daily, in the indicated doses and for a long time; during several weeks or longer, if necessary.

It is in these cases, which belong nearly all to the organic auto-intoxications, that the *adjuvant medication* of the lacto farinaceous regimen is especially indicated. This signifies medication by means of the lactic bacilli in the form of *yoghourt* or *lactic bouillons;* **for they, above all else represent chronic disinfection** in its best type.

III. EVACUATION OF THE PROTEOLYTIC MICROBES OF THE INTESTINE AND THEIR TOXINS BY INTESTINAL LAVAGE

The antiputrefactive regimen, and the critical or chronic intestinal disinfections, prevent in a very appreciable measure, the formation and accumulation of the products of nitrogenous putrefaction that appear in the intestine as a result of the action of the proteolytic anaerobic microbes.

But notwithstanding the unquestionable efficacy of these two means, they are not always sufficient to completely prevent the formation of intestinal poisons, and moreover they offer very little protection to the organism against the entrance of these poisons into the blood (intestinal auto-intoxication). The evacuation of the microbes of the colon and the toxins they secrete will fulfill this indication much better.

There are two ways of accomplishing this:

(*a*) By lavage of the intestine.

(*b*) By relieving the intestine.

1st. Lavage of the Intestine by Enteroclysis

Enteroclysis or irrigation of the intestine is particularly indicated for obtaining this result.

For, as we have seen, nitrogenous putrefaction produced by the proteolytic microbes, occurs only in the large intestine.

If by means of enteroclysis we succeed in properly washing out this portion of the intestine, we shall have the satisfaction of having fulfilled the indication presented.

Moreover, the water of the enteroclysis does not all pass out; more or less of it is retained in the intestine, sometimes as much as a half liter or more remaining behind.

This water will be absorbed and produce a lavage of the liver, kidneys and blood, as well as a rapid and abundant diuresis,

which will carry off the waste products of nutrition and the toxins which had already penetrated the organism.

Lastly enteroclysis serves as beverage and calms the thirst, inevitable during the first days of the regimen.

Therefore, in all cases of intestinal auto-intoxication, enteroclysis casts out THROUGH INTESTINAL LAVAGE, the products of nitrogenous putrefaction existing in the colon and through DIURESIS, those that have already entered the general circulation.

This constitutes the first and principal indication for intestinal irrigation.

In the second place, enteroclysis is indicated in auto-intoxication due to muco-membranous enteritis, which is characterized by the formation of mucous shreds or membranes that are gorged with bacteria. These may also be the seat of considerable putrefaction, for they sometimes remain a long time in the intestinal folds before becoming detached and cast out with the stools.

A cleaning out of the intestine by an irrigation which would at the same time rid it of the mucus, and membranes with the microbes they contain, would consequently be most useful in relieving the condition. In the third place, intestinal auto-intoxication is accompanied in the great majority of cases by a spasmodic constipation, with accumulation of fecal matters which may be dry and occasion but little fermentation, but which may also exist, higher up, above the site of the spasms in the localized dilatations of the colon, in which the phenomena of putrefaction are extremely accentuated.

Here again the regular evacuation of these matters by enteroclysis, will save the patient from complications, often serious.

Hence, the evacuation of the matters, the evacuation of the toxic products, the evacuation of the membranes, constitute the triple indication for enteroclysis. A fourth may be mentioned, but only for auto-intoxication due to chronic enteritis, this being an infectious inflammation of the intestine.

Enteroclysis, which can be made to carry the evacuating liquid up to the Bauhinian valve, may also be made to carry

medicinal and microbicidal agents that are harmless to the patient.

That is the sole indication for the use of antiseptic enteroclysis.

Evacuating Enteroclysis

Intestinal lavage is performed with normal salt solution (*7 grams of salt to one liter of well-boiled water*) at a temperature of 38° to 42° C., 100.4° to 107.6° F., according to the patient.

This solution is the one which irritates the intestine the least and which provokes the most abundant diuresis. For these reasons we prefer it to all others.

An infusion of flaxseed or marshmallow root may be added to it with advantage.

Technic of enteroclysis. To make a good lavage of the intestine, it is necessary to carry the liquid to the cæcum, but without distending or irritating the intestine.

This cannot be done with the ordinary rectal douche, with short nozzle and strong pressure.

The large intestine and particularly when diseased, is very contractile, and prolonged spasms occur in it from the slightest irritation.

Consequently, it is not surprising to see a violent irrigation under strong pressure, determine spasms that not only prevent the tube from passing, causing it to bend on itself but even prevents the water from issuing.

We make use of English catheters of small caliber (16 to 24 French scale), but 50 centimeters long for children, and 1 meter or more for adults. They are pierced with an opening at the extremity and one on the side.

The catheter is connected by a short tube with a receptacle holding 2 liters, which is hung *at the most, 10 centimeters above the patient's buttocks.* The patient should lie on the right side, with the legs flexed on the abdomen and the hips elevated.

The stopcock being opened, the catheter (properly lubricated) is introduced into the rectum for one or two inches, the flowing water opens the intestine beyond it and in a few moments more, it will be found easy to insert the catheter a little

further and so on. By introducing the catheter slowly inch by inch, waiting each time until the water shall have opened the passage or straightened the bending of the catheter, its entire length can be easily introduced, and the water carried to the cæcum without causing the patient the slightest pain or discomfort.

The quantity of water which should be introduced will vary greatly according to individuals and often in the same individual, depending on the days; sometimes it may be 500 c.c., at others 1,500 c.c.

Any back flow in the receptacle is a sure sign of intestinal spasm; if pain or discomfort of any kind should supervene during the irrigation, it should be stopped and postponed, even if the quantity of water injected is insufficient.

The irrigation should be voided by the patient at the first urgent inclination.

In most cases a good third remains in the intestine. It is well to precede the irrigation by a small evacuating clyster.

Indications for enteroclysis. We have seen that the indications for irrigation were the evacuation of the stools, membranes and toxic products.

Which means that all cases of auto-intoxication do not require intestinal lavage, and that enteroclysis in nowise forms part of its specific treatment.

We make use of irrigations in the three following conditions only:

1st. When there exists at the same time constipation and intestinal auto-intoxication characterized by high curves of the aromatic bodies; in these cases irrigations are quite indicated and they bring about a rapid improvement.

2d. Irrigations are indicated when there is a considerable degree of auto-intoxication, even though there are but few membranes and the stools are regular. Their use brings about a favorable modification in the general condition, and a disappearance of most of the discomforts.

3d. When enteritis is accompanied by many membranes and much mucus; irrigations are of great benefit, for they bring about a rapid sedation of the pains.

But when constipation is the only indication, irrigations of oil are much more active and present less disadvantages.

When the auto-intoxication is mild or benign, we do not advise irrigations, for the regimen and disinfections will suffice to bring about a cure.

As a matter of fact enteroclysis is not an indifferent remedy. Badly done, it distends the intestine and increases its atony; if too great pressure is used it increases the spasms; repeated too often it irritates the bowel and exaggerates the mucous hypersecretion; too hot or too irritating, it provokes an artificial membranous enteritis.

These various reproaches are all well founded, but as *Langenhagen* wisely remarks, it is more due to the manner in which the lavage is done than to the procedure itself.

If enteroclysis is performed with the indicated precautions, most of the disadvantages disappear; but it is none the less true that they should not be abused.

It is necessary to know when to prescribe irrigations, at what intervals they should be made and to cease when the indication disappears, so as to disaccustom the intestine to their use, for too prolonged usage of the tube maintains the intestinal irritation.

Enteroclysis should, under those circumstances, be administered every two days only then on the third day, etc., until it may be discontinued altogether.

Contraindications to enteroclysis. Irrigations are contraindicated in severe enteroptosis and in intestinal atony, when the water penetrates easily but is not voided.

When the intestine is irritable, lavage produces spasms of the colon with reflux of the injected fluid into the fountain or receptacle; the spasms are frequently painful and contraindicate the use of irrigations.

Lastly, they are contraindicated in certain impressionable patients with exaggerated intestinal reflexes in whom irrigations produce such severe pain that they are often accompanied by cold sweats, nausea and fainting.

Antiseptic Enteroclysis

1st. **Irrigations of tannin** (1 *gram to* 5 *grams per liter*) may be used in the diarrheal forms and acute outbreaks. This substance, while not greatly antiseptic is antitoxic; it precipitates the intestinal toxins into insoluble compounds and is slightly constipating. It is harmless, the only disadvantage of tannin being a tendency to slightly irritate the mucous membrane and cause intestinal spasms, often very harmful.

2d. **Irrigations with calumba** (10 *grams per liter*) offers the same advantages and presents the same inconveniences as tannin.

3d. **Irrigations with oxygenated water** (30 *to* 40 *grams hydrogen peroxide per liter*) are useful in acute outbreaks when the stools are extremely offensive.

4th. **Irrigations with ichthyol** (5 *to* 15 *grams of a* 1 *per cent. solution per liter*) give good results from the standpoint of intestinal disinfection, but they are often irritating to children.

5th. **Irrigations with borated water** (30 to 40 grams per liter) were studied and advised by *Rovighi;* they are useful but dangerous, several authors having observed phenomena of intoxication.

Résumé

When the regimen and the disinfections are insufficient to control intestinal auto-intoxication, advise the use of:

1st. Intestinal lavage with normal salt solution in the mild cases.

2d. Irrigations with ichthyol in severe cases.

2d. Relieving the Intestine

To control the constipation is for many patients and often for their physicians, the principal end to attain.

Constipation, it is true, is frequent in auto-intoxication, but as we have seen, it only plays a very obscure part in its pathogeny.

Nevertheless, it is necessary to combat constipation in all moderately severe intestinal putrefactions.

In the great majority of cases of intestinal auto-intoxication, the constipation is not of an atonic, but of a spasmodic nature.

This fact is of the highest importance from the therapeutic standpoint.

To combat constipation we employ:

A. Hygienic means.

B. Therapeutic means.

A. Hygienic Means

Mental rest. Advise a calm and tranquil life in the country free from emotions, free from the occupations and cares inherent to business or household.

Intellectual rest. In the beginning, insist upon absolute rest if it is possible.

Avoid late nights and work at night, when the usual occupation is resumed.

Physical rest. This is indispensable; in severe cases advise complete rest in bed for sometime, and lying down on a sofa or lounge afterward.

In the less serious cases forbid late nights and violent exercise. Retiring early and rising late if possible.

Forbid in all cases, exercise involving running, climbing of stairs or riding in carriages, automobiles, horseback riding and bicycling, for *the shaking and jolting of these* greatly increase the spasmodic condition of the intestine.

Rest should be particularly required of women at the time of their menstruation, for we know how frequently intestinal outbreaks occur at that period.

Psychotherapy. The influence exercised by the mind over the body is well known. The sufferer who so often is depressed and despairing, should be encouraged and cheered.

The nature of his trouble should be explained to him, the significance of the auto-intoxication which results from it, the physical and nervous symptoms which derive from it, the phobias which accompany it.

When the sufferer will have understood that he is not an exception, that the annoying symptoms which torment him are also common to others, he will become reassured. He can then be shown that the disorder from which he suffers is long in duration, that it is subject to ups and downs, to good and

bad periods, but that it is curable and that with his recovery all the symptoms which accompanied it will disappear.

It is, in fact, essential that the sufferer should have the greatest confidence in his treatment, to be willing to follow so long and monotonous a régime, to give up to it the necessary time, and to bear without despair the inevitable bad days, which come in spite of a well-ordered, well-applied and conscientiously followed treatment.

B. Therapeutic Means

We have seen that *in intestinal auto-intoxication the constipation is nearly always spasmodic*, and that this fact is of the greatest importance from the therapeutic standpoint. *It shows us that all the medicines and physical procedures employed in atonic constipation must here be carefully avoided;* for after having relieved the intestine, they leave it irritated and in consequence increase the constipation.

Irritating foods containing much cellulose (vegetables and fruits) must be forbidden.

The irritating seeds of flax and of psyllium, which are sometimes recommended and with success, in atonic constipation must be avoided.

Drastic purgatives; jalap and the salines must be prohibited.

The same may be said of hydrotherapy with its cold and violent applications, of intestinal massage, of faradic electricity applied to the abdominal walls or rectum.

Lastly, in spasmodic constipation, all the *strenuous* thermal cures, with the waters of Carlsbad, Marienbad, Tarasp, de Brides, etc., must be avoided.

All of these procedures which give such remarkable results in atonic constipation, have a deplorable effect in membranous enteritis and in the spasmodic constipation of intestinal auto-intoxication.

The only purgative which may be employed in urgent cases, the only one which is not irritating and consequently harmful, on condition of its being employed in moderate doses and not too frequently, is *castor oil.*

In children the *syrup of manna* or *manna tears* may be substituted for it in doses of 15 to 30 grams. But these two

medicines are only for urgencies, and are not to be used for the curative treatment of spasmodic constipation of intestinal auto-intoxication. We much prefer to them the *oleclysms* and the *Rhamnus frangula.*

Enteroclysm

One of the first procedures advised by authors is intestinal lavage with the normal salt solution.

We have seen that it is neither indicated nor indispensable in all cases of enteritis or of intestinal auto-intoxication, and that its principal object was not the emptying of the bowel.

But it certainly contributes to it, although it cannot be looked upon as a curative procedure of spasmodic constipation.

At all events, and contrarily to the opinion of *Lyon*, the more intense the spasm, the higher should be the temperature of the lavage (40° (104° F.) and above) and the more must the pressure and the quantity of liquid introduced be diminished (500 c.c. and even less) and the longer the water is retained, the greater the benefit to the patient.

Oleoclysm

The best remedy against spasmodic constipation is *the systematic treatment by injections of oil or oleoclysms.*

Introduced in therapeutics by *Kussmaul* and *Fleiner* they fill all the indications.

They soften the fæces, detach them from the intestinal walls which they at the same time lubricate, they calm the intestinal spasms, and diminish the absorption of the toxic substances produced by the fecal matters.

Oleoclysm may be employed as:

(*a*) Lavage of oil.

(*b*) Oil enemas.

Lavage with Oil

Lavage with oil is recommended, particularly when the seat of the constipation is very high up. For adults, from 200 to 500 c.c. of pure oil (olive, poppy, sesame) heated to 40° (104° F.)

For children, from 50 to 150 c.c. to be introduced from a fountain, the patient lying extended with hips elevated.

Bourget uses with benefit *the oil of sage.*

Essence of sage ..... 3 grams.
Oil of sesame .....1,000 grams.

The *oleoclysm* of *Bourget* may be employed for administering the lavage; it consists of a small glass recipient which prevents the rubber tubing and the receptacle from being soiled by the oil, for they are difficult to clean, particularly the red tubing; they should be cleaned with alcohol.

The oil must penetrate slowly and under as small a pressure as possible (10 to 15 centimeters), consequently it is necessary to use a long tube having a large opening and from fifteen to twenty minutes will be required for introducing the oil.

If a stool does not take place within four hours after the oleoclysm, a warm enema should be given.

The lavage with oil must be continued every day until followed by a soft, sufficient and spontaneous stool.

Their frequency is then diminished, as well as the quantity of oil introduced.

Oil Enemas

Oil enemas are sufficient when the seat of constipation is low down (in the sigmoid); they are much simpler, more easily administered and less expensive.

They are administered on retiring and when lying in bed; from 30 to 60 c.c. of warmed oil are introduced into the rectum by means of a sufficiently large glass syringe provided with a hard rubber nozzle attachment.

The enema should be retained until the following morning if possible, when it is usually voided with the stool.

Oil irrigations and oil enemas, owing to their anti-spasmodic action, may be looked upon as a specific and pathogenic treatment, of the spasmodic constipation, characteristic of intestinal auto-intoxication. But they are not always tolerated, even when an absolutely pure and fresh oil is employed; they sometimes occasion painful rectal tenesmus; in such cases their use must be suspended.

Finally, they are not always sufficient.

In these two cases, recourse must be had to medicinal agents or to thermal spring waters.

Medicinal Treatment

In such conditions we employ two mild, non-irritating laxatives belonging to the American Pharmacopœia; the

Fluid Extract of Cascara Sagrada and

Fluid Extract of Rhamnus Frangula.

These are given by drops in a little water, immediately before eating or at bedtime.

Beginning with gtt V in children and with gtt X in adults, the dose may be gradually and progressively increased, if necessary up to gtt L for children or gtt C for adults. As soon as a dose sufficient to cause a spontaneous stool is attained, it is continued until the stools become soft, then the dose is gradually and slowly diminished, a drop at each time until it can be done without.

An infusion of the herb or tea of **"Rhamnus frangula"** may also be advantageously used in mild cases, a pinch of it in a cup of hot water at bedtime.

In more obstinate cases, *tablets of Purgen* may be recommended in doses of from a half to two tablets on retiring.

Thermal Springs

Strenuous or violent thermal springs cures are absolutely contraindicated.

They should all be mild and the quantity of water drank very slight (50 to 150 grams).

Carlsbad water is greatly used in Germany for constipation and chronic enteritis.

Small doses of *Sprudel* water are given internally in conjunction with rectal irrigations of the same water (200 to 500 c.c. at 40°). (104°F.)

Marienbad and Homburg. The waters of these springs are employed in the same conditions.

Tarasp. Vulpera in Switzerland (elevation 1,400 meters) has the advantage of combining an Alpine climate with the thermal springs, the waters of which often give good results, provided, as we have said before, that they are taken in small doses only.

The tonic action of carbonic acid baths is combined with them.

As with all other thermal spring *cures*, the favorable effects are not manifested until later, for during the treatment it is not rare to find an increase in the constipation.

In France, the waters of **Chatel Guyon** are recommended for the constipation of intestinal auto-intoxication.

Chatel Guyon (*Gubler Spring*). These waters are stimulating and appear to us to be much more indicated in the atonic form of constipation of auto-intoxication than in the spasmodic form.

In spasmodic constipation, it is only when the spasmodic condition is not too intense that patients derive any benefit from their sojourn at **Chatel Guyon.**

In chronic enteritis, and in muco-membranous enteritis, the results give but very little satisfaction.

It is only when the enteritis is quite subdued and quiescent *that benefit may be derived from Chatel Guyon.*

On the other hand, these waters are particularly indicated in the hepatic complications of intestinal auto-intoxication.

Néris and Plombières. The waters of Néris, but specially those of Plombières, give better results in cases of pure spasmodic constipation. For owing to their warm temperature and to their radio activity, they exercise a very favorable action on intestinal spasm.

II. TO STIMULATE THE ACTION OF THE ANTITOXIC ORGANS AND THE EMUNCTORIES OF THE ORGANISM

A double indication presents itself here:

1st. *To stimulate the insufficient antitoxic functions.*

2d. *To stimulate the insufficient emunctories of the body.*

1st. Stimulation of the Insufficient Antitoxic Functions

We have seen the great part played by insufficiency of the antitoxic organs, in the causation of auto-intoxication.

Can we hope to control this cause at some future day?

Everything leads to the supposition, for organotherapy which promises to supplement the organic insufficiencies, is in its beginning only, and is slowly emerging from the field of empiricism.

Organotherapy

Some twelve years ago, in a communication to the Swiss Medical Congress, we proposed the term organotherapy which has since been adopted in all countries, France excepted, the term *opotherapy* being used there in preference.

Organotherapy seeks to substitute for the insufficient organ of man the healthy organ of the animal or its products.

But it is still in its empirical stage, and the favorable results obtained from organotherapy made with organs *in toto*, gives no certainty as to the method in general.

For in fact, in the application of organotherapy, it is proposed to artificially introduce an element that is normally secreted by a gland, which appears to be insufficient as a whole or in part.

But what this element is, is not known, nor what its state is when poured into the blood, nor in what quantity. All these facts are unknown and we can only draw hypotheses. Organo-

therapy is a mode of treatment from which much may be hoped, as thyroid therapy proves; but until our chemical knowledge of the organs of internal secretion is more complete, organo-therapeutic treatment can only be empirical.

In digestive insufficiency, we can actually replace the insufficient digestive enzymes.

We dispose of *pancreatin*, *taka diastase*, and *kinase* for the digestive insufficiencies due to the intestine.

Fremont's gasterin, *Hepp's dyspeptin*, like *pepsin* and *hydrochloric acid*, will render the same services in gastric digestive insufficiency.

Siegert, only lately, has shown the favorable influence exercised by *pancréone* in athrepsia and the auto-intoxication which accompanies it.

Lastly, in insufficiency of the intestinal antitoxic functions, *lecithin*, *rhomnol* and *histogenol* have each in turn been employed to stimulate the intestinal defenses.

In hepatic insufficiency, the liver extracts, *heparaden*, have been used, often with success.

In insufficiency of the thyroid, *thyroidine* has been used with brilliant results, as is well known.

In insufficiency of the supra renals, *epinephrin* has given definite results.

But to mention it again, all these empirical applications must be reviewed, and the scientific appreciation of this method can be made only on the day when the active principles of these organs will have been isolated.

Metallic Ferments

The new therapeutic chapter on metallic ferments that *Robin* has just inaugurated, opens a new horizon upon the action possible to obtain in the future by stimulating or supplementing the insufficient antitoxic organs of the body.

Stimulating the Insufficient Emunctories of the Body

The accumulation of enterotoxins and leucomaines in the blood may result, not only from an overproduction of these

poisons, but particularly when there is insufficiency of the normal emunctories; the kidneys, the skin and the intestine.

1st. Stimulation of the Renal Emunctory Functions

The renal function may be stimulated by:

1st. Intestinal irrigations.

2d. Lavage of the blood.

3d. Thermal springs.

Enteroclysis

Intestinal lavage with normal salt solution and of which we have already spoken, is an excellent method of increasing renal elimination; for after each lavage, there is always an increased excretion of urine, sometimes considerable.

Lavage of the Blood

Lavage of the blood appears to be very particularly indicated, when poisons have accumulated in the blood.

It may be performed:

(*a*) By *intravenous injection.*

(*b*) By *hypodermoclysis.*

Intravenous Infusion

"I find," says *Professor Lepine*[1], "the expression 'lavage of the blood' used for the first time by *Professor Sanguirico* in a paper upon the toxic effects produced in rabbits by various substances (strychnine, alcohol, chloral, aconitine, paraldehyde, urethane, caffein, morphine, crurare, nitrobenzol, nicotine).

"*Sanguirico* performed on these animals numerous intravenous injections of salt water; he appears to have obtained encouraging results in some cases, but as he does not state the quantity of liquid used, we have no assurance that he really practiced a *lavage of the organism*, such as *Dastre* and *Loye* have taught us.

"*Sanguirico* mentions *Sanarelli* as having attempted before him *lavage of the organism* in intoxications; but I have been unable to get at the source and I do not know exactly what *Sanarelli* attempted."

[1] Lepine: Semaine médicale. 1896. p. 233.

Be it as it may, *Ch. Richet* and *Montard Martin*[1] had previously shown that an injection of sugar solution into the veins of a dog—even when the quantity of sugar was only a few grams—at once determined a considerable polyuria.

By their very exact experiments *Dastre* and *Loye*[2] have placed beyond doubt, the important fact that a considerable quantity of salt solution—even more than two-thirds of its weight!—may be injected into the veins of an animal, *without provoking any trouble*, provided the injection is well regulated and the liquid penetrates slowly.

Since then physicians, *Sahli* chiefly[3], and surgeons, have frequently had recourse to lavage of the blood in grave intoxications and uræmic auto-intoxications with some success.

But to accomplish this, the integrity of the kidneys is necsary, because to effect a lavage of the blood, it is not sufficient that a large quantity of liquid be absorbed; an abundant urination must also take place and even that does not suffice, because with the excretion of urine, it is necessary that a corresponding elimination of toxins should also take place.

That is what is observed in interstitial nephritis, in which uræmia may exist in spite of the excretion of several liters of urine.

Finally, it must not be forgotten that in nephritis, in which a retention of chlorides exists, an intravenous injection of a 7 per cent. salt solution may be harmful and even fatal.

In consequence, this method which may be used in very grave cases of intestinal auto-intoxication, is scarcely indicated in ordinary ones.

Hypodermoclysis

Hypodermoclysis remains therefore the method of choice in intestinal auto-intoxication. The fountain or receptacle and the normal salt solution having been sterilized, the fountain is placed at a moderate elevation and a very fine sterilized trocar provided with its canula is introduced under the skin of the abdomen. The trocar is then withdrawn and the canula con-

[1] Richet: Arch. de physiol. 1881. p. 1.
[2] Dastre: Arch. de physiol. 1889. p. 283.
[3] Sahli: Corresp. f. Schweiz. Ærzte. 1890. p. 545.

nected with the tube of the fountain. If the trocar is very fine and the fountain not too high, the outflow will not be too rapid; otherwise it should be moderated by the catch on the rubber tube.

The solution should flow in very slowly, otherwise very painful tumefaction of the subcutaneous cellular tissue will take place.

The temperature of the solution should be that of the body, but if it enters very slowly it is not so essential, provided that it is warm, for the temperature is soon equalized in the subcutaneous cellular tissue.

In our clinic, we use in preference, a large glass syringe with a ground-glass piston which is easily sterilized and makes hypodermoclysis much more easy.

The quantity injected varies from 60 to 150 grams and may be repeated several times if necessary.

Under its influence, the heart's action will be seen to improve and the urine will increase in amount and even in quality, as we have many times observed.

Résumé, hypodermoclysis must always be the exceptional method and enteroclysis the usual method to employ, for stimulating the renal functions in intestinal auto-intoxication.

Mineral Springs

There remains to be mentioned treatment by the mineral waters, which act by lavage of the organism and more by what they carry off than by what they bring.

St. Evian, *Vittel* and *Contrexeville* are the waters most employed for washing out the organism. They may prove useful in auto-intoxication, but only temporarily. Only an antiputrefactive alimentary regimen can produce a deep and lasting effect in this chronic condition.

II. Stimulation of the Cutaneous Emunctories

The importance of a good function of the skin is well known.

We know the *decongestive action* that the skin, so richly provided with blood-vessels, exercises through its vasomotor nerves upon the circulation of the internal organs, and how

much it favors, when it is insufficient or its function is impaired, the congestion of the abdominal organs, the liver in particular.

We know what a *tonic action*, the skin, which is so richly provided with nerves, exercises upon the organism by regulating its loss of water and animal heat; and how much the impairment of its function relaxes and depresses the vitality of the tissues and nervous system.

Finally, we know what a *depurative action*, the skin so richly provided with glands, exercises upon the elimination of toxic substances, which have penetrated the organism, and how serious are the consequences resulting from its insufficiency. In auto-intoxication, as we have seen, the skin acts badly; it is relaxed, without tone, wrinkled and of yellowish color; its decongestive action is nil, its tonic action is impaired, and its depurative action is diminished.

This bad function of the skin is therefore a consequence of auto-intoxication, which is also increased by it; hence it is advisable in this condition, more than in any other, to combat the cutaneous insufficiency by all the means in our power.

To accomplish this we have:

(*a*) Diaphoresis.
(*b*) Hydrotherapy.
(*c*) Aerotherapy.
(*d*) Heliotherapy.

Diaphoresis

Without doubt when it is a question of acute intoxication, sweating brought on by *mud baths*, *Russian baths*, particularly *Turkish baths*, is quite indicated; for in such case, the elimination of the toxins is the first object to be attained.

In renal insufficiency and specially in uræmia, diaphoresis renders great service, but here again the desired effect is the rapid elimination through the skin, of the toxins which the kidneys can no longer throw out.

Whereas, in digestive auto-intoxication, which is pre-eminently a *chronic* auto-intoxication, we not only seek the elimination of the digestive poisons by the skin, for these are excreted much better and more thoroughly by the intestine and kidneys,

but we more particularly seek to re-establish the normal and complete function of the skin.

Hydrotherapy

We need not dwell upon this method, the practice of which has long existed and which has received a new impulse since the *Abbé Kneipp* and his medical followers have brought it into vogue again.

Hydrotherapy, when well directed and carefully applied as it should be in weakened and nervous individuals, like the auto-intoxicated, gives excellent results.

Many of our patients have derived great benefit from the hydrotherapy cures of *Divonne* in France; *Champel*, *Schoenbrunn* and *Schoenfels* in Switzerland; *Woerishofen* and *St. Blasien* in Germany.

Aerotherapy

Aerotherapy is less known, but still more useful.

While this method is greatly employed in Germany, Austria and Switzerland, it does not seem to have attracted attention in France, where, to our knowledge, air baths are only advised and practiced by *Monteuuis* of Sylvabelle, who has just published an excellent little work upon air and sun baths applied in ordinary practice[1].

Aerotherapy is much superior to hydrotherapy in the effects it produces.

In the first place, the patient as soon as he has the opportunity of comparing the two methods, very quickly prefers the air baths.

Is it because man was created to live in the air and not in the water, as *Neuens* claims? Or is it not rather because the air bath is more agreeable and gives less shock than the cold douche or pack. We frequently see patients who have learned to take air baths, not only not dread the exposure of the body to the open air, but on the contrary seek it, for the impression of ease and well-being it produces.

It is, as *Monteuuis* remarks, an important factor in the treatment of the auto-intoxicated who are all neuropathic,

[1] Monteuuis: Bains d'air et de lumière. Paris. 1906.

hard to please and sensitive to a method of treatment so new to them.

In the second place, hydrotherapy is much more active and gives greater shock than the air bath; in consequence nervous and impressionable patients cannot bear it.

When the cutaneous surface is directly exposed to the air, the layer of air immediately surrounding it, is constantly renewed and as constantly taking away its heat. The organism reacts, to make up for the lost heat, and in consequence the heart and lungs act more energetically, the circulation becomes more active and all the organs are called upon for more work, resulting in an acceleration of the oxidations and nutritive mutations.

Taken with the necessary precautions and progressively, the air bath leaves a sense of well-being and is beneficial.

Whereas the cold bath, douche, affusions, or cold packs produce a greater shock, a disagreeable sensation amounting sometimes to real suffering, owing to the body heat being too rapidly taken away.

The conductivity of water being nearly five times greater and its power of absorbing heat nearly seven hundred times greater than air, it is not difficult to understand (as *Neuens* reminds us)[1] why the sensation may be disagreeable. Of course, a well-conducted hydrotherapy cure avoids these bad features, but medical establishments for properly carrying it out are few, and most frequently in the smaller cities and even in the large ones, hydrotherapy is not directed by competent specialists, who are experienced in the use of a procedure, the action of which is not proportional to the resistance and weakness of the subject. This explains the frequent failure of douches, etc., and the great number of sufferers who derive no benefit whatever from hydrotherapy, and who not being able to support it, are obliged to give it up.

Air and sun baths are much milder and those who cannot support douches, etc., very easily tolerate the stimulating effects of air and sunlight.

In the third place, air baths may be taken anywhere and medical supervision, while useful, is not essential.

[1] Neuens: Traité de médicine naturelle scientifique. 1900.

A hydrotherapy cure worthy of the name necessitates the supervision and constant care of a specialist.

"At home," *Rikli* says, "a small part of the garden about five to six yards square and enclosed by plank walls six feet high is all that is required. Whoever has a garden can easily substitute sheets for the plank walls."

When one has no garden, a platform or balcony so screened as to insure privacy will suffice.

"In default of all these resources," as *Monteuuis* remarks, "air baths in one's own room are entirely practicable, provided the patient can move about in it and that sunlight is abundant; the windows are screened by curtains so as to afford privacy."

The last and greatest advantage of aerotherapy over hydrotherapy is that it does not merely act by abstracting heat as water does, but it also acts as *a bath of sunlight.*

As a matter of fact the **action of light** is much superior in its effects to those of air and *solar heat*, hence heliotherapy is being more and more used, and since the famous paper of *Bernhard* of Samaden, this powerful agent has become a curative means of the first order in surgical tuberculosis.

Methods of Aerotherapy

We borrow the following details from the paper of *Monteuuis;* it is the work of a distinguished physician and difficult to improve upon. *Monteuuis* makes a distinction between:

(*a*) Air baths.

(*b*) Light baths.

Properly speaking, the air bath is one in which the air plays a more important part than light. It is of short duration for if prolonged it becomes a *bath of light.*

Bath of light. This produces the same effects as the air bath, but in addition, the intensity of light plays an important part either as a cutaneous stimulant or as a microbicide. Consequently, when the air bath is prolonged, the efficacious role of light must be taken into account.

Taken altogether, the two kinds of baths may be included in the term *air bath* or (*Luft-bad*) as is done in Germany, reserving the term **light bath** or (*Licht-bad*) to phototherapy and **sun baths**

or (*Sonnen-bad*) to the method of insolation adopted in Switzerland for several years.

The Air Bath

The air bath may be taken in the open air, in a room with the windows opened or with the windows closed, and finally in a room heated according to the susceptibility of the patient.

The duration of the air bath will vary according to the outside temperature and according to the indications furnished by the temperament and power of endurance of the patient. The first bath should be short. Delicate and sensitive individuals cannot in the beginning withstand more than two or three minutes, even with windows closed, and sometimes with the room heated. For some time they may be unable to have the windows opened or to prolong the duration of the bath, for they are seized with goose flesh after a short exposure, which frictions do not dispel, and they are compelled to dress quickly.

Accustomed to a life of inactivity, weakened, and very susceptible to cold, these subjects require many precautions in the beginning, but with care they always succeed in becoming hardened and more resistant. Fortunately for these hyperæsthetics, the stimulation produced on the cutaneous surface makes up in intensity for the lack of duration. In less sensitive subjects, the air bath may be at once begun with windows open; the duration must be measured by the impression of cold they derive and by the ease with which *reaction* is established.

As soon, however, as the individual becomes more accustomed, the exposure is gradually and progressively lengthened to fifteen minutes or more, taking meanwhile every precaution to prevent cold.

Effects of the air bath. The first effect is the impression of cold and an imperative desire for movement.

Instinctively the patient will rub himself vigorously with his hands or a rough towel; to the superficial reaction thus brought about will follow the need of movement or more violent exercise.

Some will walk or exercise differently, others do gardening, digging, or saw wood.

Owing to the exercise, the feeling of coldness is quickly dissi-

pated, to reappear again after more or less time, the interval becoming longer as the patient accustoms himself to exposure.

At the time when the sense of well-being and comfort begins to disappear and gooseflesh appears anew, the patient must above all secure reaction; if a feeble or neuropathic subject by returning to bed; if more vigorous by quickly dressing and exercising sufficiently to bring it about. As to the kind of exercise, any that the patient may care to indulge in will answer.

The duration of the cold air bath will be regulated by the impression the cold makes, by the promptness of reaction and lastly by the amount of consecutive exercise the patient is capable of.

The first danger to avoid is too long an exposure to the cold air.

If too prolonged for a cutaneous surface, still unaccustomed to the stimulating effects of the air, instead of finishing his bath with a feeling of well-being, the patient will feel tired, overdone and stiffened.

Sometimes the discomfort is more accentuated, headache, pains across the back, a general weariness and a feverish sensation, but without elevation of temperature, lastly insomnia. At times a generalized erythema may be found.

A second danger to avoid is exaggeration of the exercise. Too much exercise may bring about overfatigue.

Care should be taken therefore not to overdo.

The measure of strength should not be exceeded and that of the auto-intoxicated is often limited; in consequence when the patient has become hardened and more resistant, he may sit or even lie down part of the time.

It is not unusual to see patients absolutely unaccustomed to exercise or to go about after a too prolonged or too violent exercise complain of local muscular pains, etc., which they do not fail to attribute "to cold" or a "rheumatism" caused by the cold air bath.

A last danger to avoid is an insufficient reaction.

The reaction following the cold air bath is as important as the reaction following a douche or other bath.

The vivifying effect of the bath veils the insufficiency of the reaction; hence it is important to advise the patient to dress

himself quickly as soon as his bath is finished and to take some sufficiently active exercise. The exercise must be enough to produce a general sense of warmth, and rest must not be allowed until the patient finds himself in some place where he may regain his ordinary temperature without fear of catching cold.

Duration of the treatment. It would seem that air baths might be continued indefinitely, certain temperaments can do so without experiencing the slightest inconvenience or trouble.

"In nervous subjects," *Monteuuis* states, "the stimulation of the bath may after a while bring about an overexcitation, an overdoing of the nervous system manifested by a general discomfort, muscular pains and digestive troubles.

On the appearance of these symptoms, it is better to lessen the duration of the baths, or even suspend them if the symptoms instead of decreasing become more accentuated. We generally limit the treatment by air baths to six or eight weeks, and we have never observed the symptoms mentioned by *Monteuuis*.

Heliotherapy

Sun baths have been particularly studied by *Bernhard*[1] of Samaden, and *Rollier*[2] of Leysin.

These two surgeons, by methodical and progressive insolations, obtained rapid and definite cures of tubercular ulcers and tubercular joints (tuberculosis of the knee, hip, wrist, elbow and shoulder) even in spondylitis of the same nature.

In consequence, this method has been greatly used for a large number of other affections. *Sorgo*[3] claims to have cured tubercular laryngitis by direct insolation.

We have used it in a certain number of digestive disorders with benefit.

Sun bath, method of. At daybreak all our bedridden patients are wheeled out on our spacious balconies, where they remain all day and take their meals. With the first appearance of the sun, the beds are uncovered and the patients, simply protected by small straw hats, are subjected to the beneficial action of the sun.

[1] Bernhard: Correspondenzblatt f. sch. Aerzte. 1904. p. 763.
[2] Rollier: Rev. Med. Suisse Romande. 1895. p. 602.
[3] Sorgo: Wien klin. Wochenschr. 1894.

Of course, the little patients must be progressively accustomed to the sun's action, but this comes quickly and soon the tanned and almost black skins of the patients show the powerful activity of the sun's rays.

Action of the sun bath. Does the intense tonic and bactericidal action which takes place through the skin in surgical insolation, explain the beautiful results obtained by sun baths in other chronic and deeper affections? That is not impossible.

An additional reason then—considering their innocuity—for employing the sun's rays in intestinal infections in general and intestinal auto-intoxication in particular, as we have been doing for almost a year in our clinical service.

Of course, at an elevation of 400 meters (over 1,200 feet), we do not have at our disposal the intensity of light at the command of *Bernhard* in St. Moritz, 1,800 meters (over 5,400 feet), nor of *Rollier* at Leysin, 1,200 meters (over 3,600 feet); nevertheless, the results have been most interesting, and such as to induce us to continue the experiment.

The sun baths from the standpoint of the general condition of our little patients have an unquestionable vivifying power and a most remarkable tonic effect, resulting in a veritable regeneration of the entire organism, as is manifested by an increase in the hemoglobin, the erythrocytes and the body weight.

The appetite is renewed in a most striking manner, the digestion improves and is more active and the intestinal functions appear to be favorably influenced.

The stimulating action of the sun upon the temperature of the skin is accompanied by penetration into the body of the ultra violet rays, and these stimulate the oxidizing processes of the organism. To the general action we may add the local stimulating and bactericidal effects of the ultra violet rays upon the skin, as demonstrated by *Downes* and *Blum*, later by *Duclaux* and *Arloing*.

We admit without question that the local action combined with the air bath readily explains the favorable action of the sun bath upon the function of the skin.

Of course, at the altitude in which our hospital is situated,

we can only make use of sun baths during the summer, but in the mountains where the air is dryer and purer, where the intensity of light and heat is much greater, it is possible, thanks to the exceptional climatic conditions, to carry on the insolation during the entire winter.

III. Stimulation of the Intestinal Emunctory

We have seen that the intestine is not only the source of the enterotoxins, but that in a certain number of auto-intoxicated cases, it also serves as the channel for eliminating them, and the **crises** and acute **recurrences** have no other explanation. To stimulate the intestinal eliminative functions by a daily purgation would meet the indication; it may be obtained by:

(*a*) *Daily purgation.*

(*b*) *Treatment by the purgative mineral waters.*

Daily Catharsis

Purgatives, after having temporarily increased the number of intestinal microbes, bring about their decrease after a few days, as we have seen, consequently from a theoretical point of view, their daily use might well be defended.

It is not the same from the practical standpoint; the daily administration of cathartics after a time weakens the vitality of the digestive glands and lessens their normal functions. The intestinal muscles become indolent and the assimilative and defensive power of the intestinal mucosa is diminished.

The daily use of cathartics presents many great disadvantages, and the slight benefit derived from them might be more readily obtained and with less harm by means of dry disinfections.

Hence, we have completely abandoned the method, although many other authors advise it. A teaspoonful of castor oil may be given each morning before breakfast.

German authors recommend the daily use of a small glass of mineral water to be taken in the morning.

Montmirail, Hunyadi Janos, Birmenstorff, Rubinat, Villa Cabras, etc.

Purgative Mineral Springs

The saline sodium sulphate waters are laxative and cathartic; in sufficient doses they produce numerous watery evacuations without pain or fatigue. Besides their purgative properties—not always manifested in our patients suffering from spasmodic constipation—these waters possess diuretic properties, which render them valuable in intestinal auto-intoxication. A mild and well-directed mineral springs course may give good results, provided the auto-intoxication is not due to an enteritis in an inflammatory state.

We have seen a rather large number of our patients benefited by following the course at the following thermal springs:

Brides and *Chatel Guyon* in France; *Homburg* in Germany; *Carlsbad* and *Marienbad* in Austria; lastly, *Tarasp. Vulpera* in Switzerland, which has besides the advantage of mountain air (elevation, 1,200 meters).

These various places fill in varying degrees the indications laid down and give happy results in intestinal auto-intoxication.

LACTIC FERMENTS

WITH PARTICULAR REFERENCE TO THEIR APPLICATION IN INTESTINAL THERAPEUTICS

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(WITH PERMISSION)

The name of lactic fermentation was formerly applied to all fermentations giving rise to the production of lactic acid. No attention was paid to the nature of the organism, the activity of which brought about the production of lactic acid; nor to the substances at the expense of which the organism thrived nor to the influence and action the temperature had upon it and for greater reasons no attention was given to the influence exercised by the respective proportions of the substances constituting the culture medium.

We remember that in former times, a *lactic ferment* was spoken of. It was described as a *non motile* element measuring 1.6 μ and constricted in the middle. To-day we should say that this had reference to a diplococcus. These diplococci may be observed in the soured milks of our climates, they are found isolated or linearly disposed, in contact with each other and assuming more or less flexuous chain-like forms.

This microbe was discovered by Pasteur in 1859[1] and to determine the cause of the acid fermentation of milk was the object of his first researches.

He found that the micro-organism he was studying thrived in milk owing to the transformation of lactose into lactic acid which it brought about, whence its name of *lactic ferment*.

Later this name was adopted and employed to designate all fermentations giving birth to lactic acid.

[1] Pasteur. Ann. Chim. Phys. 3ª Serie t. CCCCXI.

Unfortunately, this definition at once leads us away and greatly from the object which is itself the starting point; for as a matter of fact innumerable microbes including pathogenic species are capable of generating lactic acid but even when we leave out the pathogenic organisms, we still remain on a ground without boundaries, and we are unable to perceive the limitations that are necessary for precise definitions. We are therefore constrained to include in the same family, fermentations of most dissimilar types. Some in which the fermentating substance is not always a sugar, in which the lactic acid may exist in infinitesimal proportions and frequently accompanied by products differing greatly chemically.

It is an easy matter to verify these observations by numerous examples. Among the pathogenic organisms, the *bacillus coli communis* the *cholera spirillum*, the bacillus *anthracosis* are capable of producing lactic acid; as for the non-pathogenic, it is sufficient to cite certain ferments of cream or cheese the micro-organisms of which furnish very feeble quantities of lactic acid accompanied by odoriferous substances. Some of them even give bodies derived from an advanced proteolysis of the albuminous substances present.

Gradually, step by step and by the judicious use of systematized successive eliminations we can arrive at a more concise and more exact definition by restricting it to those micro-organisms which give *only* lactic acid to the exclusion of all other bodies. Although by so doing we are exposed to a new deception, because a given specie the sole excretion of which is lactic acid in certain media may betray its presence by other by-products when placed in other media; it therefore becomes necessary to take into account the nature of the alimentary medium as well. *Hueppe*[1] was one of the first to call attention to the importance of the culture medium.

It is even easy to foresee that a new factor—*the temperature*—will likewise intervene to a certain extent. However as the taking into account of all these elements would prove too arduous a task and as it is moreover unnecessary in practice, we shall limit ourselves to considering as a lactic ferment *any ferment capable of transforming a sugar into lactic acid.*

[1] Gesundheitsaemter t. II. 1884.

We can also foresee that this definition will bring together a number of other species differing greatly in other properties. As a matter of fact if we were to proceed in an orderly fashion we would find the *bacterium of Eberth* approximating the *bacterium acidi lactici* of *Hueppe*, the *comma bacillus* approximating certain non-pathogenic species very amply prepared for the production of lactic acid, like the ones studied by *Rist*[1] in the Egyptian leben.

These confusions would be extremely deplorable from the standpoint of biological entities and might create strange misapprehensions with regard to the application of lactic ferments in general and particularly their therapeutic use. The necessity of a classification is therefore clearly indicated.

TRUE LACTIC FERMENTS. As with Duclaux, we reserve the term of true lactic ferment to any ferment capable of cleaving the molecule of a sugar, into as many molecules of lactic acid as are necessary for its weight to equal that of the sugar from which it issued.

A hexose for example gives $C^6H^{12}O^6 = 2\,C^3H^6O^3$.

Let us at once add that this theoretical specie does not exist but there are ferments which—taking into consideration their multiplication—content themselves with a very small quantity of sugar, while they at the same time convert its almost totality into lactic acid, in conformity with the preceding equation; to such we reserve the term of *true lactic ferments*.

Notwithstanding the severe restrictions placed upon their definition these species nevertheless exceed 150 in number. The appreciation of the quantity of lactic acid furnished is, of course, subordinate to the neutrality of this acid as fast as it is formed. All arrest in the vitality of the ferment by reason of a too great abundance of lactic acid is thus avoided. It is in fact well known that the content of the excretions of a living cell or living being limits its evolution when it reaches a determined point for *there exists an equilibrium which is vital*.

Among the true lactic ferments may be mentioned those of *Hueppe*, of *Pottevin*[2] and of *Rist*. We have also isolated from

[1] Etude sur le leben Egyptien (brochure).
[2] Ann. Inst. Pasteur, t. XII. 1898.

the Bulgarian soured milks a *bacillus* and a *coccus* belonging to the same category.

The oriental soured milks are generally very rich in *true lactic* ferments, these moreover are very active and powerful as we shall see further on.

PARALACTICS AND PSEUDOLACTICS. At the side of the *true lactic ferments* and responding to our general definition of lactic ferments, there appear other organisms which also act upon sugars while giving but more or less reduced quantities of lactic acid.

We apply the term of *pseudo lactics* to those ferments which give only traces or a few hundredths (up to 3 or 4) of lactic acid and the term of *paralactics* to those whose production rises gradually to the theoretical requirements.

The *pseudo lactics* have very numerous representatives and are very widespread; some may be isolated from certain cheeses. The *bacillus* of *Freudenreich*[1], the *bacillus coli*, the enterococcus of *Thiercelin* belong also to this class.

They are found with *paralactics* and sometimes with *true lactics* in the fermentation waters of beans, peas, boiled rice, fermented beet juice, ensilated vegetables, sauerkraut, bread yeast, etc. Some confer upon these liquids a more or less great degree of resistance to putrid fermentations; most of the lactic ferments belong to the *pseudo lactics*.

The *paralactics* also present an imposing array. We may mention the one isolated by *Pottevin* which furnishes 62 per cent. of *dextro acid* at the expense of mannite and dulcite.

Generally the two last species (*pseudo and paralactics*) adjoin divers compounds of lactic acid. In composite culture media as for instance, nitrogenous media, they have a marked tendency to attack the other substances as well as the sugars. Many *true lactics* do likewise but to a lesser degree.

Lactic acids and lactic fermentations. The general definition we have adopted does not confer any exactness upon the nature of the lactic acid produced nor the nature of the sugar fermented All sugars in $C^2C^6C^9C^{12}$ are *fermentable* and furnish lactic acid. On the other hand all the lactic acids are susceptible of being

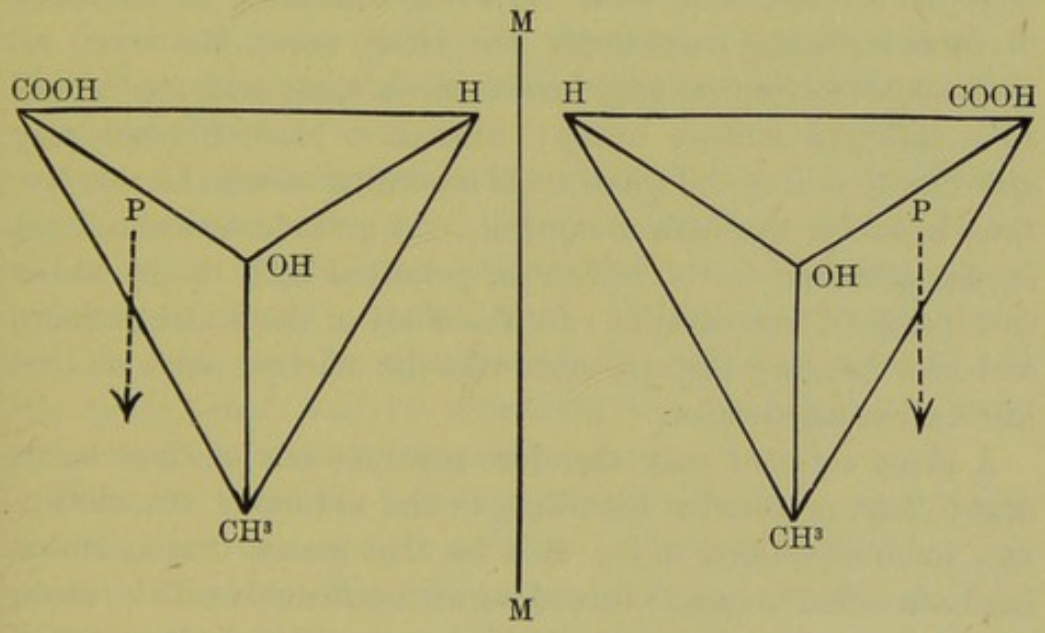
[1] Ann. de Micrographie.

generated by lactic ferments. The lactic acids as we know, are four in number: the *dextro rotatory* or *sarcolactic*, the *levo rotatory*, the *inactive acid* by *compensation* and the *passive inactive acid*.

The last of these acids has the constitutional formula CH^3, OH, CH^2, COOH.

The first three have the formula CH^2, CH, OH, COOH.

From the point of view of their properties they differ only in their rotatory power on polarized light. They have the same plane formula but not the same formula in space. Analogous facts are not rare in chemistry. This has led to the construction in space of symbols representing the constitution of the bodies, which, while acting in a different manner upon polarized light have nevertheless the same plane formula. The constitutional radicals are situated at the apices of a regular tetrahedron the center of which is occupied by a dissymmetrical carbon. Thus the lactic acids which actually concern us may be represented by the following schemas:



The carbon of C. H. being in the center of these two tetrahedrons. These two figures are not identical, they are symmetrical with regard to the fictitious mirror M. M., one being the image of the other, but they are not superimposable. Moreover, if we grant to the two radicals placed at the apices of the

two tetrahedrons, their ponderal value and if we seek the centers of gravity P. of the two heterogenous tetrahedrons so constituted; we will be able to observe that one of the centers is to the right of the plane of symmetry passing through the apices O.H. CH^3 being the figurative center, the other center of gravity is situated to the left of the same plane, so that obeying the resultant forces passing through the centers of gravity, one of the figures turns from left to right; this is precisely the one which represents the acid deviating the polarized light to the right (*dextro rotatory*), the rotation of the symmetrical figure representing the *levo acid* taking place from right to left (*levo rotatory*).

The third lactic acid having the same formula is the result of the combination in equal proportions of the two preceding ones; it is a body *inactive by compensation.*

We have taken pains to recall this stereochemic theory because it is closely related to the fermentations and because it is well to understand the meaning of the terms *dextro acid, levo acid* and *inactive acid,* terms recurring constantly in the study of fermentations, particularly the lactic ones; the more so, since some one ferment may furnish one of these acids exclusively from different culture media; whereas a same ferment may give rise to one of the three acids according to whether it vegetates in this or that culture medium. A great historical interest is also attached to the action on polarized light of the bodies susceptible of fermentation; for the study of the dextro rotatory and levo rotatory tartaric acids was the starting point of *Pasteur's* great discoveries.

A given ferment may therefore generate one of these acids, *dextro, levo,* or *inactive* according to the nature of the alimentary medium offered to it. It is for that reason that attention has been called to species furnishing an *inactive acid* with levulose, *dextro acid* with glucose; this is the case, for instance, with the *bacillus coli communis* which besides offers us an example of the influence of the medium upon the kind of acid produced.

Through the action of one of the ferments of *Pottevin* (*a paralactic*) mannite and dulcite furnish a little alcohol, acetic acid, formic acid and 62 per 100 of *dextro lactic acid.* The same

organism when placed in a peptonated solution (2 per 100) mixed with 3 per 100 of *calcium mannate* furnishes alcohol, 16 per 100 of acetic acid and 24 per 100 of formic acid *without any lactic acid.*

Kayser[1] has also shown that the lactic acid may likewise vary in nature when the sugared medium is or is not peptonated.

ACTIVITY OF THE LACTIC FERMENTS

The activity of *the lactic ferments* is nearly always increased by the presence of peptone; it even augments up to a certain point as the medium becomes progressively richer in peptone; this to a degree varying with the nature of the ferment. But in order to measure the comparative activity of the lactic ferments a medium containing only the experimental sugar and free from all other substances must be used. The cultures are placed in the incubator at a fixed temperature in the presence of carbonate of lime in excess. The output of lactic acid is then noted and the measure of greatest activity is accorded to the ferment showing itself to be the most apt of its congeners for the production of lactic acid under the requisite experimental conditions.

Power of the lactic ferments. The power of a *lactic ferment* should not be confounded with its *activity*. The power is measured by the resistance of the ferment to the increasing proportions of acid excreted by it. Experiments must therefore be conducted by withdrawing the carbonate of lime (all else being equal) and by measuring the lactic acid produced when no more is being formed.

The most powerful ferments are generally the most active as well, but frequently the activity proceeds inversely with the power. These two propositions, however, are in nowise absolute.

Power of multiplication. When examining the specific characters of a ferment we must also take into account its ability to multiply. The ferments that multiply the most are not the ones that give at the same time the most lactic acid. The reason of this can be understood, for owing to the fact that the

[1] Ann. Inst. Pasteur, t. VIII. 1894.

building of the cells is in large part performed at the expense of the sugar, the sugar serving for this purpose cannot simultaneously serve any other.

Influence of time. The element of time has a variable influence upon the vitality of the lactic organisms. Their longevity is dependent not only upon the particular specie but also and particularly upon the nature of the medium in which they are imprisoned. It has been said that their resistance or duration was generally speaking a direct function of their ability to withstand temperature; but our experiments enable us to state that it is the nature of the culture medium which exercises the preponderating influence. It is thus that some species numbered among the most resistant and selected from Oriental soured milks find their duration increased from three to nine weeks when they are placed in bouillons prepared according to a special technic. Most frequently their longevity is also in direct relation with their *power* and *activity*.

Importance of the culture medium. The longevity, activity and power may each be developed to a maximum by a judicious choice of the *culture medium* for a determined specie. A very slight variation in one of the aliments forming part of the medium sometimes suffices to bring about a very notable variation in the lactic acid output. For example, a *true lactic* ferment taken by *Pottevin* from fermented onion juice and inoculated in lactose, saccharose, maltose, glucose, galactose, mannose and invertine; these different sugar media being mixed with 2 per 100 peptone furnishes nearly 100 per 100 of lactic acid (*inactive*), whereas only 90 per 100 of lactic acid (*dextro acid* in this instance) is obtained when the proportion of peptone is reduced to 1 per cent. Generally speaking peptone increases the different positive functional characters of the lactic ferments, when its proportions are increased to a certain maximum, this varying according to the specie.

It is a very remarkable fact that with certain *true lactic* ferments, the lactic acid output may exceed 100 per 100 in the presence of peptone and this without giving rise to any simplified nitrogenous product nor to any putrefactive one particularly. These *lactic acidogens* evidently utilize the peptone not only

for the construction of their cells but also for the formation of new quantities of lactic acid at its expense.

The role of peptone in culture media is of interest because of the increasing application of the lactic ferments in intestinal therapeutics in which they are each day taking a more and more prominent part.

Given an abundance of alimentary sugars and in the presence also of the intestinal peptones, *the activity will remain an increasing function of the multiplication of the ferment.* It will even be proportional at all times with the number of active cells, the identity of which can be admitted. Consequently, a ferment prepared and adapted for existing in the intestine, one having lived in a peptonated medium and trained or accustomed to anaerobiosis[1] and capable of thriving in a temperature of 37° C. may thrive and continue to multiply for a very long time in the intestinal medium and in sequence produce lactic acid constantly, at the expense of the fermentable sugars forming part of the alimentation and to a certain extent at the expense of the peptones, the last being, moreover, exempt from all putrefactive processes in the presence of *true lactic ferments.* It may also be said that the activity is not liable to be interfered with by reason of an overproduction of acid, for this is always limited by the alkalinity of the intestinal media.

The physical state of the culture plays a considerable part. Ferments obtained in a dry state by filtration, by mechanical precipitation, by agglutination or else by desiccation at low temperatures or by a combination of these or other methods, last much longer than cultures in liquid media, the maximum duration of which is about three months. The duration of the dry preparations is so to speak almost unlimited because of the latent life imposed upon them. Per contra, when they are placed in conditions of active life their activity and power of multiplication is always inferior to that of the liquid cultures; these facts must be recognized outside of any theory.

We can understand that a seed taken from an Egyptian tomb and equally as old, will germinate with more difficulty than a

[1] Oxygen also plays a rôle in the life of most of the lactic ferments.

fresher one, or that an organism condemned to a long period of repose will take up with greater difficulty the full exercise of its functions. Be it as it may, it is only by a more prolonged use, a more sustained application by a greater insistence so to speak, that we may finally obtain from the dry ferments results equal to those obtained with the liquid cultures.

CONCLUSIONS

We propose to divide the ferments capable of generating lactic acid at the expense of sugars, into three categories.

1st. True lactic ferments a denomination already adopted by Duclaux.

These ferments are characterized by their ability to transform a given sugar and furnishing the theoretical or almost theoretical quantity of lactic acid.

2d. Paralactic ferments : Those which cleave a given sugar into small quantities of a certain number of bodies (alcohol, acetic, formic, malic acids, etc.) and a proportion of lactic acid which, although it never approaches the theoretical quantity is nevertheless rather high at times (50, 60, 70 per 100 of the theoretical amount).

3d. Pseudo lactic ferments. Those which give rise to only small quantities of lactic acid (1, 2, 3 per 100) or else traces which accompany or precede the formation of substances differing greatly according to the case.

Natural state and application. The lactic ferments are extremely widespread. They are found in milk in which they bring about acid fermentation, in cheese, butter, certain species being responsible for the bouquet to which some of these articles owe their reputations. Generally speaking they are found in a very large number of the spontaneous fermentations undergone by organic substances when deprived of life, and from the organic matters derived from them.

As long as these acidogenous fermentations continue the putrefactive proteolyses are inhibited or rather they succeed and only take place when the first are terminated.

It is thus that we can explain the very clear and well-defined anti-putrefactive action exercised by the lactic ferments when applied to the treatment of intestinal disorders. An action which becomes all the clearer if judicious choice is made of the most suitable of these ferments for the part intended for it.

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