

The cause of the coagulation of the blood : being the Astley Cooper prize essay for 1856, with additional observations and experiments, and with an appendix, showing the bearings of the subject on practical medicine and pathology / by Benjamin Ward Richardson.

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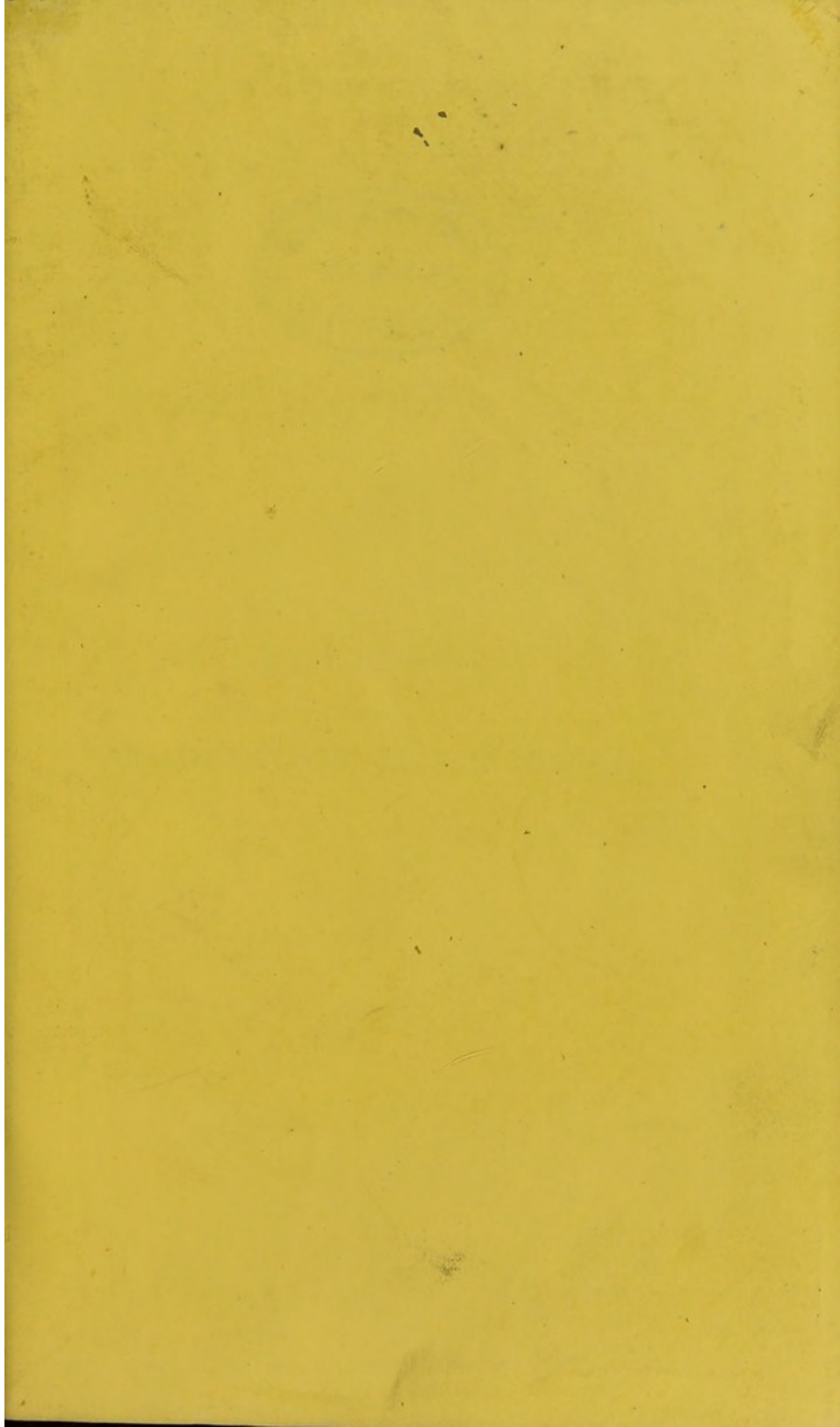
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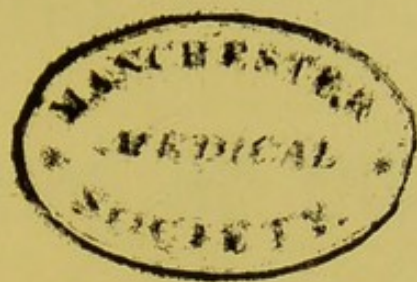
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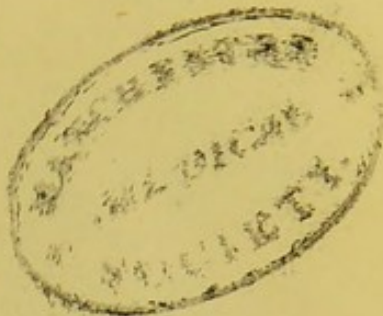




THE CAUSE
OF THE
COAGULATION OF THE BLOOD.

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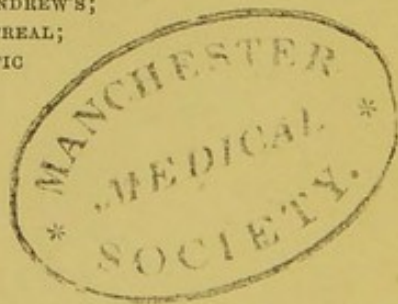


BEING
The Astley Cooper Prize Essay for 1856,
WITH
ADDITIONAL OBSERVATIONS AND EXPERIMENTS:

AND WITH
AN APPENDIX,
SHOWING THE BEARINGS OF THE SUBJECT ON PRACTICAL
MEDICINE AND PATHOLOGY.

BY
BENJAMIN WARD RICHARDSON, M.D.,

LICENTATE OF THE ROYAL COLLEGE OF PHYSICIANS OF LONDON;
PHYSICIAN TO THE ROYAL INFIRMARY FOR DISEASES OF THE CHEST; LECTURER ON PHYSIOLOGY,
AND ON HYGIENIC MEDICINE, AT THE GROSVENOR PLACE SCHOOL OF MEDICINE: FELLOW
AND A FOTHERGILLIAN GOLD MEDALIST OF THE MEDICAL SOCIETY OF LONDON;
HONORARY FELLOW OF THE PHILOSOPHICAL SOCIETY OF ST. ANDREW'S;
HONORARY FELLOW OF THE PATHOLOGICAL SOCIETY OF MONTREAL;
CORRESPONDING FELLOW OF THE SOCIETY OF SCIENTIFIC
MEDICINE OF BERLIN.



"God loves from whole to parts; but human soul
Must rise from individual to the whole."—POPE.

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TO THE
PHYSICIANS AND SURGEONS OF GUY'S HOSPITAL,

AND TO
BENJAMIN GUY BABINGTON, M.D., F.R.S.,
PRESIDENT OF THE EPIDEMIOLOGICAL SOCIETY, AND LATE
PHYSICIAN TO GUY'S,

THIS WORK IS WITH SINCERE RESPECT INSCRIBED.

ERRATA.

Page 123, line 6, for "effects", *read* "effect".

Page 215, line 24, for "32°", *read* "52°".

Page 328, line 13, after "water", *add* "at or below 60° Fahr."

Page 339, line 20, after "favour", *add* "or retard".

Page 439, line 1, for "alkali", *read* "antimony".

P R E F A C E .

IN the forthcoming Essay, I lay before the reader the results of some inquiries, which, commencing in the year 1850, have been carried on so steadily to this date, that in reviewing the long interval, I can scarcely recall a day, some portion of which has not been set aside to the study of one or other of the subjects hereafter to be described. But the work has been so deeply interesting and progressive, that the years seem gone as an hour; and if I have one regret at this moment, ~~it~~ is, that the same years with their labours cannot return.

In 1853, I became for the first time aware that the subject of the next Astley Cooper Prize, was "The Cause of the Coagulation of the Blood." Working on as I had previously done, I arrived in 1855 at what seemed to me to be a rational and true explanation of the phenomenon of coagulation. I therefore decided to send in an Essay in competition. This Essay, to which the prize was awarded in 1856, is here produced, with numerous additional experiments and ob-

servations (marked off by brackets to distinguish them from the original), and with an Appendix which is also new.

I have been rendered fortunate and happy, in the whole course of these labours, by the kindly interest and willing assistance which have at all times been afforded to me by those numerous professional friends and *savans* who have come forward to witness and assist in my experiments, and to tender their opinions and suggestions. I have referred to many of these in the text, and return to all my warmest thanks.

To my colleagues of the Medical Society of London, I can never, in this respect, be too grateful. Before them, as an entire stranger, I laid timidly the first fruits of these inquiries, and as a friend the latest. But, from first to last, their fair criticism, kind encouragement, and scientific interest, have been the same,—to me invaluable. I return also my best thanks to the Council of the Royal College of Surgeons, for having granted me the free use of their great library; and to their learned librarian, Mr. Chatto, for the courteous assistance which he has often rendered me.

To Dr. R. Willis, of Barnes, my hearty acknowledgements are specially due. Working together for many years in the same field of practical labour and observation, many of the facts relating to disease, recorded in these pages, were common to both of us, and afforded matter for our mutual study. Here the more extended learning of my fellow-labourer came willingly to my

assistance, and helped me not a little in the first steps of the way.

To Drs. Snow and Thudichum, and to Mr. Thomas Taylor, Lecturer on Chemistry at the Middlesex Hospital, I express equal gratitude.

In the past three years I have received the able assistance of Dr. Alexander Henry and Mr. Wentworth Scott; and I can never forget or overestimate their unwearied and efficient services. The former in literary matters, the latter in experimental, have lent me their ready skill in the same free and unanimous spirit, and with the same intelligent industry and interest. During publication, too, Dr. Henry has relieved me of much anxiety, by undertaking the revision of the press—a labour in which he is a perfect master. In his laborious and learned way he has, moreover, carefully perused the historical chapters, so as to ensure for them the greater accuracy and value.

To Dr. Barker, of Bedford, my further thanks are due for carrying out at my request several experiments which required much time, expense, and trouble. Engaged as Dr. Barker is with the harassing duties of the busy medical practitioner, I can better feel than express the friendly manner in which he undertook, and so efficiently performed, the experiments recorded in this work as having been conducted by him.

I have to offer a word of apology and explanation for the delay which has occurred in the publication of this Essay. The work was intended for the latter part

of last, or, at latest, the beginning of the present year, and it was sent to press with this intention. But having given at the Cheltenham meeting of the "British Association for the Advancement of Science" an exposition and full abstract of the Physiological part of this work, many inquiries soon began to be made of me, by medical friends, as to the bearings of the physiological question on Pathology and Practice. I was thus led into new lines of experimental inquiry, the result of which has been the preparation of the Appendix herewith published. This preparation, in the midst of other pressing scientific concerns, has taken up more time and work than I ought, in strict prudence, to have devoted to it, and is, after all, but an instalment of a wider series of inquiries. But if, as it is intended, the subject matter of the Addendum should ultimately prove of service to pathological and practical medicine, the good-natured Reader will, I hope, forgive the delay, in consideration of the labour which has called for it.

Whatever position the views published in this work may now or in after time take, I, as their author, can state thus much; that they have been deduced without any preconceived ideas, and in an earnest attempt to follow out the pure inductive method of research; that if they gain ground, the success is entirely due to the inductive principle; and that if they fail, the failure is exclusively my own.

As the conclusions at which I have arrived are based on experimental evidence, so I hope to see them tested

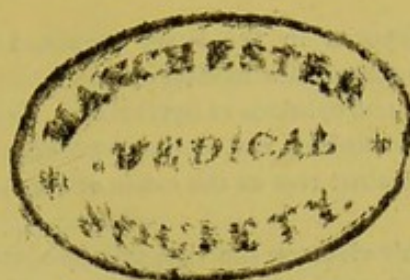
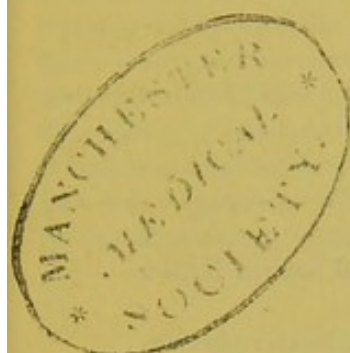
by similar evidence ; and I wish this remark to apply, not to the phenomenon of coagulation alone, but to every other experimental inference, and specially in regard to the artificial production of certain diseases explained in the last part of the work ; since this latter point bears the same relation to Pathology as the preceding to Physiology, and, in a practical sense, is equally important. The experiments have all been conducted with the utmost regard to simplicity of detail, and are described as they were performed, so as to render their repetition the more ready.

And whereas it is the business of no man here to set himself up as the prophet of Nature, nor to run before her, and so far to dominate over her as to dogmatically assert that she does things which she does not, because he has given the *ipse dixi* ; so, in now recording certain new interpretations of some natural phenomena according to my best ability and closest observation, I hold myself still the servant of my divine mistress, ready at any moment, as I grow older and more learned in the knowledge of her laws, to be corrected by her, and to accept her, but none other, as umpire on each and all interpretations which are submitted to the reader. For I know that a true interpretation of a natural phenomenon is in the end irresistible, and that whatever is not true will fall of itself, unsustainable in the presence of the immutable and constantly recurring fact.

To the true scholar, Nature, the manuscript of the Supreme, is the only book of reference. To him, the

Elements are the letters of this book—their combinations the words—their manifestations or phenomena the thoughts. Turning up but a brief sentence of this inexhaustible work, I have tried its interpretation with willingness and industry, but with much more of reverence and admiration. How feeble my efforts are, how infinitely poor my abilities for the task, how marked my shortcomings, I know better than the most unfriendly critic could suggest. For it is the peculiarity, nay, the fatality, of natural and experimental studies, that the more one learns from them, the wider and wider expands the argument, and the stronger and stronger becomes the consciousness of the mind's limitation, and of the facts, that the phenomena of the universe admit of no isolation, and are seen but as material visions, beginning in the unknown, ending in the unknown—having to us, indeed, no beginning and no end.

12, Hinde Street, Manchester Square,
December 21st, 1857.



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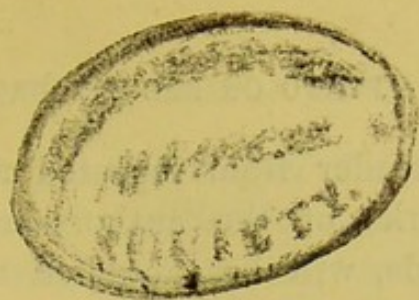
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Of these illustrations, the coloured plates are by Tuffen West; and, like all the productions of that excellent artist, are close representations of nature. The microscopical drawings are by Mr. Lens Aldous; the mechanical by Mr. Barrow. Both have been executed in wood with great skill by Mr. Hart, of Gloucester Street, Bloomsbury.



COAGULATION OF THE BLOOD.

CHAPTER I.

HISTORICAL MEMORANDA ON THE SUPPOSED CAUSES OF THE COAGULATION OF THE BLOOD.

"Every physician will and ought to make observations from his own experience; but he will be able to make a better judgment and juster observations by comparing what he *reads* and what he *sees* together. The searcher of authors has the benefit of other men's experience as well as his own, and it is by the joint concurrence of these that we can hope for any considerable advancement in knowledge. Were it not for this, the oldest practitioner would always be the best physician, and there would be little difference, even as regards the scientific part, betwixt an old woman and the most regular professor."—FRIEND.

It is not my intention in this chapter to follow up in chronological order the labours and discoveries of those who, either in ancient or in modern times, have endeavoured to solve the problem of the cause of the Coagulation of the Blood. My object in these memoranda is simply to collate the various theories and hypotheses, which have been advanced regarding coagulation. The authors, advocates, or opponents of such theories or hypotheses will, however, receive attention incidentally, as they may have originated, supported, or opposed the various opinions or arguments which have to be narrated. It will be my endeavour to condense what has here to be said, as far as is consistent with plain writing and with fairness of description; while, to prevent the interruptions which always

occur to the reader from repeated references to foot-notes, the works of the authors mentioned, as the history proceeds, will be tabulated at the end in an alphabetical list. Should it happen that the views of any writer are omitted, I crave pardon, and explain that as this essay is mainly the record of an original inquiry, no strain has been made towards historical display. I place before the reader, in fact, in acknowledgment of good and learned assistance, the names merely of such authorities as have answered fully to certain matters of fact and argument, which I was anxious to obtain before embarking in original work, and to bear in mind afterwards. For I hold it as a rule, that no one can pursue an original inquiry, who does not know that true originality of thought includes two principles; the one consisting in a knowledge of what is not original, *i. e.*, of what has been done; the other in an appreciation of what remains to be originally done, and how to do it.

The subject of the coagulation of the blood did not escape the attention of the old physiologists of Greece; and even at the early period when they lived, the cause of this phenomenon was supposed to depend on a net-work or fibre in blood, which, by coming together and contracting, gives rise to coagulation—a supposition which has been sustained to the present day. Plato, in his *Timæus*, very distinctly remarks, that throughout the blood are scattered a number of fibres, which give to the fluid certain measures of tenuity and density; so that it may neither flow through the “thin” structures, nor, from its density, become unadapted to motion, and thus find a difficulty in flowing back by the veins. And he further observes, that the blood is

under the natural guardianship of the fibres ; because, if these are collected together in dead blood, all the remaining blood becomes diffused ; and when blood is let out quickly, it coagulates in consequence of the cold surrounding it.

Dr. John Davy points out also that Aristotle paid attention to the same question, and considered that a substance in the blood, which we must believe to be the same as that now called fibrin, is liquid so long as the blood is in motion in the living body, like the matter of curd in uncoagulated milk, and solid only and fibrous after extraction, the coagulation being the effect of the change.

The process of coagulation did not, however, receive much further attention until the Harveian discovery of the circulation. This discovery acknowledged, certain pathological states of the blood became subjects of special study ; and Malpighi was led to discover and point out accurately the fact, that the buffy coat is made up of a substance natural to the blood, its concrete or reticulated part, and identical with the white clots not unfrequently found after death in the circulatory system, and particularly in the heart.

Again, even for a long period after Malpighi, great confusion existed regarding the different parts of the blood. A few observing men, it is true, distinguished correctly the differences between corpuscles, serum, and “spontaneously coagulable lymph”, but their views were not accepted. By other men, serum and “spontaneously coagulable lymph” were confounded as one and the same. By a third and more numerous body, this lymph was ignored altogether, and the globules were turned to as everything, so that the phenomenon of coagulation was

considered merely to consist in an aggregation of these, brought about by some force of attraction. There is not a more interesting historical subject in physiology than the one here noticed. But I do not discuss it at length, because Mr. Gulliver, in his introduction to Hewson's works, has said all that can be said, with such masterly judgment, candour, and critical learning, that it were impossible to dwell on the topic without trespassing on his domain.

Referring to the views, correct, at least, in part, of Malpighi, Lower, Borelli, Boyle, Collins, Ruysch, Petit, Butt, Glaubius, and Quesnay; and to the incorrect and confused views of Leeuwenhoeck, Boerhaave, Haller, and Senac, Mr. Gulliver shews that the speculations connected with Leeuwenhoeck's microscopical researches supplanted accurate experimental inquiries into the properties of the blood. When, therefore, "the errors consequent on this state of things began to wane, the blood sank into neglect, and the just observations of Malpighi, Lower, and Borelli were lost for the greater part of a century." In England, the errors continued to the year 1760; on the continent, even later than 1771, the year when Hewson first published his labours. To Dr. Richard Davies Mr. Gulliver assigns the credit of "having revived and established that correct knowledge of the three parts of the blood which was taught afterwards by Hewson, Fordyce, and the Hunters." This may be so; and, indeed, Hewson himself laid no claim to the discovery of the constituent parts of the blood, but I take it, that he (Hewson) held more correct views on this matter than any of his predecessors. He described *the red or colouring part*—red corpuscles; the *lymph*, or spontaneously coagulable part—fibrin (so called

thirty years later by Fourcroy); and the *serum*; the latter containing, as he taught, a constituent which, agreeing with the white of egg, remains fluid when exposed to the air, but coagulates when exposed to heat—albumen. It is but fair, moreover, to give to Hewson the credit of having been the first to demonstrate that the transition of the coagulable lymph from the liquid to the solid state, is an essential and independent part of the process of coagulation. This view was theorised on before; but was not proved by experiment until Hewson skimmed off the size from the blood of a phthisical patient, and observed its spontaneous separation into colourless clot and serum.

Since 1771 there has been confusion again; some sort of retrogression towards Leeuwenhoeck's speculations; some progression, without experiment, into profound and mystical controversies and descriptions. So science, like the great ocean, fluctuates; but, by fluctuating, encroaches and advances, her vitality and sign of existence being her unceasing unrest. At the present moment, Hewson's definition of the parts of the blood is the one generally accepted.

Historically, then, we start with the knowledge, that the first true steps in the problem on which we are engaged have consisted in the discoveries of the "blood-fibre" (in this day called fibrin); of the tendency of this fibre to coalesce under certain favouring conditions; and of this coalescence as one cause of the phenomenon of coagulation. The next step in the inquiry, Why does the fibrin concrete at all? is continued to modern times, and opens for consideration numerous experiments, theories, and hypotheses.

THE VARIOUS THEORIES AND HYPOTHESES.
TEMPERATURE.

The first, and possibly the oldest hypothesis, is that which attributes coagulation to loss of *temperature*. This seems to have been the hypothesis held by the Greeks, and is in strict accordance with the general doctrines regarding heat held by some of their philosophers, such as Heraclitus, who supposed—not incorrectly in the abstract—that heat was the elementary and moving principle of all things. Thus Plato remarks, as I have already quoted, that the blood, “when let out quickly, coagulates in consequence of the cold surrounding it.” Aristotle and Hippocrates seem to have entertained a similar opinion; and the same was received, in after days, by the discoverer of the circulation of the blood himself. I need scarcely repeat the well known fact, that the fallacy of this hypothesis was satisfactorily disposed of by Hewson, who proved, indeed, that the very reverse obtains; and that, while an increase of temperature favours the tendency to coagulation, a great decrease causes the blood to remain longer in a fluid state. The following experiments, performed by Metcalfe, and described in his work *On Caloric*, published in 1843, confirm, in a manner too striking to be omitted or forgotten, the correctness of Hewson’s views.

“A healthy pigeon”, says this writer (Metcalfe) “was immersed in water at 47°, with the exception of its head, when a thermometer *in recto* fell from 108° to 74° in twelve minutes; and the poor bird presented all the symptoms of approaching convulsions, coma, and death. In this state it was decapitated, and its blood made to flow into

three saucers, one of which was placed in water at 130° , another in water at 110° , while the third was exposed to the temperature of the room at about 60° ; when the blood in the first saucer began to solidify in three minutes, that in the second in four minutes, and that in the vessel at 60° but slightly in seven minutes." In another experiment, where a pigeon was treated in the same manner, but without previously reducing its temperature, the blood coagulated sooner at 110° than at 60° , sooner at 130° than at either point, and more firmly in five minutes than the blood of the other pigeon at the expiration of thirty minutes. In another experiment, Metcalfe found that, when half an ounce of blood from the divided vessels of the neck of a healthy sheep was put in a small tin cup, and surrounded by a freezing mixture of snow and salt, it began to solidify just perceptibly in three minutes, and was quite frozen in six minutes. After remaining in this state above an hour, it was gradually thawed by exposure to the atmosphere (which was at 51°), and formed a loose coagulum. After narrating several experiments of a most conclusive kind, Sir C. Scudamore, in his *Essay on the Blood*, states that the conclusion is clear, that a remarkably high temperature hastens the coagulation of the blood; and conversely, that the retarding influence of cold is still more marked.

The effects of temperature have moreover been inquired into by various physiologists, in relation to the coagulative power of the blood of warm and of cold blooded animals, and to the effects of cold or of changes of temperature on animals themselves: and it has been shewn, first, that in cold blooded animals, *cæteris paribus*, blood coagulates more slowly than in the warm blooded;

and, secondly, that the blood of an animal, if drawn when the temperature of the body is low, coagulates much more slowly than when the temperature is high, or at the natural standard.

The condition of the blood in the fluid state, in animals hybernating, has often been adduced to shew that the effect of extreme cold on the blood is that of preserving this fluid in an uncoagulable condition.

The opinions of many writers, then (opinions which receive, by the way, the support of no less distinguished a writer than John Hunter), all go to shew that the ideas of the first physiologists, with regard to the effects of loss of temperature on the blood, are absolutely incorrect; and, although they do not lend support to a modern view, that temperature has no effect, they indicate that an increase of temperature, whether derived from animal heat or from external sources, tends, under favouring conditions, to increase the rapidity of coagulation in healthy blood.

The following statements, according to Metcalfe, form a *resumé* of the leading facts connected with the effects of temperature on the blood, whether in or out of the living body:—

“ 1. The contractile power of the blood when removed from the body, like that of the muscular fibres, is in proportion to the quantity of respiration, mean healthy temperature, and aggregate energy in the different orders of animals; being greater in birds than in mammalia, and greater in the latter than in reptiles and fishes.

“ 2. As the temperature of arterial is greater than that of the venous blood, so does the former coagulate more quickly and firmly than the latter.

“3. As the vital energy of animals is always diminished by reducing their temperature below the natural standard, so is the coagulation of the blood retarded by the same means, and wholly prevented by long-continued cold.

“4. The blood of individuals belonging to the sanguine or dynamic temperament, coagulates sooner and more firmly than in such as are of a weak and phlegmatic constitution, while its contractile power is diminished by whatever impedes the function of respiration, as in phthisis, asthma, disease of the heart, the cold stage of fever, and all diseases of long standing, by which the powers of life are greatly reduced.”

Regarding the influence of temperature on the blood as it escapes from the body, Lehmann observes that we are still ignorant how far this may affect the period of coagulation, and he points out the difficulties that stand in the way in the investigation of this problem. The question, whether, during coagulation, heat is evolved from blood, has been discussed on many occasions; Hunter and Dr. Davy took the negative view of this question. Dr. Gordon and Sir Charles Scudamore were of opinion that a slight evolution does take place.

EXPOSURE TO THE AIR.

Having disproved the ancient notion concerning the effects of temperature, Hewson raised a theory of his own regarding coagulation, which attributed the occurrence of the phenomenon mainly to the air. He seems to have been led to this conclusion by discovering that blood, retained or tied up in a vessel—say a vein—of an animal, coagulates much more slowly than when ex-

posed to the atmosphere, and by observing the negative effects of a low temperature. This theory has not been very favourably received by succeeding physiologists, who have shewn that blood, effused into serous cavities or cellular structures, does sometimes coagulate, though not exposed to the air; and that even in the veins themselves, this change may take place during life; a fact which Hewson admitted.

The condition of the blood when placed *in vacuo* has also been inquired into by various experimenters. Lehmann states that blood coagulates rapidly *in vacuo*, in consequence of the violent action induced in the molecules of the blood by the rapid development of vesicles of gas and of aqueous vapour. Scudamore (p.27) came to three conclusions on the effect of exposure *in vacuo*, viz.: 1. That at a reduced temperature *in vacuo*, coagulation is hastened. 2. That atmospheric air being simply excluded in a stoppered bottle, the temperature not being reduced, coagulation is retarded. 3. That all communication with atmospheric air being prevented, the temperature not being reduced, coagulation is much retarded. This author was also of opinion that the extrication of gases, especially of carbonic acid gas, from the blood, influences materially the period of coagulation. Simple exclusion from the air, without the vacuum, *retards* coagulation, in the opinion of Dr. Carpenter, who observes, that if blood be received in a vessel under oil, its coagulation will take place slowly, a fact first noticed by Dr. Babington.

The question of the effect of exposure to the air on coagulation was further inquired into by Sir Humphry Davy, who found that the mere exposure of blood to the atmosphere, nitrogen, nitrous acid, nitrous oxide, and various other gases, does not materially affect the process.

REST AND MOTION.

Another theory on the process of coagulation has been that it arises simply from absolute rest. I do not know who originated this theory; but it has been referred to incidentally by various authors. Thus Lancisi, in speaking of aneurism, remarks on the separation and coagulation of glutinous chyle in aneurismal cavities; and implies that, as this is merely held in mechanical suspension in the blood, it is prone to separate and become deposited whenever the motion of the blood is slow. He compares an aneurism to a lake formed in the course of a river; and concludes, that as the insoluble substances, which are mechanically suspended in the natural current of the river, where the motion is rapid, are laid down on the sides of the lake, where the motion, from well known dynamical causes, is slow, so the blood, when flowing through the arteries, holds in suspension its solid constituents, while, in flowing through an aneurism, where the motion is impeded, it deposits these constituents on the sides of the sac. Rest and cold were assigned by Davies as the causes of coagulation.

Dr. S. Collins, in his work on *Anatomy*, written in 1685, contends that polypous concretions in the heart are identical in structure with the buffy coat of coagulated blood, and that they arise from a languid motion of the blood current, being deposited from the blood in a manner analogous to the formation of stone in the bladder. Dr. Brown, too, writing in 1684, remarks that depositions of fibrin and firm clots of blood are most commonly found on the right side of the heart, and most frequently in the right auricle; an effect due mainly to the slow motion of the returning blood through these parts of the circulation. Spallanzani

also taught indirectly that rest is the cause of coagulation; since blood stagnates and coagulates most quickly where its motion is slowest, as in the extreme parts of the circulation. The same view has been supported by more modern physiologists and pathologists, who have argued that the tendency to coagulate is greatest in weakened animals. Magendie, who entertained a similar opinion, made an experimental trial by introducing a tube into the two extremities of a divided artery, and found that the blood remained fluid only so long as the action of the heart continued to drive it forward. Magendie also, with J. Simon and Carswell, refer to the experiment of passing a ligature, or needle, transversely through an artery, and to the fact, that a coagulum of fibrin forms upon the foreign substance thus introduced into the circulating current. On a similar basis of reasoning, reference has often been made to the frequent coagulation of blood on the valve cords of the heart, on indurated valves, and on any other points in the circulatory apparatus which, from retarding the blood current, form favourable *points d'appui* for the formation of fibrinous clots.

Dr. Bostock, in summing up the causes of coagulation, supports the view that the process depends on cessation of motion. He remarks, "that, as fibrin is gradually added to the blood, particle by particle, while this fluid is in a state of agitation in the vessels, it has no opportunity of concreting; but when it is suffered to be at rest, either within or without the vessels, it is then able to exercise its natural tendency. In this respect," he adds, "the coagulation of the fibrin of the blood is very analogous to the formation of organised solids in general, which only exercise their property of concreting or coalescing under certain circumstances, and when

those causes, either chemical or mechanical, which would tend to prevent the operation, are not in action. Upon this principle, we shall be induced to regard the coagulation of the blood as analogous rather to the operation by which the muscular fibre is originally formed, than to that by which its contractile power is afterwards occasionally called into action."

On the other side, it has been forcibly urged that the mere statical condition of the blood has little, if anything, to do with its coagulation. The fact stated by Hewson, and supported by Scudamore, and lately by Stromeyer, that if a portion of blood be tied up in the vein of a living animal it does not coagulate for some hours, unless let out, when it may coagulate rapidly, is thought by some to settle negatively the stasis theory. Instances have been related, moreover, where blood effused into the cellular tissue, or other soft parts, has remained fluid for weeks, and has coagulated immediately on being let to escape into a vessel. There have thus been adduced, to oppose the theory of rest as a cause of coagulation, the very arguments which have been brought forward by its supporters as fully *substantiating* their idea. It has been further urged, that if the particles of fibrin were merely mechanically suspended in the blood, they would be as easily distinguishable by the microscope in an isolated form as are the blood corpuscles. Some interesting inquiries on this point, favouring the mechanical suspension view, have been made by Dr. A. Buchanan; and Dr. Milne Edwards is inclined to believe that fibrin, like the proper globules, is merely suspended in the mass of the blood in a state of extreme subdivision, and possessed of transparency too perfect to be distinguished in the surrounding fluid.

VITAL FORCE.

The idea that the coagulation of the blood is due to some peculiar principle of vitality, is included in the well known hypothesis of John Hunter. However carefully the works of this physiologist are studied, one finds a difficulty in understanding what he precisely meant by the "vital principle," or its effects in promoting the coagulation of blood. In one sentence he remarks, "This disposition to coagulate, when out of the vessels, or when retained in them without motion, till the consciousness of the use of motion, and, of course, of fluidity, is lost, is one of the effects of the life of the blood." This sentence, obscure as it is, includes, as fully as any other, Hunter's view. That he himself was not satisfied, is obvious; for he proceeds to remark on the use he has made of the word "consciousness," explaining that he has employed that term because we have no language existing answerable to all his views of the animal economy; and that to coin words would not answer his purpose, because he must then have a dictionary of his own. In a further sentence, Hunter speaks of coagulation "as a species of generation, or as the first action or establishment of a power of action within itself, so as to form itself into muscular fibres—the only powers in an animal." The only explanation of this hypothesis that can be arrived at, is, that it supposed to exist in the body a separate principle or entity, which, although taking part in, and overruling all the organic processes, is yet distinct from them, and is itself unmodified by the changes it excites. This principle, therefore, acts on the blood in the body so as to form it into the various structures;

but when blood is removed from the vessels, this fluid, being still acted on by the living principle, undergoes coagulation—an analogous phenomenon.

In order to add force to his hypothesis, Hunter relates several cases, where death took place from the instantaneous and complete abstraction of the presumed vivifying principle. A gentleman in perfect health dies instantaneously from passion; and death takes place in every part at once. A healthy woman, in giving birth to a child, dies instantaneously. A soldier receives a blow on the pit of the stomach, and succumbs at once. An animal is struck dead by lightning. Two deer are hunted to death; in which case they acted till every power of action ceased. In all these cases, the blood was in a fluid state, and did not coagulate on being exposed; and the muscles were not rigid—a result due to the rapid abstraction of the life of the solids and of the blood. In other cases, he adds, where an animal dies in the common way, the vital actions are first destroyed, but life still exists: for the muscles contract and the blood coagulates.

In other parts of his works, Hunter dwells on the same hypothesis. "Coagulation," he remarks, "I conceive to be an operation of life; and I imagine it to proceed upon the same principle as the union by the first intention. It is particle uniting with particle by the attraction which in the blood forms a solid."

To these opinions of Hunter, regarding a vital influence, strict obedience was for many years paid. They lost ground as the labours of Magendie became more prominently marked, and as the solution of the chemical problems of life advanced. In these present days, they are again being reverted to. Franz Simon, in his

desire to avoid particularising the causes of coagulation, says, in a word, "it is a vital process," and Dr. Carpenter, in one place, speaks of the coagulation of blood as an evidence of vitality, and says that a deficiency of coagulating power in blood is due "to the want of due elaboration in the fibrin alone, or to the destruction of its vital endowments by some agent which has a noxious influence upon it."

NERVOUS INFLUENCE.

Thackrah was of opinion from his experiments, that blood, placed in an organised structure removed directly from the body of a living animal, coagulated less speedily than when it was placed in a similar structure from which the vitality had absolutely passed away. These conclusions receive opposition from certain experiments of Scudamore directed to ascertain the same point.

But Thackrah's views being in harmony with the hypothesis of the existence of a nervous force, generated in the medullary substance of the nerve-centres, and communicated by the nerve-cords to all parts of the economy, supplying or governing nutrition, secretion, circulation, and all the organic processes, it has been argued from them that the fluidity of the blood in the living body is kept up by this nervous force, which has been supposed by some to be communicated to the blood in the lungs by the nerve-filaments. To this hypothesis a kind of force has been added, by the argument that the blood is found fluid in cases of death from electricity, and where life has been destroyed by sheer exhaustion—in the parlance of the neuro-physiologists, by *nervous* exhaustion. This hypothesis, which is now well-nigh exploded, has not unfrequently been confounded with

the vital hypothesis of Hunter, whose writings, indeed, tend not a little to support such a confusion of ideas. Thackrah's summary runs thus: "I conclude that the vital or nervous influence is the source of the blood's fluidity." (*Essay*, p. 91.)

CHEMICAL HYPOTHESES.

The advance of modern chemistry has led to not a few theories, or rather hypotheses, regarding the cause of coagulation. One point that has been forcibly urged, is, that the blood, when drawn from a vessel, is prevented from coagulating by the addition of certain salts and other chemical substances. Thus it has been stated, that the fixed alkalies completely prevent coagulation; and that some of the vegetable acids, as the acetic, have the same effect. The various salts which are said to have this property are, common salt, the tartrates and borates, nitrate of potash, acetate of potash, chloride of potassium, sulphate of copper, acetate of lead, tartrate of potash, ammoniacal sulphate of copper, nitrate of lime, chloride of iron, sulphate of potash, sulphate of magnesia, and chloride of ammonium. Among the vegetable salts are nitrate of strychnine and nitrate of morphine, and the vegetable alkaloids, nicotine and morphine. Mr. Blake found that the blood was not coagulated after injection into the veins of caustic soda, carbonate of soda, sulphate of soda, ammonia, nitrate of silver, sulphate of zinc, sulphate of iron, phosphoric acid, arsenic acid, arsenious acid, oxalic acid, infusion of galls, infusion of digitalis, and alloxan. Magendie found a fluid condition after injection of putrid matters into the circulation.

It has been stated that coagulation is favoured in

drawn blood by the addition of acetate of morphine, solution of sugar, alcohol, ether, tannin, starch, alum, benzoic acid, or iodine. Magendie observed that the injection of a solution of bichloride of mercury into the veins was followed by the coagulation and separation of fibrin. In the hands of Gaspard and Mr. Henry Lee, the injection of pus into veins, or its addition to blood drawn from the body, has produced rapid coagulation. The injection of brain substance into the veins has led to a similar result; and Mr. Blake found the blood coagulated after the injection of the following matters: liquor potassæ (firmly), carbonate of potash (firmly), nitrate of potash (firmly, blood scarlet), nitrate of soda, nitrate of ammonia, nitrate of lime, nitrate of baryta, chloride of calcium, chloride of barium, chloride of strontian, sulphate of magnesia, sulphate of copper, acetate of lead, arsenite of potash, nitric acid, narcotine, tobacco, strychnia, conium, hydrocyanic acid, euphorbium, and water in quantity. On the subject of salines and their effects on the blood, Nasse comes to a general conclusion, differing, indeed, in a great degree from that of any other observer. He argues that almost all salts, when not used in too large quantities, accelerate coagulation, though in small quantities they may retard it. Nasse believes, too, that water in small quantities hastens coagulation, and in large quantities retards it. (Lehmann, vol. ii, pp. 197-8.) Gulliver points out that blood may be kept fluid for weeks by the neutral salts, and may then be coagulated by dilution with water.

It will be observed, that various contradictions exist in these statements; and that the effect which is produced by a given agent in drawn blood in one experiment, seems to be just the reverse of what occurs in

other experiments when the same agent has been injected into the living circulation. Franz Simon, in fact, seems to experience so much difficulty in accounting for coagulation on the chemical process, that he refers it to the old doctrine of vitality, as I have before shown. Other physiologists and pathologists, however, more daring than Simon, seizing on the fact that the blood, when drawn from the body, may be kept from coagulating by some alkaline solutions, have argued that upon alkalinity of the liquid part of the blood depends the non-coagulability of that fluid during life: in short, that fibrin is chemically dissolved in the living blood. Dr. Fuller, in his excellent work on *Rheumatism* (1st edition), accepts this theory, and argues that the cause of the deposition of fibrin on the valves of the heart is due partly to its presence in unusual quantity, and partly to the weak state of solution in which it is held, in consequence of that extreme acidity of the system, which is so well marked in acute rheumatic affections.

Further experimental researches of a chemical kind relate to the effects of gaseous substances in retarding or increasing the coagulation of the blood. I have already referred to the experiments of Sir Humphry Davy on this point, which shewed that the exposure of drawn blood to nitrogen, nitrous acid gas, oxygen, nitrous oxide, carbonic acid, carburetted hydrogen, and atmospheric air, did not modify coagulation. Other experimentalists have shewn that the process is not retarded by the fluid being placed *in vacuo*. From a long series of experiments performed by Dr. Polli of Milan, with great care, it would seem that coagulation takes place with equal freedom in pure oxygen, nitrogen, and atmospheric air; but that the presence

of carbonic acid always impedes it. Carbonic acid gas, according to this author, is always given off from blood during coagulation; and the more quickly this occurs, the more quickly the blood coagulates. The more carbonic acid gas the blood contains, the more slowly it coagulates, according to Polli, and the greater chance is there of a buffy coat being formed; while a buffy coat, formed over a dark clot without froth, is always a sign of the blood being surcharged with carbonic acid.

On the subject of the effects of gases on the blood, Lehmann also remarks that, since the blood contains gases, the different quantities in which they occur modify coagulation; hence blood rich in carbonic acid coagulates less rapidly than when the contrary is the case. Scudamore, in his *Essay on the Blood*, in referring to carbonic acid, states that he feels himself fully authorised in concluding that the period of time in which the blood coagulates depends, in a great measure, on the quick or slow extrication of carbonic acid gas. The evolution of this gas takes place most freely as the blood begins to concrete, and ceases when coagulation is completed. It is evidently, he presumes, an essential circumstance in the process of coagulation, as the same causes which retain the carbonic acid in the blood delay coagulation.

In relation to the point now before us, there is an interesting and curious paper in the *Philosophical Transactions* (vol. for 1818, p. 81), from the pen of Sir Everard Home, which I notice here incidentally only, but to which Scudamore refers at length. Sir Everard, in giving an account of the evolution of carbonic acid from the blood during coagulation, relates some experiments made at his request by Professor Brande, from which it was inferred, not only that carbonic acid

gas exists in both the venous and the arterial blood of man, but that as much as two cubic inches could be extracted from every ounce of blood. Sir Everard did not use this statement as one particularly bearing on coagulation, but as supporting an hypothesis that as, in the coagulation of dead blood, channels are made in it by the escape of carbonic acid, so in the living body effused blood may be made vascular by the blood-vessels transmitting blood into it, by channels similarly produced.

Mr. Bauer seems to have been the first observer who stated that blood in coagulating exhales carbonic acid.

Contrary to the views of Scudamore regarding carbonic acid, Dr. John Davy held that the agitation of carbonic acid gas with blood does not retard coagulation; that newly drawn blood really *absorbs* carbonic acid; and that water charged with this gas and added to blood does not affect the coagulating process.

Without endeavouring to define its nature, Spallanzani conceived that there was in blood an elastic invisible gas. In this view he was supported by his English translator, Dr. Hall, who urged this point on the notice of physiological inquirers, as one deserving special notice, and as promising to explain many of the phenomena connected with the blood and circulation.

In speaking of the various chemical hypotheses which have been raised regarding coagulation, it would be an error to omit that which is held by Schmidt and Schulz, and in some degree supported by the writings of Mulder; viz., that fibrin, *per se*, does not exist in the circulating living blood at all. Schmidt's arguments are intended to prove "that, as blood escapes from the circulation into a cup or other vessel, an acid albuminate of soda, which previously existed in a state

of solution in the blood, becomes disintegrated into its component parts in such a manner that a less acid, neutral, or basic albuminate of soda remains dissolved; while the other atom of albumen separates under the form of protein, which we call fibrin." The fibrin thus *formed* and separated, afterwards contracts into the smallest possible volume, just as freshly precipitated silica, alumina, and phosphate of lime contract when isolated. Respecting this peculiar hypothesis, Lehmann, to whom I am indebted for its history, observes, that if we watch the separation of fibrin into filaments during coagulation, it will be seen that "the analogy with hydrated alumina affords no special support to this hypothesis, which, at first sight, seems sufficiently plausible."

EFFECTS OF ELECTRICITY AND GALVANISM.

Gerhard and Hufeland, according to F. Simon, have shewn by experiment that an electric current, continuously passed through blood, tends to keep that fluid in an uncoagulable state. Scudamore tried the effects of both electricity and galvanism on drawn blood. The results of his experiments, with reference to electricity, differ from those of Hufeland and Gerhard. He found that blood exposed to the electric current gained in temperature two degrees on the introduction of the current, but coagulated as soon as did other blood removed at the same time from the same person and allowed to concrete naturally; and again, that the blood treated by electricity coagulated more firmly. In experimenting with the galvanic current, he found also that the temperature of the blood was raised. In one case there was a copious evolution of gas at the negative pole, and in all cases the current gave rise to a peculiar process of coagulation and decomposition.

PHYSICAL INTERCHANGES IN THE CONSTITUENTS OF THE BLOOD.

Of late years, an hypothesis has been gaining ground, that the fluidity of the blood is sustained during life by the constant abstraction of fibrin from the circulation for the purposes of nutrition. This idea was hinted at indeed very broadly by Dr. Bostock, in the passage I have already quoted from his work. "As fibrin," he says, "is gradually added to the blood, particle by particle, while that fluid is in a state of agitation in the body, it (the fibrin) has no opportunity of concreting." The idea present in Dr. Bostock's mind evidently was that fibrin passes from the heart to the extremities of the circulation without any change by the way; and that, having arrived at its destination, it enters into the construction of such solids as receive it as a part of their structure.

By another and more extended view, it has been conceived that the liquor sanguinis, being constantly pervaded by the red blood corpuscles, is elaborated by them, and that the coagulable part is thus taken up as quickly as it is formed. This view is maintained by Mr. Wharton Jones, who does not, however, here undertake to answer the question, whether the process of coagulation be a vital or a physical one? but prefers to explain, as above, why the blood circulating in the living body does *not* coagulate. By an extension of this view, Mr. Jones argues further, that the elaboration supposed to be performed by the red corpuscles is probably the conversion of one protein compound into another, albumen into fibrin, a less into a more highly organised proximate principle.

Mr. Gulliver points out that this hypothesis is an old

one revived; that it was virtually advanced by Quesnay in 1750, and by Bordenave in 1787. He objects to it, as well as to the hypothesis that fibrin is elaborated by the white corpuscles, on the ground "that fibrin and its fibrils may be produced merely by mixing together certain varieties of serum, in which, before mixing, no fibrinous particles can be discovered by the microscope." Mr. Dowler shewed that in the fluid produced by a blister there exists a fibrous part, which can be extracted by squeezing the fluid strongly through a fine linen cloth. The fibrous part is left on the cloth, and resembles the fibrin of blood. This observation, though important, is, however, less pointed, since it may be urged that coagulable lymph is effused, under the blister, with the serum.

An hypothesis of the physical kind which is advocated by some authorities is, that the period and the intensity of coagulation depend on the quantity of fibrin, in relation to the blood corpuscles and water. When the corpuscles are few in proportion to the quantity of fibrin, the molecules of fibrin become more densely compressed together, and thus render the formation of the clot more marked, and its structure more firm. (Lehmann, vol. ii, p. 199.)

A further hypothesis, which is in part physical and in part chemical, is advanced by Dr. Carpenter: viz., that coagulation consists in the passage of blood from the soluble to the insoluble state, in which transition it is not formed into an amorphous coagulum, but into a network of fibres more or less definitely marked out. In a former page we saw that Dr. Carpenter considered coagulation to be a *vital* process. However, we now find him defining the process on simple principles.

Prevost and Dumas, in speaking of coagulation,

thought that the red corpuscles were essential to that process. They contended that "the attraction which keeps the red matter fixed around the white particles having ceased when blood is drawn, together with the motion of the fluid, these parts remain at liberty to obey the force which tends to make them combine and form a net-work, in the meshes or amid the plaits of which the colouring matter is included, with a quantity of particles which have escaped this spontaneous decomposition." This speculation, as M. Edwards indicates, was entirely disproved by Müller, who shewed that when the blood corpuscles were filtered off from newly drawn blood, prior to coagulation, the fibrin now left with the serum alone spontaneously solidifies. It was further disproved by Dr. Babington, to whom we owe the term *liquor sanguinis*, as distinguishing the fluid in which the red corpuscles float during life. This liquor sanguinis he believes to be no mere mixture of fibrin and serum during life, but a homogeneous mass, which, after the vital force is removed, separates into two distinct parts; one part spontaneously coagulable, the other fluid at ordinary temperatures—fibrin and serum. Dr. Babington skimmed off the liquor sanguinis from blood, and observed the coagulation as a process independent of the corpuscles.

SPECIFIC GRAVITY.

The specific gravity of the blood, or of its parts, has been thought to bear some relation to the rapidity and cause of coagulation. On this point it has been shown that viscid solutions, such as albumen, or thick solution of gum, introduced into newly drawn blood, tend materially to retard coagulation; and that by this means a buffy coat may be produced from healthy blood. Hence it has

been inferred, that the density of the serum, relatively to the density of the other blood constituents in various kinds of blood, has something to do with coagulation. We have also seen that a large dilution of blood with water is said to retard the coagulating process. On these points, Scudamore has the following observations, which embody much that has been written before and since his time. "Blood," he says, "possessing the highest specific gravity, coagulates the most quickly. In blood of this description, there is the largest proportion of red particles, which are the heaviest part of the mass. Blood which gives the fibrinous coat in a great degree, has a lower specific gravity than healthy blood, and is slower in coagulation. Fibrin is lighter than the red particles, and also lighter than serum." He further says that for the most part the specific gravity of the serum is higher, in proportion as the quantity of fibrin is natural. Hunter states that dilution with water rather hastens coagulation, but makes the clot neither firmer nor looser in texture. Scudamore's experiments led to an opposite result.

With regard to the blood corpuscles and their specific gravity, Lehmann remarks that they sink just as rapidly and just as slowly in defibrinated blood, as in blood containing its fibrin. Hence, the fibrin exerts no influence on this part of the phenomenon. The blood corpuscles unite and sink, in great part, from the difference between the density of the cells themselves, and of the intercellular fluid.

OTHER CIRCUMSTANCES RELATING TO COAGULATION.

There are yet a few points of a minor kind regarding coagulation, which deserve notice, because they have

been almost unanimously agreed upon by various writers, whose opinions on other matters of higher importance have been widely different.

These points, which we may call *facts*, are:—

1. That blood drawn in a quick stream coagulates more slowly than blood drawn in a gradual current. This fact has been accounted for by the supposition that when the fluid flows slowly, and is thus exposed freely to the air, it gives off with greater ease the carbonic acid or other gases, and the aqueous vapour, which it contains.

2. That the shape of the vessel into which the blood is received makes a great difference in the time of coagulation; *i. e.*, that coagulation is retarded if the blood is received into a tall and narrow vessel; but that the reverse obtains if it is received into a wide and shallow vessel. This is accounted for as being due to the evaporation of gases, and of aqueous vapour, on the principle laid down in the last paragraph. Lehmann states that in a long and narrow vessel the blood corpuscles sink rapidly, leaving the fibrin above to coagulate alone.

Dr. Babington, in referring to the effect of differently shaped vessels on buffy blood, argues “that the space left by the gravitation of the red particles, bears a proportion to the whole perpendicular depth of the blood, so that in shallow vessels scarcely any buffed coat may appear, where the same blood, in a deep vessel, would have furnished such a coat of considerable thickness. It is a fact”, he continues, “that the quantity of crassamentum is also dependent, within certain limits, on the form of the vessel employed. If this be shallow, the crassamentum will be abundant; if

approaching in form the cube or sphere, it will be scanty. This difference is owing to the greater or lesser distance of the coagulating particles of fibrin from a common centre, which causes a more or less powerful adhesion and contraction of those particles."

3. That moderate agitation of the blood in the open air quickens coagulation; that agitation in a closed vessel somewhat retards it; but that if the blood be briskly whipped, ordinary coagulation is altogether prevented. This latter fact is easily accounted for by the separation of the molecules of fibrin, and by their adhesion to the rods or stick employed.

PHYSIOLOGICAL INFERENCES FROM PATHOLOGICAL DATA.

The fact that the various pathological conditions of the blood have a great influence on the process of coagulation has long been known, and upon it various opinions have been based. These opinions relate to the blood in two conditions, as it is drawn from the living body, and as it is found in the bodies of the dead.

Regarding blood drawn from the living body during the presence of pathological conditions, the observations that have been made refer in great part to that modified form of coagulation which is characterised by the formation of what is called the "buffy coat".

The identity of the buffy coat with the coagulable part of the circulating blood was shewn, as I have before said, by Malpighi, who further traced out its identity with the fibrinous concretions sometimes found in the heart after death.

Regarding the cause of the buffy coat, most writers are agreed in these particulars.

1. That it occurs in blood from the human subject

chiefly in cases where the fibrin is either actually or relatively increased, as in acute inflammations (hyperinosis); in pregnancy, plethora, albuminuria; and in some instances where great loss of blood has taken place.

2. That the formation of the buffy coat is dependent on, or at least coincident with, a *slow* process of coagulation, as a general rule.

3. That the specific gravity of the buffy coat is lower than that of the serum and blood-cells.

4. That the appearance of the buffy coat is owing, simply, to the separation of fibrin in a tolerably free state, *i. e.*, unmingled with the red corpuscles, and freed of serum.

5. That the tendency to the distinct separation of fibrin is greatest, *cæteris paribus*, in those animals in which the average amount of fibrin in the blood is highest, as in some of the herbivora, and especially in the horse.

6. That in cases where the blood presents the buffy coat from mere richness or excess of fibrin (hyperinosis), the blood corpuscles are below the average in amount; and *vice versâ*, that when fibrin is decreased (hypinosis), the corpuscles are increased above the natural quantity.

These opinions, which, by the strength of the evidence brought to support them, may almost all be received as facts, would have a direct and most important bearing on the coagulation of buffy blood, were not some other considerations in the way, which I now proceed to notice.

It has been argued that the white substance met with floating on the top of the serum of blood, is not invariably composed of fibrin alone, but is often made up of other principles, either combined with, or absolutely distinct from, fibrin.

Mulder contends that the buffy coat is formed of two compounds of protein, in a higher state of oxidation than fibrin, viz., of the tritoxide and binoxide of protein; the former of which is soluble in boiling water, the latter insoluble. The terms binoxide and tritoxide, as applied by Mulder, do not, however, bear the chemical interpretation ordinarily placed on them. They mean that the binoxide contains one, and the tritoxide two equivalents more of oxygen than is present in fibrin itself.

Remak of Berlin has contended that the buffy coat, as obtained from the horse after repeated bleedings, is made up of an excessive quantity of lymph corpuscles, and of but little coagulated fibrin. He predicted that he should be able to distinguish between a buffy coat formed by an excess of parent cells, and one consisting of fibrin proper. He thought that the looseness of the buffy coat in some cases is due to the presence of lymph cells in large proportions.

M. Bouchardat endeavours to prove that the buffy coat is made up of three proximate principles. (*a.*) A substance identical with pure non-coagulated albumen, which he would call albuminose. (*b.*) A network, enclosing the albuminose, composed of gelatine and of a substance (*c.*) possessing all the properties of the epidermic formation—epidermose. These substances are not, however, to be considered as peculiar to the buffy coat, but to represent an analysis of fibrin itself, when freed from fatty substance. (*Comptes Rendus*, 1842.) According to Mulder, the gelatinous matter, thus described by Bouchardat, is merely the hydrated tritoxide of protein.

There are still some other hypotheses respecting the

composition of the buffy coat and of fibrin ; such as, that the fibrinous coat is nothing more than a modification of albumen, and that the cause of the lighter specific of the fibrinous coat is due to the presence of fat cells and water ; but on these particulars it is unnecessary specially to dwell.

Returning to the cause of this peculiar separation of the fibrin coat and its mode of formation, it is to be remarked, that as many hypotheses have been advanced on this subject, as on the composition of the coat itself. Hunter was of opinion that the blood in an inflammatory condition has a greater tendency to divide into its component parts ; and that as this blood coagulates more slowly, the red corpuscles have time to subside, and the coagulable part is therefore left free at the top of the fluid. Hewson and others have attributed the separation of the fibrin to its lower specific gravity and its excess. Henle and Nasse state that the time in which the blood corpuscles sink bears an inverse ratio to the time in which the fibrin coagulates. They found that they could produce an artificial buffy coat in ordinary blood by retarding coagulation. Müller pointed out also that if, to a little recently drawn blood, a strong solution of carbonate of potash be added, the coagulation is retarded, the corpuscles have time to sink, and the clot is colourless at its upper part ; while Dr. Babington discovered that by receiving blood under oil he could bring about the same result, viz., a buffy coat.

Our countryman, Mr. Wharton Jones, who may be ranked as one of the first and ablest in observing the process of coagulation systematically by the microscope, believes that in buffy blood there is, with a diminution in the quantity of the red corpuscles, an exaltation of

their natural disposition to run into rolls; and that these, again, forming a spongework, squeeze out by their closer aggregation the liquor sanguinis, and by their greater specific gravity rapidly subside. Upon this the liquor sanguinis, which is in such cases proportionally in greater quantities, collects at the top, and the fibrin, coagulating, forms the buffy coat. The opinion, as to the increased attraction of the red corpuscles for each other in inflammatory blood, was pointed out by Mr. Hunter; and even the mottled appearance of buffed blood was described and explained by this physiologist, as attributable to the red corpuscles attracting each other, and forming spots of red. (Hunter's *Works*, vol. i, p. 235.) Zimmermann concludes that the appearance of the buffy coat is owing to slow coagulation; and that this slowness is brought about by three causes: 1. By an increase of fibrin: 2. By the diminution of the blood corpuscles and their tendency to adhere to each other: 3. By some peculiar properties of the fibrin itself. The blood vesicles, he adds, act as points of crystallisation, just as a straw thrown into freezing water accelerates the formation of ice. He further maintains, that, in coagulated healthy blood, the lowest portion of the clot is the heaviest, the proportion of fibrin in healthy clots being, as proved by experiment, 2·7 in the lower part, and 7·3 in the upper; while in inflammatory blood from a pneumonic patient, it was as 3·3 in the lower portion, and 14·8 in the upper. There is thus, he says, in inflammatory blood an increase of fibrin, a tendency on the part of the corpuscles to sink, and on the part of the fibrin to rise; hence the result.

In these narrations are embodied the more important speculations with regard to the formation of the buffy

coat. In reference to the modifications arising from the mode of bleeding, the vessel in which the blood is received, and so on, the same remarks apply as were made when treating on the coagulation of healthy blood. One observation more is alone required: viz., that the mere agitation of hyperinotic or sisy blood will tend very much, by hastening coagulation, to prevent the formation of the buffy coat. This fact is described by Sydenham in an interesting passage, in which, after describing the blood as drawn in *pleurisy*, and the white or tough skin of sanguineous fibres which rises upon *pleuritic blood* if the current flow freely, he adds:

“Quinimo cùm hoc ipso modo extrahitur, si orificium angustius, sive quid aliud, obstiterit, quò minus pleniori exeat gurgite, neque hic sanguis *pleuriticorum* sanguinem colore æmulatur, neque æger par exinde commodum capit. Observavi etiam, quòd, si sanguis recens extractus, quocunque demùm modo fluxerit, immisso digito agitetur, superficie rubenti ac floridâ, ut in aliis morbis quibuslibet, spectabitur.” (*Observationes Medicæ*, sect. vi, cap. 3.)

STATE OF THE BLOOD IN THE BODY AFTER DEATH.

Regarding the condition of the blood in the body after death from various diseases, many important facts have from time to time been observed. Some of the German writers have recently endeavoured to shadow forth a kind of system, or set of fixed principles, on this important point. It would divert me from my present purpose to dwell on this subject; I therefore shall only refer to a few general observations which have at various times been made.

In the first place, it has been argued by Hunter and

other observers, that in death from shock, lightning stroke, electricity, and *coup de soleil*, the blood remains fluid after death ; as also in cases where the fatal result has occurred from sheer fatigue. This point has been contradicted by other authors, who have found the blood coagulated after these forms of death. Morgagni has described the blood as quite fluid after death in only four instances ; all these were cases in which death ensued from slow arrest of the respiration. Drs. Peters, Goldsmith, and Moses, three American physicians, have published a report on the appearance of the blood in seventy cases of death resulting from the excessive use of ardent spirits. In every case, the blood was fluid and dark, was of a cherry-juice appearance, and shewed no tendency to coagulate. Magendie produced a fluid state by injecting putrid matters into the veins of animals. In deaths from the narcotic poisons, from delirium tremens, typhoid fever, and yellow fever, the blood is generally described as thin and uncoagulable. Dr. John Davy found the blood fluid and uncoagulable on exposure, in cases of drowning, hanging, suffocation from the fumes of burning charcoal, and effusion of blood into the pulmonary air cells. Mr. Gulliver narrates an instance, in which a man and his three children were suffocated in a burning house. In all, the blood in their hearts was fluid, and remained so permanently. In a case of hanging, Mr. Gulliver met with the same fluidity ; but in kittens killed by hanging and drowning, he has seen coagulated blood in the heart.

In cases of an opposite type, viz. acute inflammatory disorders, hyperinosis, the blood has generally been described as firmly coagulated, or with the fibrin more or less separated in the form of concretion.

Altogether, the experience and observation of the majority of writers tend mainly to sustain the following conclusions.

1. That in cases where immediately previous to death the fibrin is increased in quantity (whether from active hyperinosis or from a relative excess of the fibrinous constituent), coagulation is firm, and the disposition for separation of fibrin, in the form of concretion, is well marked.

2. That in some cases, where the blood current is impeded, as in an aneurism, or in the heart where the valves are rigid, or in very feeble states of the heart, the fibrin has a tendency to separate from the other blood constituents, at the point of obstruction, and to form itself into distinct masses—fibrinous concretions.

3. That after the introduction of some poisonous agents, as pus, into the circulation, and the death resulting therefrom, there is often a distinct separation of fibrin, and firm coagulation generally.

4. That, in instances where the death of the body is produced by an interference with the natural chemical interchanges between the blood and oxygen, as from impeded respiration, great fatigue, the use of ardent spirits, and the inhalation of volatile narcotic agents, as carbonic acid, the process of coagulation is often materially retarded, and is imperfect.

5. That in some special diseases of the hypinotic class, such as scurvy and typhus, the consistency of the blood is diminished, and its coagulation in a great degree prevented.

6. That in instances where death occurs from the abstraction of water from the blood, as in cholera, the entire fluid is left in a dark, tarry, and semicoagulable

condition, but attended occasionally with separation of fibrin in the heart.

7. That in examples of *instantaneous* death from such causes as shock, suffocation, or lightning stroke, the blood oftentimes, but not invariably, remains fluid in the circulatory system.

COAGULATION OF BLOOD IN THE LIVING BODY.

Of late years, an old question has been revived, whether the blood does not sometimes coagulate in the body during life? This question is now pretty clearly answered in the affirmative. M. Velpeau, in the year 1846, related a case in the Academy of Medicine in Paris, of a woman, from a vein in whose arm a long coagulum of blood had been extracted, and who ultimately recovered. But pathological observations have afforded further evidence in proof, from the condition of the blood in some aneurismal cavities; from the appearance of the arteries, and the formation in them of firm clots of fibrin, in cases of gangrene of the parts which they supplied with blood; and from the construction of the fibrinous masses found in the heart after various diseases, together with the symptoms which in such diseases preceded death. From the results of these observations many facts, opinions, and discussions have been elicited by Gould, Templeman, Kerckringius, Tulpius, Pasta, Haller, Morgagni, Götz, Brown, Burserius, Queye, Cullen, Huxham, Corvisart, Stewart, and Chisholm, in a past age; and in the present day by Meigs and Dana, Baron, Fredoult, Bouillaud, Andral, Grisolle, Gaspard, Gulliver, Davy, Burrows, Fuller, Simon, H. Lee, Paget, Crisp, Hughes, Barclay, Corrigan, Fletcher, Kirkes, Hasse, Wagner, and Rokitansky.

I have myself for several years past paid attention to this subject, and have communicated numerous papers upon it, in the affirmative view, to the Medical Society of London. The results of these labours will be given in another place.

From the various arguments and facts put forward by the above numerous authorities, it has been no slight task to make such an epitome as shall fairly represent the meaning and end of their labours. The task, however, has been undertaken, and the inferences obtainable from a review of the whole, to the best of my judgment, are these:—

1. That the blood may, in very rare instances, coagulate in the ordinary way, *i.e.*, as a red clot, in the body during life.

2. That the fibrin alone may separate in the form of concretions during life; this result being theoretically attributable (*a*) to mere slowness of motion, as in the aneurismal tumour; and as in some cases of slow death; (*b*) to absolute or relative increase of fibrin itself; (*c*) to a peculiar kind of coagulation arising from chemical or physical changes incident to the mixture of some poisons as pus with the blood; (*d*) to the neutralisation of those alkaline constituents of the blood, which hold the fibrin in chemical solution, by some free acid, as lactic, generated in the body superabundantly; (*e*) to an extreme tenuity of the serum in which the fibrin is distributed, with a feeble resistance against the natural attraction of the molecules of the fibrin and their consequent aggregation; (*f*) to a supposed disorganisation or disintegration of the blood, under the influence of certain diseases, as typhus and scurvy, whereby it has a tendency to divide into its constituent parts.

3. That these depositions of fibrin may, like the buffy coat, differ in constitution; that they may be more or less coloured, from enclosing in their structure modified red corpuscles; that they may become softened in structure, such softening being most marked in the centre; that they are often accurately moulded to the cavity which contains them; that they may be developed both on the venous and arterial sides of the circulation: that they sometimes become firmly adherent to the walls of the heart, by interlacing with the muscular fibres; and that, in some rare instances, the adhesion which they have formed with the heart may become united by vessels, so that the deposit itself ultimately assumes an organised character.

En resumé, we see that in regard to the causes of the coagulation of blood, both in and out of the body, the explanations that have been adduced rest on one or other of three grand theories: the vital, the physical, the chemical; and it is to be observed, that in the order of time in which these theories have influenced physiological inquiries in general, so have they specially influenced those which relate to coagulation. How far each or all of the speculations which have now been recorded have a bearing on the question at issue, is a subject which must be considered in a distinct chapter.

CHAPTER II.

CAUSE OF THE PHENOMENON OF COAGULATION.

PRESENT POSITION OF THE QUESTION.

"The past deserves that men should stand for a time upon it, to view around which is the best way; but when the discovery is well made, they should stand no longer, but proceed with cheerfulness."—LORD BACON.

IN the last chapter, I have written simply as the historian, putting together systematically such thoughts and opinions as the learning of previous times has produced on the subject of coagulation, and offering no comments or criticisms thereupon. In the present chapter, I shall reverse this order, taking what has been already written for a text, and discussing it unreservedly, both in detail and collectively.

Fibrin essential to Coagulation. Whatever may be the cause of the aggregation of the molecules of fibrin, the evidence is overwhelming in regard to the fact, that upon this aggregation one part of the phenomenon of the coagulation of the blood depends. This opinion, which I have shewn to have been shadowed forth by Plato, is proved, both on the strength of positive and of negative evidence. The proofs are: *first*, that if the fibrin is whipped out of the blood, ordinary coagulation does not take place; *secondly*, that if the fibrin of any quantity of blood rises to the surface, the natural process of coagulation is modified, and the fibrin, blood

corpuscles, and serum, are left in separated conditions, the fibrin only in the concrete form; *thirdly*, that in a red clot of blood, the corpuscles, and, for some little time the serum also, are retained in the meshes of the fibrin, and that the blood-corpuscles may be washed out of the clot, leaving the fibrin free; *fourthly*, that the blood corpuscles being removed by filtration, the fibrin will coagulate in the serum, and, contracting more and more, and squeezing out the serum from itself, will remain ultimately a separate and distinct substance.

The question whether or not fibrin exists at all in blood circulating in the vessels of the living body, which some have raised, does not at this point require consideration. For, however much opinions may vary as to the state of the liquor sanguinis during life, there are no differences of opinion as to the fact, that, *when blood is drawn*, a certain substance, called blood fibre, spontaneously coagulable lymph, fibrin, or by any other name, exists in the blood as a distinct thing; that the particles of this substance possess, under such circumstances, a force of aggregation and contraction; and that to such aggregation and contraction the phenomenon of coagulation is demonstratively attributable, whatever may be the variations occurring in the development of that phenomenon. Further evidence, after facts so obvious, is unnecessary; and hence we start fairly with the general principle, that upon the aggregation of the molecules of fibrin coagulation ultimately depends; and that whatever may solve the problem of the cause of this aggregation, solves at the same time, of necessity, the cause of the phenomenon altogether, as far at least as we can at present foresee.

Temperature and its Effects. As far as written evidence goes, it proves, 1st, that the process of coagulation is retarded more or less by a decrease of temperature below the natural standard of the body, such retardation being more marked as the freezing point is approached; 2ndly, that blood brought down to a temperature of 25° Fahr. may become frozen, but not coagulated, coagulation being possible, however, when the frozen mass has been thawed by exposure to a higher temperature; 3rdly, that, at certain temperatures above the natural standard, the process of coagulation is hastened, *i. e.* it takes place more quickly at 110° than at 90° or 100° , and more quickly at 120° than at 110° . These conclusions are corroborated so fully, that they may be received with confidence; for, although the ancient philosophers took an opposite view, their opinions are here of no weight, since their arguments were based on a general and vague inference, while the modern view rests firmly on direct experiment. Why temperature influences coagulation, in the way we have seen, is a great question. Its effects do not in themselves explain the phenomenon to the observer; nor do they chime in with the other hypotheses and theories which have been advanced, save with one, that, namely, which relates to the escape of gaseous matter from the newly drawn blood. In relation to the speculation about a loss of vital force as a cause of coagulation, the experiments regarding temperature are, on the contrary, in direct opposition. For, as the vitality of an animal is impaired in proportion as its temperature is reduced below the natural standard, so, according to this hypothesis, should the tendency to coagulation of its blood be hastened by a similar reduction. But the reverse obtains.

Exposure to the Air. The experiments of Hewson on the exposure of blood to the air are at once striking, simple, and ingenious, and, as far as they go, convincing; they afford at the least some evidence of a circumstantial character. His hypothesis has failed to convey full conviction; first, because it does not attempt to explain the act of coagulation, but certain conditions only under which the act is possible; secondly, because it does not in truth include all those conditions; and, again, because it does not show the reasons why the conditions which it presumes to be necessary, *are* necessary. It is argued, that the exclusion of air from blood retards coagulation, and that exposure to air increases it. But it is clear that these observations, however accurate, prove but little when taken alone. For, in the mere act of enclosing blood in an air-tight vessel, certain physical or chemical changes may be prevented from taking place. On the other hand, the free exposure of blood to air admits, as seems well proved, of an escape of gaseous matters. When to these arguments there is added the further proof, that blood coagulates as rapidly *in vacuo*, or when exposed to carbonic acid gas, to carbonic oxide, or to oxygen, as it does in common air, the hypothesis becomes limited in its application and meaning. But as a fact observed is often far more valuable than the inference made from it by the observer, and even remains when the inference is disproved, so we may accept the observation of Hewson without binding ourselves strictly to his deduction. The effects of exposure to air, like those of temperature, chime in well with the hypothesis of gaseous evolution; and it is curious that Scudamore did not see the matter in this light, and give another reading to the vacuum experi-

ment. For, as free gases act as vacua to each other, so the escape of a gas from the blood should, *a priori*, be favoured by exposure of blood to air or to any gas; the only additional effect of the vacuum being its assistance in extricating the gases from the blood itself.

The experimental facts which indicate that blood received, under oil, or in long and narrow vessels, or in vessels tightly closed, coagulates slowly, all go to support Hewson's view, when received with its necessary limitations.

The Theory of Rest as the main cause of Coagulation leads us at once into the sphere of physics. It offers two propositions: first, that by motion the blood is prevented from coagulating; in other words, that the molecules of fibrin are prevented from coming together: secondly, that when this motion is suspended, the mechanical force, by which the molecules of fibrin are separated, is removed; that the mutual attraction which they possess for each other is permitted; and that the first step in the process of coagulation is thus set up. In this line of argument we rest, at all events, upon simple physical principles, which admit of plain discussion, and of direct experiment.

We have already seen that so powerful was the strength of this mode of reasoning felt to be by some of the older physiologists, that they adopted it as the only satisfactory explanation of coagulation; in which view they have been in part followed by Dr. Bostock. The circumstances favouring the view are important.

In the first place, pathology has shewn very clearly, that whenever the circulation of blood through the heart, or other part of the circulating system, is diminished in force, a decided tendency to coalescence

amongst the particles of fibrin ensues, giving rise to the formation of what are now called fibrinous concretions. It has been shewn, also, that when the circulation of blood is completely arrested in its course through the vessels, as when a ligature is applied, the formation of a coagulum of blood at the obstructed point is the ordinary fact; again, that in aneurism, where the current is impeded from its passing through a dilated vessel, a deposition of the fibrin is common at the most depending part, as a result of the languid motion; nay, more, that any direct obstacle to the course of the blood in its vessels, say an indurated valve, or a thread stretching across an artery or vein, is sufficient, under some conditions, to produce at the point where it obstructs a kind of coagulation.

In the second place, it has been very properly urged, that the mere act of suspending coagulation for a time by the agitation of blood in a closed vessel, is a proof that absolute rest has to do with the coagulating process. For, although the fibrin may either eventually cling to the side of the vessel in which the agitation is kept up, or float to the top of the fluid, these results are slowly induced, and depend, indeed, on the fact, that the fluidity of the blood has been kept up for a length of time sufficient to permit the red corpuscles to subside, and the fibrin to exert at leisure its specific property of molecular attraction.

Thirdly, the experiments which shew that the blood in a glass tube affixed by its two extremities to the free ends of a divided artery, does not coagulate, so long as it is passing through the tube, have been adduced in favour of the correctness of the theory now being considered.

Against it there stand out in bold relief; first, the valid objections derived from the facts Hewson discovered and dwelt upon so forcibly, viz., that blood retained in a state of rest in a vein coagulates very slowly so long as it is thus confined. Secondly, that blood extravasated into the living cellular tissue may remain fluid for weeks, though at perfect rest, but being let out will coagulate while still at rest in the receiving vessel. Thirdly, that blood drawn from the body cannot, by any kind of motion or agitation, be held in the same fluid condition as during life; *i. e.* with its fibrin distributed throughout the whole fluid as a part of the homogeneous liquor sanguinis. To all these arguments double force is added by the overwhelming evidence in favour of the view, that, in the circulating system, during healthy states, the fibrin is as certainly in solution as is the albumen or the soluble salts. If so, then, the force which can thus hold fibrin soluble is sufficient of itself, is chemical rather than physical in kind, and is independent of motion.

Such is the conflicting evidence on the subject of the stasis theory of coagulation. Fact meets fact in collision. Taking it all in all, however, unless something more can be said in its favour, the theory fails to account in full for the phenomenon of coagulation. But like the theory relating to exposure to air, it may comprise so much of truth, that, in the presence of the whole truth, the arguments and facts on which it has been founded would be easily read off and understood.

Hypothesis of the Vital Principle. If writers who speak of a vital force, or principle, could define what they mean by the term, or could even agree to a kind of

hypothetical definition in regard to it, we might be able to treat more satisfactorily of this hypothesis. Or if, in using the term "vital principle or force", they would rest content to let it stand to express, in a general sense, the aggregate of all the phenomena observed in the living body; or if they would only use the term to explain any operation, whether chemical or physical, which occurs in the body, simply because it does occur in it; if these definitions were admitted, there would be fewer difficulties in the way. But so far is this from being the case, that we find even those who speak of the vital principle in connexion with coagulation, assigning to it two distinct and directly opposite functions. It is plain that Mr. Hunter held the vital principle, *i. e.* its presence, to be the cause of *coagulation*; for he compares the change that occurs in the blood removed from the body to certain transformations or changes which occur to it in the body during life. On the opposite principle, the older physiologists thought that the living blood was retained in a state of *fluidity* by the presence of the vital force, and that the act of coagulation, in blood at rest, arose purely from the loss of the vitality which ensued upon its removal from the living structures; and it is evidently towards this latter view of the vital hypothesis that Mr. Thackrah, Franz Simon, and even Dr. Carpenter, incline. Our modern physiologists are, however, much less consistent than were those of old; for, although they defend the idea of the existence of some peculiar principle, or entity, which they call vital, they at the same time do not omit the attempt to explain the nature of the vital act itself on physical or chemical grounds. Into this peculiar mode of reasoning Dr. Carpenter very obviously falls, without seeming to

be conscious that to offer a physical or chemical explanation of any obscure phenomenon, is to admit that the phenomenon itself is the result of physical or chemical causes. Thus, unhappily, whenever a very hard and peculiar problem relating to organised structures has to be solved, writers are apt, in a dilemma, to beg the question by referring the cause of the phenomenon to the "vital principle" as to an entity, or ruling force, which, being vital, is open to any definition, or to none. It is clear, however, that to bring a problem to such an ultimatum as this, is merely equivalent to saying that nothing is or can be known about it. For, as the physiologist is prevented by the limitations of his science from instituting any but chemical or physical inquiries as to the causes of natural phenomena, it were vain for him to institute such inquiries at all, unless he felt that by them he might unlock possibly a chemical or physical secret bearing on the point. Nay, should he fail by such inquiries to solve the questions before him, what would this negative result indicate? That the cause of a phenomenon is referrible to an indefinable principle? Certainly not. But rather that his knowledge of physical or chemical laws is simply insufficient for carrying him to the goal he has in view.

In relation to coagulation of blood, the vital hypothesis is entirely disproved; nay, it would never have been advanced but for the coincidence that the phenomenon occurs in blood newly drawn, and without man's interference. If an experiment were wanted, if blood had to be raised in temperature to 150° or 160° , to make its *fibrin* coagulate, in the same way as is necessary with the serum when its *albumen* is made to coagulate by heat, the idea of vitality would be ridiculous.

Yet the albumen of the serum comes from the living body the same as the fibrin. But why argue the point thus, when experiment answers for itself? Hewson, Hunter, John Davy, and others, have frozen blood, and have kept it, thus frozen, from coagulating. They have then thawed the frozen mass, and the fluid has thereupon coagulated. Does the coagulation of blood that has been frozen (and even frozen and thawed three times successively) depend on the presence of vitality, or on the loss of vitality?

One further disproof is conclusive, without more. Dr. Davy and Mr. Gulliver have both shown that fresh blood may be held fluid for weeks by the addition to it of certain salts, and may then be made to coagulate by the addition of water. "Some horses' blood," says Gulliver, "which I had kept fluid with nitre for fifty-seven weeks, readily coagulated when diluted with water." Did this blood, kept fluid fifty-seven weeks, coagulate from the presence or from the abstraction of the vital principle? With this query the hypothesis of the vital force may be safely left to its advocates, for once and for good.

Hypothesis of a Nervous Force. The idea that the nervous system supplies something to the blood which keeps it in the fluid state, though less mystical than the vital hypothesis, is still very poor and improbable. What is the nervous force? Is it analogous to electricity? If so, then the effects of electricity on drawn blood shew nothing positive on the subject. Is it a force in itself special? If so, how does it affect the blood, and where? Instead of the "nervous influence" keeping the blood in a fluid state, from what we know regarding the effects of cutting off the nervous commu-

nications from any part or organ, and the deficient or imperfect nutrition, or transformation of blood into solid structure (which, by the way, as John Hunter said, is a kind of coagulation) which ensues, the inference would tend towards the opposite point; viz., to prove that the nervous influence should favour the process of coagulation, rather than that blood should coagulate from the withdrawal of it.

Chemical Theories. The chemical theories regarding coagulation relate specially to the effects of various chemical agents on blood drawn from the body. It is obvious, at the outset, that many of the results that have been narrated can have no direct bearing whatever on the question under discussion. It will be seen by reference to the first Chapter, that various experimentalists, in endeavouring to ascertain what chemical agents would hold the fibrin of the blood in a state of solution, have employed a variety of substances, such as nitrate of potassa, nitrate of soda, nitric acid, etc., substances which in no way enter into the composition of living blood, and which cannot therefore have any influence on the fluidity of the blood during life. These experiments are vague to the last degree, and can lead to no important results. In other cases, where solutions of salts or alkalies, which do exist in the blood, have been added to drawn blood, little or no accurate attention has been paid towards making these artificial solutions resemble, in point of strength, the natural solutions of the salts as they really exist in the blood circulating through the body. It may be true, that a certain powerful, perhaps saturated, solution of common salt will suspend coagulation. But what has this to do with the question? Does not the proof rather lie in the experiment

whether an admixture of the salt with the blood, in the proportion of some three or four grains to the thousand, will lead to such a result?

In treating, too, on such discrepant statements as those which have been recorded in preceding pages, I have well founded suspicions that much of the discrepancy has occurred from the simple fact, that the chemicals employed by various experimenters have not always, and, indeed, have not often been, of the same chemical quality or purity. The results obtained by two observers have thus been very different; for the explanation of this there is no great difficulty.

To show how probable are the grounds on which this supposition is based, I may relate an illustrative incident. I was anxious to ascertain the effect of nitrate of potash on freshly extracted fibrin. I obtained two specimens of this salt from two different chemical establishments. Both specimens were warranted as carefully prepared. With each of these specimens I made a solution, in the proportion of ten grains of the salt to one ounce of distilled water. Into each solution I then dropped two grains of moist fibrin, derived from the same blood, and left them standing side by side under the same conditions. In three days I found that the fibrin in one of the solutions was in a great measure dissolved; in the other it remained unchanged. This difference arose from the fact that the salt which had dissolved the fibrin contained free potassa; the other salt did not.

F. Simon, in commenting on an experiment by M. Denis, remarks incidentally on the possibility of an error from a similar cause. (*Animal Chemistry*, vol. i, p. 19.)

In reviewing the experiments that have been conducted in relation to the effects of chemical agents

on the blood, the only essential fact which seems to me to have been attained as bearing on coagulation is, that simple alkaline solutions, both weak and strong, of potassa and soda (one of which has been thought to exist in blood), have the effect of dissolving fibrin. In all other cases where, under the influence of certain chemical substances, the tendency to coagulation has been retarded or increased, the substances in question either have not been those of the normal blood; or, if so, they have been used in amounts remote from the natural proportions in which they exist in normal blood; *ergo*, the effects obtained are only of an indirect value at the most.

However, if it be simply true that free soda and potash dissolve fibrin and suspend coagulation when added to blood, here at all events is a fact, and one that must not be disregarded. But, unfortunately, it fails at once to explain coagulation. For, although the serum of the blood remains slightly alkaline after its abstraction from the body, such alkalinity is obviously not sufficient to prevent the separation and coagulation of the fibrin which was, during life, in solution in the liquor sanguinis. If it were, there would be no coagulation at all. *Ergo*, during life there must be a more decided alkaline principle preventing coagulation, than that which afterwards remains in the serum, if alkalinity be the real cause. Again, if the solvent effect of a fixed alkali is even admitted as a cause of the fluidity of living blood, it remains a question how the effect of the alkali is developed; *i.e.*, whether it dissolves the fibrin, and so holds it in solution, or whether it acts indirectly, by modifying the chemical combinations of the other blood constituents.

The hypothesis which refers to carbonic acid the property of sustaining fluidity deserves to be remembered. It remains to be seen whether the slow coagulation of the blood richly charged with this acid be a coincidence or a result; since it is said that blood will coagulate in the presence of the acid. But it is easy to imagine that blood, drawn from a vein charged with carbonised material, would almost of necessity coagulate more slowly than richly oxygenised blood; since the same chemical effects in the body, which would charge the blood with carbonic acid, might lead also to a reduction or to important modifications of fibrin. In truth, we find that the formation or elaboration of fibrin can be arrested by slowly reducing the process of respiration. Hence, possibly, one reason of the fluidity of the blood in some cases of death from chloroform and other narcotic vapours, as well as in instances where life is put out by failure of the respiratory organs, such as Morgagni has related. Still, the evolution of carbonic acid from blood is important as opening the question whether some other volatile or gaseous agent may not also be thrown off by the blood after its abstraction from the body, and which may by its presence influence fluidity, and by its escape give rise to coagulation. Here is new ground for minute investigation; for, while many striking facts, such as the effects of exposure to the air or to the vacuum, and of temperature, as connected with the process, point markedly in this direction, there has, as yet, been no very elaborate attempt made to ascertain what really are the products evolved from drawn blood. I shall bestow much labour on this subject in the end.

For the reasons assigned above respecting the dif-

ferences in the qualities of the chemicals, which may have occurred in the hands of different experimentalists, it is difficult to draw many safe conclusions from the materials before us. The following are those most worthy of notice:—

1. The alkalies, potash and soda, dissolve fibrin, and, added to newly drawn blood, hold it fluid.

2. Several salts, such as the chlorides of potassium, sodium, and ammonium, added in free quantities to blood, sustain fluidity.

3. The evidence in favour of the extrication of carbonic acid from newly drawn blood seems well supported; but there is no proof that upon this extrication, *per se*, coagulation depends.

4. Blood held fluid by a salt may, after many weeks, be made to coagulate on the addition of water.

5. The exposure of newly drawn blood to various gases, such as nitrogen, oxygen, nitrous oxide, carbonic acid, and carburetted hydrogen, does not affect coagulation.

The hypothesis which supposes that fibrin does not exist as such in circulating blood,—but is formed after the blood is drawn by the transformation of an acid albuminate of soda from a soluble into an insoluble and neutral state, and the subsequent separation of a portion of albumen under the form of fibrin,—admits of no experimental proof whatever, and is utterly inconsistent with the clearest and best observed facts in nature. If it were true that the fibrin does not move along in the blood-stream, in the same manner as the albumen and certain of the blood-salts do, how is it that it becomes deposited in aneurisms? Why should it attach itself to a thread carried through an artery? Why should it

seal up an obstructed vessel? Why should it even exude as plastic lymph? Or, lastly, why should it exert its peculiar power of contraction in blood retained in the vessels of the dead body?

Electricity. On the effects of electricity but little has to be observed. The electric has been identified with the nervous or the vital force by those who have spoken of it in connexion with coagulation; and the remarks which have already been made in reference to these forces bear equally on the electric force. It may, however, be observed, that although, as a general rule, the blood is fluid after death from electric shock, or its analogue the lightning stroke, this rule, which is now proved to be not without its exceptions, would bear but lightly on the question, even were it universal, since a fluid state of blood is common to other forms of death.

Physical Interchanges. The hypotheses regarding the physical interchanges in the constituents of the blood are important. In one respect, some of these interchanges, whatever their intimate nature may be, must be considered, at least, as having an influence in sustaining fluidity during life. For, as it is clear that fibrin must be constantly thrown into the circulation, so it is equally clear that it must be taken up, and either applied to some purpose as a product of nutrition, or carried away as a product of elimination. Were there no provision for removal of this kind, the fibrin in the blood must soon exist in such superabundance as to nullify the effect of the process, whatever it may be, by which its molecules are kept from aggregating, and the healthy blood is maintained in a fluid condition.

In reference to the special process, or processes, by which the fibrin itself is elaborated or removed, there

is nothing to be said positively, and any lengthy remarks would tend only to lead away from the immediate subject of this chapter.

Specific Gravity of the Blood. The experiments of Nasse, on the specific gravity of the blood, and the differences arising under varying specific gravities, point to certain physical, or rather, mechanical results. That coagulation is retarded in cases where the specific gravity of the liquor sanguinis is raised by the addition of dense viscid solutions, is a receivable fact which carries with it great weight. It tends, possibly, to show either that the particles of fibrin in drawn blood have for each other a natural attraction, which can be temporarily broken by placing in the way a mechanical obstacle; or that the added solutions hold for a time the gases which escape from blood spontaneously. It should, however, be borne in mind, that the specific gravity of blood, when made higher than is natural by the addition of viscid solutions, is very different from that increased specific gravity which is sometimes met with in diseased blood. The results, also, in the two cases are different; since coagulation is retarded in the former case, and is hastened in the latter; a difference explainable on the ground that, where the specific gravity of the blood is *artificially* increased, the serum is the portion densified; while in cases where the specific gravity is *naturally* increased, there is an excess of blood corpuscles.

On the effect of dilution with water, experimenters vary in their statements. But the evidence, taking it all in all, is in favour of the conclusion, that a free dilution with water hastens ordinary coagulation, and brings about the process in instances where it has been suspended by saline substances. This dilution acts, it

might be inferred, by distributing the solvent of the fibrin over a large surface. It is impossible, however, to argue safely on this point, because the experiments related are not sufficiently circumstantial. The exact quantities of water and blood added together by various experimentalists are, as a general rule, indefinitely stated; nor are we always told whether distilled water was employed, or spring water having salts in solution.

The remark made by Lehmann, that the corpuscles sink as speedily in blood containing fibrin, as in defibrinated blood, will be recognised as contrary to the idea generally received. The question really resolves itself into this. In ordinary coagulation, with the formation of red clot, does the entanglement of the red corpuscles with the fibrous network depend on the rapid contraction of the fibrin, or on the slow gravitation of the corpuscles? Weighing the proofs on both sides, it seems pretty clear, (*a*) that the corpuscles do not, in ordinary blood, sink rapidly, and that the fibrin has therefore time to enclose them in its meshes; (*b*) that in buffy blood the corpuscles do sink more rapidly, and so leave the fibrin to contract without them; (*c*) but that if the fibrin of natural blood be held in solution for a longer time than usual, as by the addition of carbonate of potash, or by viscid mixtures, the corpuscles have time to sink naturally and before the concretion of the fibrin, which then concretes alone. Thus the appearance of a coagulum may vary from differences in the fibrin in one case, in the corpuscles in another.

Minor Facts. The facts recorded in the last chapter, on the slower or quicker process of coagulation in cups differently shaped; in blood drawn with different degrees of rapidity; and in blood subjected to agitation in

various ways, are of value, though subordinate in kind; and when the greater elements of the problem of coagulation are considered, they may, in an incidental way, render important evidence. They would point towards the hypothesis which connects coagulation with the evolution of carbonic acid, and would give this hypothesis strong support if it were itself sound, and if it admitted of satisfactory proof by experiment, which we have seen, from the labours of Dr. Davy, not to be the case. If the current of blood be slow, and if the receiving vessel be broad and shallow, *i.e.* if the blood be exposed over a wide surface, coagulation is quick; and again, if the blood be agitated in an open vessel, by which means a wider surface is exposed to the air, the coagulation is hastened. It is unnecessary to describe at length how compatible these facts are with the idea of gaseous extrication, and how little compatible they are with any other view that has been propounded.

The Pathological Arguments which have been brought to bear on the problem of coagulation are all most interesting. They tend, at first sight, to support the theory, that to a dynamic force must be attributed some direct or indirect influence in keeping blood fluid. They shew, for instance, that when blood, by passing through a dilated vessel, is impeded in its course, a separation of fibrin, or, in other words, a form of coagulation, is the result; that when, from languor of the circulating system, blood flows slowly through the heart or vessels, the fibrin again begins to separate in the parts where the languid motion is most marked, as in the auriculæ and in aneurismal cavities. Pathology indicates also that when fibrin is abnormally increased, its peculiar tendency to separate, whether

within or without the body, is manifested by the formation of a distinct fibrinous clot *in* the body, by the development of the buffy coat *out of* it; two facts which have both a chemical and a physical meaning.

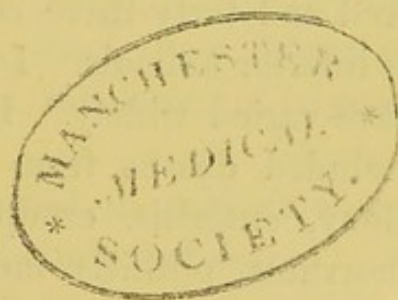
But neither the phenomenon of coagulation of fibrin in the living body, nor the formation of the buffy coat out of it, are sufficient in themselves to give satisfactory proof in favour of the statical theory, inasmuch as the fibrinous concretion or the buffy crust are possibly never formed from blood which is in quality absolutely normal. If fibrin be in excess,—if the tendency to aggregation amongst the blood corpuscles be increased,—if, as some presume, a free acid exist in the blood under certain forms of disease, in which the tendency to fibrinous separation is marked,—if any of these conditions exist, the chemical properties of the blood, as well as the physical, are so obviously modified, that to speculate on the one modification without the other, is, of necessity, a failure. Neither is it logical to deduce ordinary principles from extraordinary phenomena; for, except in rare cases, a correct knowledge only of a natural law explains in full the causes of its variations.

In summing up the various theories and hypotheses that have been propounded by different authors on the cause of coagulation, it is to be observed, that those who have advocated the doctrine of a vital or other indefinable cause, have done so mainly to bridge over the difficulty which has, up to this time, stood in the way of discovering an agency more simple and definable. The arguments of these may therefore be fairly eliminated.

On the other side, the supporters of either a special physical or chemical hypothesis, or theory, while

they have brought together very cogent reasons in defence of their own views, and in opposition to those against which they have written, have at the same time failed altogether in establishing any essential position. The inference from this fact is, that, a soul of truth exists in both lines of argument, and that a correct explanation of the problem might probably blend them harmoniously into one.

If, however, we might venture empirically to isolate physical and chemical principles,—if, according to common acceptation, we were to look upon physical science as mere mechanical science, then we must, perforce, in this problem of coagulation, place the chemical argument in the first position. Neither does this apply to the present problem alone. It is a rule of general application. For it is probable that there is no mechanical force or principle that cannot be traced back ultimately to chemical agency; and that chemical force can never be developed without the development of some mechanical, or, in other words, physical demonstration.



CHAPTER III.

THE AUTHOR'S PERSONAL OBSERVATIONS AND DEDUCTIONS ON THE CONDITION OF THE BLOOD IN THE BODY UNDER VARIOUS PHYSIOLOGICAL AND PATHOLOGICAL STATES.

"In considering any complex matter, we ought to examine every distinct ingredient one by one, and reduce everything to the utmost simplicity; since the condition of our nature binds us to a strict law and very narrow limits. We ought to compare our subject with things of a similar nature, and even with things of a contrary nature, for discoveries may be and often are made by the contrast which would escape us on the single view. The greater number of comparisons we make, the more general is our knowledge likely to prove, as built upon a more extensive and perfect induction."—BURKE.

IN the course of my inquiries into the causes of the coagulation of the blood, I have observed with special care the condition of that fluid after death in five hundred and forty-three cases, occurring either in man or in inferior animals. In these cases the forms of death have varied widely. In the human subject they have included deaths from sudden syncope, epilepsy, apoplexy, enteritis, croup, pneumonia, bronchitis, bronchorrhœa, phthisis, mesenteric disease, purpura, acute rheumatism, dropsy following scarlet fever, cyanosis, hæmoptysis, failure of the heart from fatty change, cancer (the epithelial and medullary forms), aneurism of the aorta, atheromatous and ossific disease of the aorta, adhesion and ossification of the pericardium, simple starvation, cirrhosis, degeneration of the heart

from drunkenness, hydrocephalus, lateral compression of the chest, ulceration and stricture of the œsophagus, icterus, general dropsy from mitral disease, dilatation of the right side of the heart, senile decay, and hanging. In the human foetus I have examined the state of the blood in the sixth, seventh, eighth, and ninth months of development; as well as in cases where death has occurred, at or soon after delivery, from extravasation of blood on the brain, from syphilis, from mere premature birth from atrophy arising from disease of the placenta, and from mechanical injury to the head during labour.

In various inferior animals, including pigs, sheep, oxen, dogs, cats, rabbits, guinea-pigs, and birds, I have observed the blood after death from the following causes: hæmorrhage, intestinal obstruction, poisoning by narcotic gases (viz., chloroform, ether, smoke of puff-ball, carbonic acid, tobacco smoke, antimonuretted hydrogen, and prussic acid), poisoning by solid opium, by salts of ammonia and potassa, and by antimony; strangulation, both rapid and slow, drowning, electric shock, simple exposure to cold, peritoneal dropsy naturally and artificially produced, shock from blows on the head, extraction of the kidney, inhalation of oxygen, and inhalation of chlorine.

I have also examined the blood in various stages of development, in the foetal pig, lamb, and dog.

Speaking generally, in regard to these inquiries, I note, in the first place, that the conditions of blood which I have found are as follow:—

1. The whole blood firmly coagulated, without any apparent separation of its constituent parts. Or as a simple contracted red clot, lying loose in the cavity,

and from which the serum seemed to have been removed by absorption, either into the structures immediately surrounding, or into the capillaries.

2. The fibrin separated and distinct at different parts ; this separation being most commonly seen in the heart, but sometimes in the arteries and veins. The separated fibrin being either (*a*) in the form of a layer or series of layers upon a red clot ; or (*b*) isolated, and itself filling a cavity, as the right auricle ; or (*c*) modeled into a cylinder, and surrounded or grooved by a red clot ; or (*d*) in the form of a hollow cylinder, more or less perfect, adapted to the vein or artery in which it is situated, and having a cord or column of coagulated red blood running through it ; or (*e*) merely fringing a valve ; or (*f*) laid down on the endocardial surface in the form of a membrane ; or (*g*) lying loose as a cord in one of the large vessels, the remaining blood being either coagulated or fluid.

3. The blood as a loose clot, composed of serum, corpuscles, and fibrin, but all so lightly held together as to be broken up by mere removal ; or even so loose, and the contractile properties of the fibrin so reduced, that the whole fluid was brought down to a mere sticky or tarry consistency.

4. Absolute fluidity of the blood in every part, without any discernible trace of separation.

To avoid as much as possible the differences which might occur from the circumstance that the blood in each instance could not be observed at the same period after death, I have taken care, in cases where the coagulation was not well marked, to preserve a portion of the blood, and to watch the processes through which it might pass for at least three days afterwards ; this

being the longest period after death at which any of the inspections have been made, except in one or two instances, where the foetus was the subject of inspection.

Referring in detail, but briefly, to the forms of death in which the variations I have thus sketched out have been met with, certain important facts relating to the cause of coagulation stand prominently forward.

I. NORMAL COAGULATION OF BLOOD IN THE BODY.

In instances where life is terminated suddenly, without any long or serious prostration beforehand, or where the respiratory organs have not been primarily implicated in the result, the blood left in the vessels in the normal condition passes, after it is at rest, and if sufficient time be allowed, through the same simple process of coagulation as it does when drawn from the living animal into an open vessel ; that is to say, it coagulates first into a simple red clot, afterwards the serum is squeezed out and left free, and ultimately the fibrin and corpuscles remain as a contracted clot. In the body, however, the serum does not always escape rapidly; and, when it does, it must, I think, be taken up by osmosis into the capillary system. This supposition is rendered probable, and may be demonstrated, as I have often found, by the experiment of injecting the vessels of a dead animal with serum or water. The fluid injected disappears in the course of four or five hours ; if it is injected into the arteries, it finds its way into the veins, and for a time fills them more or less.

The cases in which I have met with this, the simplest form of coagulation, have been cases of death by syncope, by rapid hæmorrhage, whether internal, as from rupture of the heart or of an aneurism, or external, as

from wounds. The best illustration that can be met with, indeed, of this form of coagulation in the body, occurs in the slaughter-house, after death by the knife. Much, however, depends on the way in which the blood is drawn ; for, if a large incision be made, with the head of the animal depending, the loss of blood is sometimes so great, that scarcely any trace of it is met with in the larger vessels, except perhaps here and there a thin cord of red coagulum.

II. SEPARATION OF FIBRIN WITHIN THE BODY.

In cases in which the blood after death is found to be separated into its constituent parts, *i. e.* where the fibrin is more or less distinctly divided, either into layers, clots, tubes, or cords, the modes and causes of death are generally very distinctly marked. This condition of the blood occurs, I believe, under three series of conditions : first, in instances where the fibrin is present in the blood in quantities abnormally great ; secondly, in instances where amount of fibrin is relatively increased ; and thirdly, in cases where some obstruction is thrown in the course of the circulating current, and interferes with or impedes the stream.

Positive Increase of Fibrin. Where the quantity of fibrin is positively increased, the process of its separation appears to be identical with that which occurs out of the body, in the formation of the buffy coat. The cases are also in themselves such as would give the buffy coat, were blood extracted during the patient's life ; *i. e.* they are mostly examples of diseases of the acute inflammatory class, hyperinosis. The causes, also, are possibly identical ; viz., increase of fibrin, and an increased attraction of the red corpuscles for each other.

The separation of fibrin in such cases in the circulatory system takes place under two conditions.

1. When the excess of fibrin is slight, the separation may occur after death. The fibrin then lies as a mere layer on the uppermost part of a red clot, thus resembling the buffy coat, except that the cupped appearance is not present, and that the serum, from causes which I have already explained, is abstracted.

2. When, again, there is a great excess of fibrin, the separation may take place gradually during life. In such instances, the fibrinous formations are widely different in their physical conformation from that simple separation described above. These differences arise from obvious causes. In the former example, the fibrinous clot or stratum forms while the blood is in a state of rest; in the latter, it is formed from blood in a state of motion. The differences thus produced are, in truth, so marked, that from the appearance of a fibrinous concretion alone, one may easily tell whether or not it preceded death. If it have been formed from blood at rest, that is, after death, it will be a simple coating on and above a red coagulum; if it have been formed from blood in motion, that is, before death, it will be modeled to the containing vessel or cavity, will be adherent to the walls of the cavity, or will be grooved by the blood currents that have passed along it; while in some examples, where it has been laid down in a vessel, it may be found as a perfect tube enclosing a column of blood, and resembling, in fact, an inner and additional coat of the vessel in which it is deposited.

It would appear, further, that a fibrinous formation occurring during life, takes its root, to use a common phrase, at some point where the current of blood is

most feeble. The auricula of the right auricle offers many advantages in this respect; the blood is here driven into a corner; the surface over which it passes is inlaid with bands, and the contractile power of the wall is feeble. The consequence is, that more than half the concretions found in the right side of the heart have an attachment to this part of the circulating organ; and so firm is the union, that I have been occasionally able, by pulling at a concretion arising from this point, to turn the auricula inside out.

A *second* point, favourable to these formations, is the funnel-shaped space running up from the right ventricle to the pulmonary artery. A *third* point is the corresponding space running from the left ventricle to the aorta. A *fourth* is afforded by the edges of the valves, and the muscular and tendinous cords. Lastly, any form of obstruction, whether direct, as from an indurated valve or atheromatous deposit, or indirect, as from the dilatation of the heart or its vessels, is

at all times favourable to the construction of a fibrinous concretion.

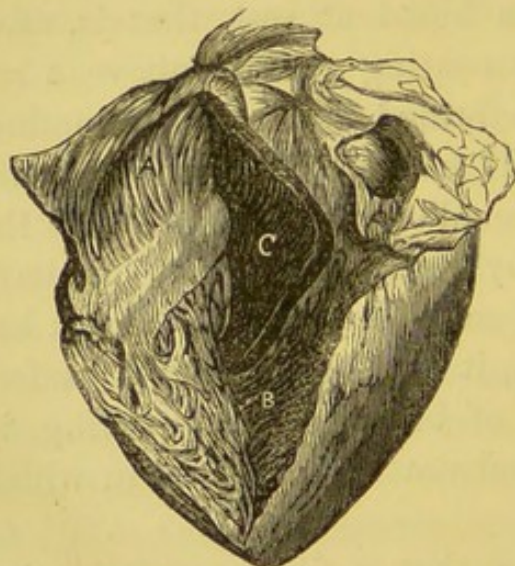


Fig. 1.
A. Cavity of right auricle. B. Cavity of right ventricle.
C. The concretion.

In a specimen now before me, a concretion on the right side of the heart takes its rise in the auricula of the auricle, runs down by the wall of the heart, and, passing over a section of the tricuspid valve, finds its way

round in the course of the circulation into the pulmonary artery. This concretion was obviously a de-

velopment antecedent to death. As will be seen in the preceding representation, it was in itself of sufficient size to fill the auricle. It was not surrounded by blood, but was directly overlaid by the wall of the heart, and firmly attached at its upper part in the auricula; it was modeled to the surfaces over which it passed, was firm and fibrous in structure, and yellowish white in colour. The blood in the large veins in this case was firmly clotted, but without any separation of fibrin.

In cases of death from acute croup, I have twice found the cavity of the right auricle filled, and even distended, with a concretion. In both instances the concretion was grooved by the currents of blood from the inferior and superior venæ cavæ. The current from the superior cava passed along the upper surface of the concretion, almost in a straight line; that from the inferior grooved the under surface, and made a gentle curve. The grooves were both filled with red blood clot. In the auricula, the concretion in each case had a firm attachment to the muscular wall. The concretions, together with the one precedingly named, and, with the others described below, were exhibited in their fresh state to the Fellows of the Medical Society of London.

In another instance, I found the right auricle inlaid with a complete fibrinous layer, from two to three lines in thickness, firm in structure, adhering closely to the muscular wall, perforated at the openings for the entrance of the two great veins, at the auriculo-ventricular opening, and containing within a firm red coagulum. Here the deposit had been laid down as in aneurism, except that it lined the cavity throughout, that it was more adherent to the wall, and that the auricle was of normal size. It was a false endocardial lining.

If in these examples of deposition of fibrin from circulating blood, the process of deposition commence at the root of the pulmonary artery or of the aorta, the formation of a tube, more or less complete, is often the result. These tubes are sometimes beautifully modeled to the vessel; and I have seen them admirably adapted at the semilunar valves, the clot being constricted at this part, and the impression of the valves being left marked upon it. If the concretion be a hollow cylinder, red coagulated blood may be found only in its central part. I met once with the most perfect hollow fibrinous cylinder of this kind in the body of an aged lady, who died suddenly, after a brief illness, the symptoms of which afforded no obvious reason for the rapidly fatal result. On a *post mortem* examination, I found that the aorta was dilated in the ascending and transverse portions, and that its inner surface was thickly studded with bony deposit. In this dilated portion there lay a fibrinous cylinder, which completely filled the vessel. On examination, this proved to be a distinct tube of fibrin, with a cord of coagulated red blood running through the centre. By a sudden dislodgment of this concretion, it had been carried to a point where the calibre of the vessel became narrower, upon which the circulation was at once arrested, and death instantaneously ensued. In another case, where a fibrinous tube laid down in the pulmonary artery was dislodged from its attachment, and carried by the blood current along the vessel, the death was not so instantaneous, and the tube was surrounded externally by a layer of red blood, which had floated between the deposit and the side of the vessel after dislodgment.

When attaching itself to a mere projection, standing

at an angle with the current of the blood, the concretion may simply float loosely in the direction of the stream, and may be merely composed of a few layers of deposited matter, or it may be affixed firmly to the projection by mechanical or even organic adhesion.

In the cases I have here been specially describing, the formation of the concretion seemed due in great part to an excess of fibrin in the blood. They were all inflammatory cases, in which what has been called *hyperinosis* by Franz Simon was present. In twenty-three cases of death from acute inflammation of the respiratory organs, and which ended fatally in the first stages by rapid sinking, I found in every case a fibrinous concretion, answering to one or other of the above named varieties; and, in the blood which remained in the form of red clot, the proportion of fibrin was far above the normal amount. These observations are confirmed by Grisolle; who, however, assigns for the concretion a different cause, viz., pulmonary obstruction.

Since the time of Pasta, a dispute has been going on in the medical world, as to the existence or non-existence of these fibrinous masses previous to death. I have explained that there are two definite forms of concretion; one formed from blood at rest—after death; the other from blood in motion—before death. I think, for my own part, that the arguments are conclusive which explain the probability of these last named depositions; for, could a concretion seize firm hold upon the walls of the heart, or become modeled into a hollow tube, or be grooved by blood currents, when all motion has ceased? Still, as the settlement of this dispute has not been definitely made as yet, I have thought it well to push the matter to a more perfect demonstration, by

inquiring whether a concretion could not be artificially produced in an animal, and be laid bare in its heart while the animal had not fully ceased to live, and while its heart was still pulsating.

Assuming, therefore, as a basis of experimental research, that in inflammatory cases the deposition takes place from an absolute increase in the amount of fibrin in the blood, and having repeated with satisfactory and affirmative results some of the interesting experiments of Dr. Gairdner,* in which he showed that by inhalation of oxygen gas the fibrin could be increased in quantity, I carried out a series of experiments with animals on the inhalation of oxygen, in which the inhaling process was continued for a period long enough to produce a decided class of symptoms, which were considered to afford evidence of fibrinous deposition. Then I rapidly destroyed the sensation of the animal, and at once laid open the heart.

Before passing to the details of experiment, it is necessary to premise, that many of the statements ordinarily made, to the effect that oxygen is a narcotic poison, are fundamentally incorrect. This error has arisen from the mode in which the experiments which led to it have been performed. I found, in the very first step of my labours, that, if an animal were placed in a jar of oxygen, with lime water beneath to remove the carbonic acid, in a short time the animal became subjected to symptoms of asphyxia and insensibility, notwithstanding the fact that a taper placed in the jar would burn more brightly than in common air. But I found, further, that when these symptoms presented

* Essay on Gout, 2nd Edition.

themselves, they could be at once removed *by the admission of more oxygen*. Hence the inference was clear, that the animals were either suffering from carbonic acid gas, or from the exhaustion of the gas, incident to its being turned rapidly into carbonic acid, and being removed by the lime, while no new supply was forthcoming. I therefore modified the experiment, and, instead of placing an animal in a closed chamber filled with oxygen, subjected it to a constant stream of the gas; or, in other words, kept it in a room ventilated with oxygen.

I had made a chamber with glass sides, capable of holding 3,350 cubic inches of gas. The chamber was air-tight, except at the top and the bottom. In an opening at the top a tube was inserted for the introduction of the gas. From an opening at the bottom, beneath a perforated zinc stage, another tube ran downwards, for the escape of the current. This tube dipped to the extent of an inch into some lime-water held in a beaker beneath. When this arrangement was completed, a large Pepys' gas-holder, capable of receiving 2,000 cubic inches of gas, was charged with oxygen made by the decomposition of chlorate of potash.

EXPERIMENT I. All being prepared, I introduced into the chamber, at 9 P.M., a full grown healthy cat. The escape tube from the gas-holder was connected with the tube at the top of the chamber, and a free current of oxygen was constantly driven through. The apparatus played well, and bubbles of gas were kept always escaping through the lime-water, no care being taken to save the gas. If at any time the lime-water became changed in colour, the ventilation was increased; and thus the animal was soon in an atmo-

sphere of pure oxygen, always newly supplied. By means of an additional gas-holder, I was further enabled to keep up the current steadily, since one was always ready when the other was exhausted of its gas; while, by means of a funnel-tube, running perpendicularly from the top of the chamber to a saucer inside, food was supplied. The drawing beneath represents the chamber and its appliances, while the experiment was progressing.

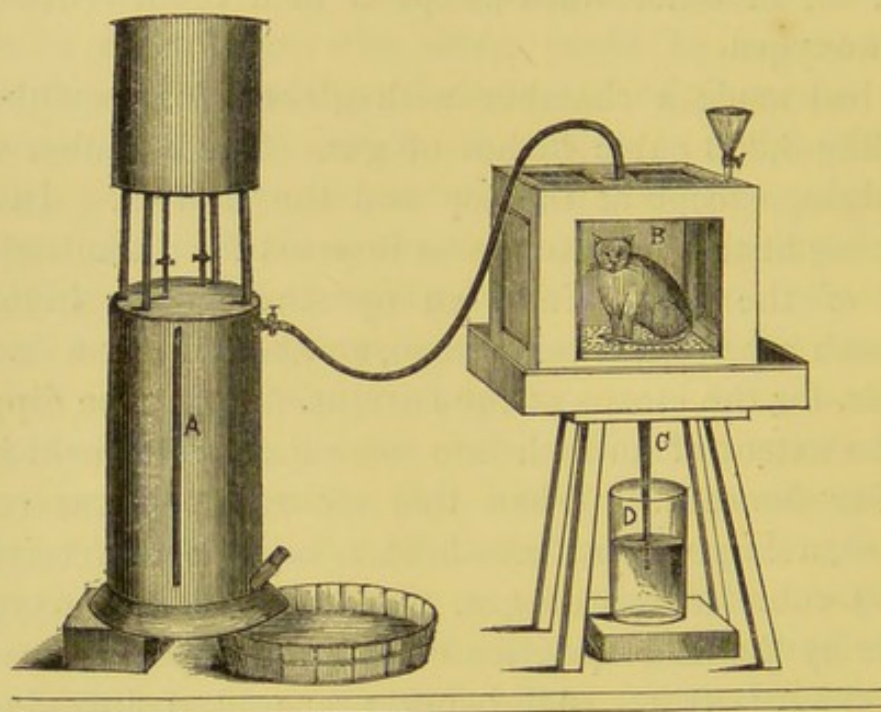


Fig. 2.

A. Gas-holder containing oxygen. B. Chamber containing cat. C. Tube for escape of gas.
D. Vessel containing lime-water.

After the animal had been breathing the oxygen for an hour and a half, the number of respirations was markedly increased, and the act of inspiration was accompanied by a dry harsh sound. The creature was excited and thirsty, often licking the sides of the chamber. At the end of seven hours, she became restless, and slightly convulsed. The supply of oxygen was now

cut off, and she was allowed to breathe the ordinary atmosphere quite freely. For three hours later, she continued in a restless, sinking state, and died.

About two hours after death the body was opened, and carefully examined.

The brain and spinal cord were perfectly natural throughout. The lungs were intensely red, but showed no indication of structural change. The blood in the veins was firmly coagulated. In the portal vein there was a thread of fibrin. The right auricle was literally choked with a tough fibrinous mass, which was firmly adherent to the wall of the auricula. It was covered on its superior surface by a thin layer (about a line in thickness) of red blood, which was easily removable. A prolongation of this fibrinous concretion passed into the ventricle, and curved upwards to the pulmonary artery. In the left auricle also there was a concretion, but of less size. The tricuspid and mitral valves were fringed with fibrin; and, at the root of the pulmonary artery, there was a small cord of the same kind, which adhered by its lower extremity to the cardiac wall. No trace of organic disease existed; but the muscles of the body and the vascular organs were unusually red. The bronchial membrane was dry throughout, but in no way red or congested.

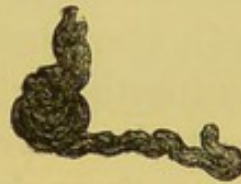


Fig. 3.
Fibrinous concretion in the
right side of heart.
Natural size.

Here there was a case of hyperinosis artificially produced, and fibrin was deposited in the heart.

[It was unfortunate that this experiment was not sufficiently conclusive; for, thinking that the death would not be so rapid, the animal being left in the open air, I, tired with watching all night, went for about

two hours to sleep, and when I awoke death, and even firm rigidity, had occurred. I therefore carried out the experiment again on various occasions, and with slight modifications, so as to husband the gas.

Of these experiments, I shall trouble the reader with two only, since they alone conclusively establish the position they were intended to support. In conducting them, as will be seen in the next diagram, a slight difference was introduced; but the principle remained the same.

EXPERIMENT II. *Inhalation of Oxygen.* I constructed an apparatus consisting of a glass chamber, of smaller dimensions than that used in the preceding experiment. The chamber was capable of holding three hundred cubic inches of gas; it was connected with a large Pepys' gas-holder, charged with oxygen, from which the current passing through it was obtained. By a further arrangement, the current, after leaving the chamber, was made to pass through hydrochloric acid, contained in a potash bulb tube, and was then received into another gas-holder, made for a different purpose, as will be described in another place. This third gas-holder secured a reserve fund of oxygen, which had only to be washed freely with lime water, for the removal of carbonic acid, to be rendered fit for retransmission to the first reservoir, and so again through the chamber. The hydrochloric acid was used to absorb any ammonia that might be thrown off into the air of the chamber from the breath or other excretions of the animal.

The subjoined drawing shows the apparatus as in action; the artist, Mr. Aldous, having been present when the experiment was progressing.

The apparatus being ready and the gas-holder

charged with oxygen, made by the decomposition of chlorate of potash, a full-grown healthy guinea pig was placed in the chamber, and a current of the gas

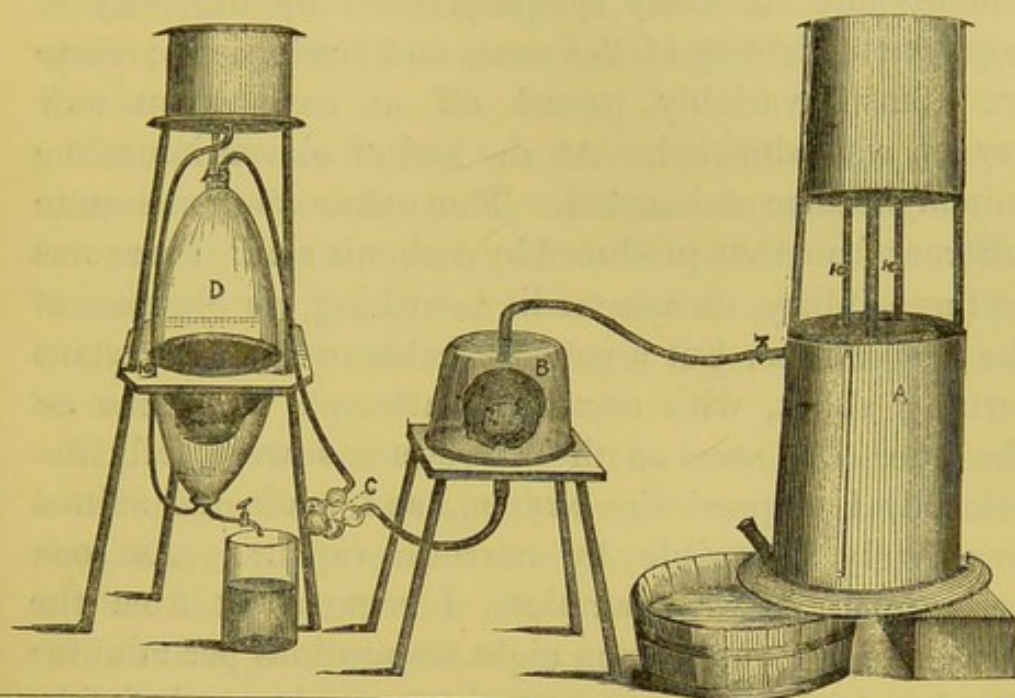


Fig. 4.

A. Gas-holder containing oxygen. B. Chamber containing animal. C. Bulb tube containing hydrochloric acid. D. Reserve gas-holder.

was driven steadily and constantly through the chamber, at the rate of 150 cubic inches per hour. The experiment commenced at half-past one in the afternoon. During the first half-hour the animal breathed with considerable rapidity; then this quickened respiration subsided, and an excited condition followed, the animal frisking about and seeming thirsty, often licking off the moisture on the sides of the chamber. But this condition also subsided; and, after an hour, the creature appeared, for a very long period, to exist in the natural state. For two hours the current of oxygen was kept constantly passing through, a new portion being gene-

rated as occasion required. Once or twice in the course of the proceedings, when the oxygen ventilation was for brief intervals suspended, the effects of carbonic acid became markedly symptomatised by difficulty of respiration, lividity of the nose, and restlessness; these symptoms invariably passed off at once when new oxygen was admitted. At the end of eleven hours the animal became exhausted. The exhaustion was quite different from that produced by carbonic acid. There was no insensibility, no spasmodic breathing, no blueness of the feet or nose, but a general feebleness, and constant turning about, with occasional attempts to recline on the side. As soon as these symptoms were fully developed, I stopped the oxygen, and made the animal completely insensible by narcotic vapour. As soon as insensibility was complete, I removed it from the chamber. It was making eight respirations per minute; the heart-beats being irregular, quick, and feeble. I now, with one or two sweeps of the knife, removed the ribs anteriorly, and laid the heart bare; it was seen pulsating quickly. The right auricle was much distended. The cavities were immediately laid open; a watch-glass full of blood, caught from the superior vena cava, coagulated firmly in two minutes, the clot being intensely red. In the right auricle there was a little fluid blood. In the auricula there was a clot of fibrin, distinctly separated, modeled to the part where it was found, and of about the size of a large hemp-seed. The inner surface of the auricle was coated with a fine layer of fibrin, which was easily removable with the point of the scalpel. In the left cavities, fine web-like cords of fibrin were interlaced with the chordæ tendineæ. To the free margins of the aortic valves there were

firmly attached three semi-transparent beads of fibrin, each of the size of a small pin's head. The aortic valves were fringed, on their free margins, with fibrinous beads, one valve having also a swollen and reddened appearance. In the aorta there lay a thin but long thread of fibrin.

The lungs contained some blood, but were not congested. They were, however, firmer in structure, and less elastic than natural. They floated in water. The vessels of the brain were congested. All the other organs were natural in structure, but unnaturally red in colour.

The operation of laying open the heart extended only over one minute; the organ was opened while yet briskly pulsating; and several attempts at respiration were made by the diaphragm and the chest muscles after the fibrinous deposition had been exposed to view.

EXPERIMENT III. *Inhalation of Oxygen.* By means of the apparatus described in the last experiment, I subjected a pigeon to the influence of oxygen gas. The experiment commenced at 11 a.m. For six hours after the inhalation but little change was observed in the animal; but at this time, the administration of the gas having been suspended for ten or fifteen minutes while the gas-holder was being re-supplied, a severe paroxysm of dyspnœa supervened, but disappeared immediately when a new charge of gas was driven through. At 8 p.m. (nine hours after the commencement of the experiment) the creature became feeble, and each inspiration was attended with a peculiar croupy sound. The respirations were now 28 per minute, and the croupy sound, which was so loud that it could be heard through the walls of the chamber, continued well marked for two

hours. There were the same indications of thirst as were noticed in the guinea-pig. The peculiar noise in the breathing subsided gradually, as a sleep supervened which lasted until half-past eleven, and was remarkably natural. On waking up at the hour named, the creature was less embarrassed in the breathing than it had been before, but it was much exhausted and restless. Its feathers were widely expanded out, and at times it reclined partially on one side. The beak, the eyes, and the feet were intensely red in colour, an appearance which commenced about four hours after the inhalation, and which continued to the end. At 12 o'clock, midnight, (*i. e.* thirteen hours after the inhalation began) I produced rapid narcotisation. As is usual in birds, the effects of the narcotic were at once developed, and in one minute and a half I removed the animal from the chamber perfectly insensible. The inspirations taken before the body was opened were three in the quarter minute, and deep. The chest was now quickly opened, and the heart laid bare. The muscular action on both sides was rapid. The right auricle, on being opened, was found in great part filled with a firm coagulum, modeled to those parts of the heart-wall against which it had rested. The clot was coloured by red matter. From this coagulum a cord ran downwards into the right ventricle, and, taking the course of the circulation, curved thence upwards for a short distance. But the most remarkable appearance was met with in the left ventricle. Here a firmer coagulum took a bulbous origin at the lower part of the cavity; from this there ran upwards a neck, which, as it approached the auriculo-ventricular valve, divided and ran along the borders of the valve, making a circle or ring from

which a prolongation was sent upwards into the aorta. At the point where this prolonged cord crossed the aortic valves, it narrowed evidently from the valves having closed upon it during the time the heart was acting, and above expanded itself so as to fill up a fourth of the diameter of the artery. This concretion, at its lowest or bulbous part, was beautifully moulded to the adjoining muscular wall, and it was so firmly attached to the muscular structure that it could not be removed without risk of breaking it away. It was also firmly attached to the valve. The side sketch gives a perfect representation of this concretion.

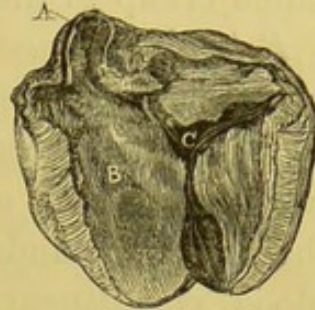


Fig. 5.

- A. Aorta, with prolongation of the concretion traversing it.
 B. Cavity of right ventricle.
 C. Concretion, with bulbous root in lower part of ventricle.

In both sides of the heart there was, in addition, some fluid red blood, of the same colour on each side. This, on being removed into a watch-glass, coagulated (at a temperature of 60° Fahr.) in fifty seconds; the clot being very firm, and no serum exuding ultimately from it. The blood corpuscles seemed to have undergone no modifications. The other organs were intensely red: and in the upper and lower parts of the trachea, for the space of half an inch, there were distinct exudations of plastic lymph; in the upper part the exudation blocked up the passage to a considerable extent; thus accounting in full for the noisy inspiration which had been so marked in the course of the experiment.

These experiments, then, definitively settle in the affirmative the question;—Whether coagulation of blood and separation of fibrin may occur in the body during life? The pathological conditions produced in all the animals, may be considered as those of active hyperi-

nosis; while in the pigeon the local manifestations rendered the case a very correct imitation of the disease called croup in the human subject.]

Relative Increase of Fibrin. The second class of cases, to which I referred at a previous page (64), are those in which the excess of fibrin is relative only; that is to say, the quantity of fibrin itself is not absolutely above the natural standard, but the serum and some other blood constituents are reduced below their natural figure. The results in such examples are the same, under certain circumstances, as in the last instance; *i. e.* the fibrin is laid down in a separate form in the circulating organs. This kind of separation not uncommonly occurs upon the setting up of profuse colliquative sweating or purging, as in the latter stages of phthisis pulmonalis, and also in cases of cholera, where a separated clot of fibrin is by no means unfrequent in the right side of the heart, and even in the aorta, albeit the remainder of the blood is in a semi-coagulated condition. In one case of phthisis pulmonalis, ending rapidly from diarrhœa, I found both sides of the heart filled completely with firm fibrinous coagula, which, when weighed after removal, were found to exceed 200 grains. The remainder of the blood was also firmly coagulated. The lungs were less changed in structure than is usual in fatal cases of phthisis; the characteristic signs of the disease being confined mainly to the apex of the left lung. The rapidity of the fatal event had, indeed, resulted more from the profuse elimination from the skin and the bowels, and the consequent formation of the concretions, than from the failure of the respiration.

Deposition from Obstruction. In the third place, I infer, from numerous observations, that the deposition

of fibrin may take place, from what may be called, in a general way, obstruction of the circulating current. [By this term I do not restrict myself to the idea of a direct obstacle lying in the course of the current, such as an indurated valve, or a bony mass, but include every cause which may lead to languid motion of blood, either generally or at any special point. Thus I include under this reading, cases where the muscular power of the heart is reduced to a dangerous degree, and cases where there is a dilated portion in the circulatory canal, as in the aneurismal cavity, and where the blood, for well-known physical reasons, flows slowly, as well as cases where the obstructing cause is direct.

Instances, in which fibrinous deposits form as the result of a languid motion of the blood arising from simple failure in the heart, are exceedingly common; indeed, in the majority of slow deaths, where the struggle for life is prolonged, and the patient lies prostrate with death written on his countenance, in Hippocratic delineation, for many hours, there is generally some tendency to a separation of fibrin, be the disease what it may. This may not only obtain in instances where the fibrin remains normal in amount, but even when it is reduced below the normal standard, as in purpura and typhus. In the *Dublin Hospital Gazette* for December 15th, 1845, a case of typhus is narrated occurring under the care of Dr. Corrigan, in which, after death, there was found in the right ventricle of the heart a bulbous-shaped firm concretion of fibrin, which passed into the pulmonary artery and continued its ramifications along the arterial branches. This concretion was made up of several distinct layers of fibrin, easily separable,—a fact showing the formation to have taken place whilst the blood was

in motion. I met once with an extreme case of purpura in a child. The body was covered with the dark patches, and even firm pressure with the finger on any clear spot of skin would give rise to a temporary blotch. After many weeks of suffering and distressing languor, death occurred one evening suddenly. On inspection, I found the right auricle filled with a fibrinous concretion, made up, as in Dr. Corrigan's case, of separate

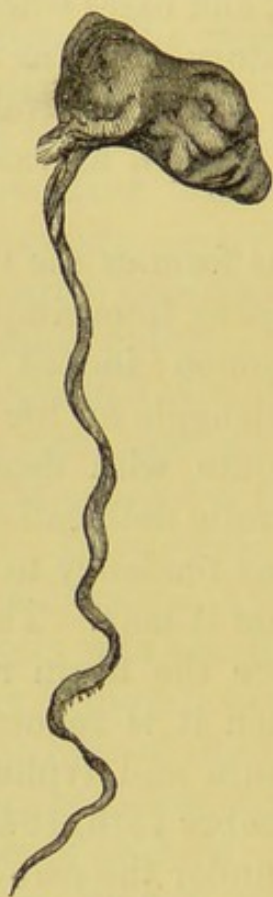


Fig. 6.

Fibrinous concretion, with prolongation into inferior vena cava.

layers. A very short prolongation of this concretion extended upwards into the superior vena cava, and a much longer prolongation, arising from a point near to the short one, extended downwards into the vena cava inferior.

In cases where no obvious disease is present, where life goes out passively in the seventh stage of its existence, falling like the full ripened fruit, in these cases death is often very prolonged, and fibrinous formations are deposited from the feebly circulating blood. In such examples, the development of the concretion will be in a great measure governed by the condition of the respiratory organs. If the respiration be free and the air-passages unloaded, so that such blood as does make the pulmonic current is oxidised, in such cases the concretion will frequently be firm, of large size, and strongly attached to the heart wall, if it be situated in one of the cavities of that organ. On the other hand, if the respiration is

to a great extent cut off, and is carried on with considerable difficulty long prior to death, such concretion as may form will be imperfect, its layers will be less compact, and it will have much more feeble hold upon any part with which it may come in contact. I will relate a few examples of these different classes of cases.

A man died in his eighty-second year; he had been long declining, but active disease of any kind was not to be detected. He had well marked arcus senilis, and the usual tissue collapse of old age. The veins were flaccid and distended, the skin shrunken. He took, as he thought, slight cold, lay prostrate for a day or two, then began gradually to sink. The breathing was unimpeded, and the action of the muscles of respiration was more fully sustained by far than of any other set. The last muscular energies of the man were expended and concentrated in the respiratory group. When the heart beat had ceased altogether, I observed that one or two efforts were made to inspire. On opening the body of this man, I found an immense concretion. It commenced in the left ventricle, it extended upwards into the aorta, crossed the arch, sent branches along the ascending vessels, and terminated in the descending aorta, making in its entire length eleven inches. This was one of the "serpents" of the old writers. Examining it closely, I found that it was made up of distinct layers, and that it was not a plug filling the vessel (for if it had been so, the circulation must long before have stopped, and indeed the thing could not have formed in that situation as a solid cylinder), but that it was a perfect hollow tube, that through its centre a cord of red blood remained, and that it had, in fact, been laid down layer upon layer from within, as

though it were a false vessel. I demonstrated the tubular character of this concretion at the Medical Society of London.

A middle-aged man, who from excesses in intoxicating drinks, from the effects of syphilis as a positive poison, from mercury as a kill or cure, and from anxieties about business, had become prematurely old, suddenly dropped one day into a state of hopeless prostration, with complete general paralysis of the right side of the body. He was well plied with supporting substances, but to no purpose: he sank listlessly away. The absolute symptoms of death extended over three days; the force of the circulation being far inferior to that of the respiration. The nurse used to remark, in common parlance, that he was dying by inches, and it was so; for the circulatory stream shortened in its circuit step by step, and the lower limbs were unnourished and dead first. When after the death I opened the body, I found in the aorta a concretion answering almost entirely to the description of the one previously given. This, too, was a hollow cylinder made up of layers, containing in its centre a cord of red blood, and formed by deposition from within.

A middle-aged man, greatly debilitated by harass, some excesses, and constant exposure to the night air, suffered from malaise, as if from cold, and soon showed signs of prostration. I suspected that the walls of the heart had undergone fatty softening. He became prostrate, suffering acutely at times with colicky pains and slight serous purging. The lungs became congested, the breathing enfeebled, and the skin acted at times profusely. He was supported by quinine and the acids, but sank. On examination, I found the heart of this

man literally worn out. The walls of the ventricles were thin, and their structure so softened, that they could be torn like saturated paper. In the aorta, as in the two preceding cases, a hollow cylinder of fibrin was deposited. It was looser and softer in texture, however, than the preceding, and had no firm adhesion to the muscular wall of the heart at its point of origin.

Lastly, in the case of a man who was worn out from intemperance in the use of spirituous drinks, whose end was quickened by an attack of bronchitis, and who died very slowly, I found the blood in the veins, as in the cases described by Drs. Peters, Goldsmith, and Moses, uncoagulable, and resembling treacle more than anything else. But in the right auricle of the heart there was a large soft fibrinous clot, slightly adherent to the wall; while in the pulmonary artery there was a half tube of fibrin modeled to the posterior half of the vessel.

I need enumerate no further examples of these forms of concretion. But I must add a word about the condition of the remaining blood in cases of this kind. As a general rule, the concretion is an index itself of the state of the blood surrounding it or near to it. If the concretion is firm and well developed, the blood is firmly coagulated also. If the concretion is loose in structure,—if it is formed into an imperfect tube or a semi-tube, the blood is more or less uncoagulable, and sometimes is quite fluid, yielding no trace of fibrin. Indeed, it is not impossible that the fibrin which the blood should contain is in some such cases removed, and that it exists in the concretion.

It may be urged, that in some instances where in

protracted dying the fibrin is thus separated, certain modified conditions of blood may obtain, and may favour the tendency to separation. It has long since been shown, that in scurvy the fibrin may separate spontaneously, and in the venesection of scurvy patients, the blood stream has been observed of a white and a dark shade; hence it is possible that the blood in this as in other disorders where disorganisation has occurred, may divide into its parts coincident with the languid motion, rather than as the sequence of such languor. But, that slow motion of blood is of itself favourable to the deposition of fibrin, is fully indicated in the case of aneurism; since there can be no reasonable doubt that the depositions of fibrin layer upon layer, which occur in the aneurismal sac, are greatly influenced by the slowness with which the blood circulates through the dilated part.]

It seems, in truth, that whenever and wherever there is an unnatural dilatation of the circulatory system, there there is obstruction, and there the deposition of fibrin is under favouring circumstances imminent. In the case of a child who died under my care with physical evidence of extensive dilatation of the left side of the heart, the symptoms immediately preceding death indicated to my mind clearly, that the cause of the failure of the circulation arose almost exclusively from the fibrinous separation. There were obstructed circulation, pulmonic congestion, and ultimately a sudden syncope. The *post mortem* examination proved the correctness of the diagnosis: the endocardial surface of the left ventricle was inlaid with fibrin, deposited in three layers or strata; while the cavity itself contained a rounded concretion, attached firmly to the tendinous

cords of the mitral valve. This concretion weighed seventy-five grains.

In this instance, there were no preceding symptoms indicating hyperinosis, or of any such modification in the character of the blood, as would lead to deposition, nor was the remaining blood unnatural in character.

In describing the formation of hollow cylinders of fibrin, page 68, an illustration was given from a case in which such a hollow cylinder was found in the dilated and roughened aorta of an aged woman. This case affords another example of the tendency of fibrin to deposit in parts of the circulatory apparatus, where an impediment lies in the way of the blood current.

[Thus there have been sketched out samples of the three conditions in which fibrin may be deposited directly from the living blood. In the first and second of these conditions, there is excess of fibrin, and the heart, to use a common phrase, *churns* out of the blood the concretion. In the third variety, the deposition is passive in character. These conditions may of course occur together.

The concretions of fibrin, to which I have here directed attention, must be considered as distinct deposits from the blood, and are not to be confounded with those small bead-like formations which occur in endocardial inflammation, and are supposed by some pathologists to be exudation products. I am in no position to deny the idea of fibrinous exudation on the endocardial surface; but the matter thus thrown out, if it is ever thrown out, must be limited, and can never build up a large concretion. At the same time, it is possible that such an exudation, in a disease of the acute inflam-

matory type, may form a favourable basis for a larger concretion deposited out of the blood.

There have been, indeed, certain instances recorded, in which a fibrinous mass has been found in the heart, having a direct connexion with that organ by blood-vessels, and having an organised character. It is fair to assume that, if such connexion may exist, the union might be accounted for on the principle here supplied. One of the best histories of an organised fibrinous mass in the heart, with which I am familiar, is given by Mr. James Stewart in the *Edinburgh Medical and Surgical Journal* for April 1817. Here the right and left ventricles contained each a concretion, attached by several peduncles to the heart wall. This concretion when cut into was found exceedingly vascular. Mr. Stewart's case was related with every evidence of care and of truth, and other pathological observers have reported similar observations. Still the evidence has been doubted. I have, however, myself met with one positive proof of the possibility of such organisation. An old lady, a patient of my friend Mr. Beresford, of Narborough near Leicester, died suddenly. On opening the body, the heart was found softened in structure, flabby, and collapsed. In the left ventricle, suspended from between the segments of the mitral valve by a fine peduncle, was a large pear-shaped white body, which moved easily by its neck. The entire heart was brought away by my friend Mr. Thomas Taylor, who was present at the *post mortem* examination, and who gave the heart to me. The growth in question was unmistakeably, for I examined it minutely, fibrinous. It was connected with the heart at its peduncular part by vessel, and, throughout its structure, vessels

could be distinctly traced. The diagram beneath gives a fair idea of the size, shape, and position of this concretion.

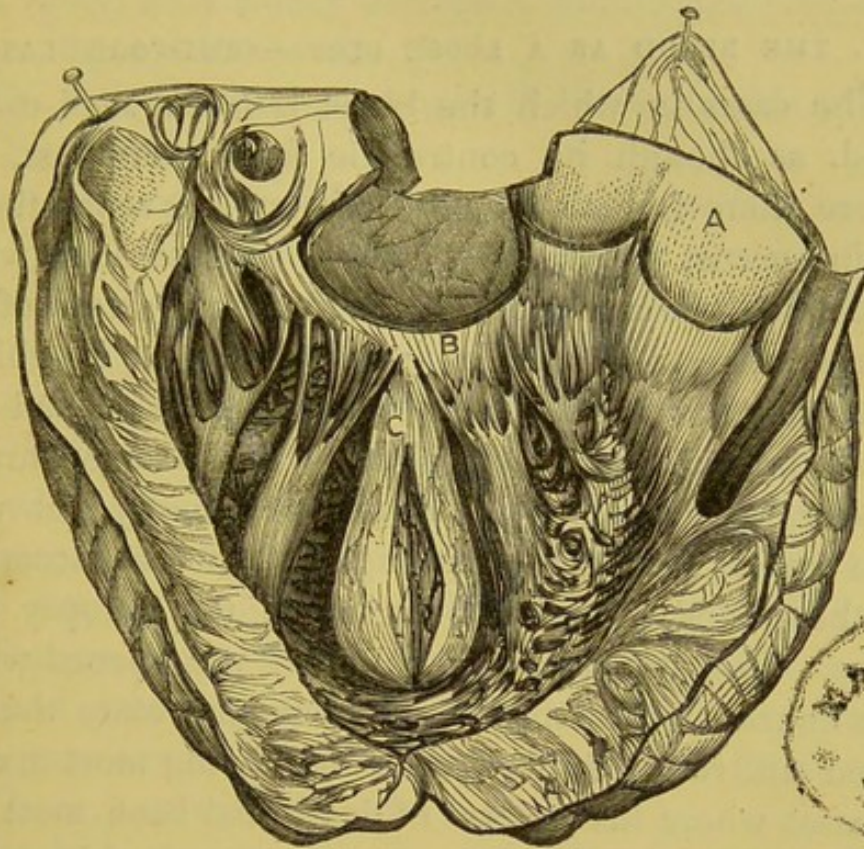


Fig. 7.

The heart, with the left ventricle exposed to view.

A. Aortic valves laid open and reflected back. B. Part of mitral valve.
C. Concretion.

A few years ago, my friend Dr. Sayer kindly showed me a concretion which he had once removed from the right ventricle. The symptoms indicative of the presence of concretion had been present many months, and the base of the mass was so firmly attached to the heart wall, that it was torn away on removal. I examined the specimen carefully, and exhibited it at the Medical Society, but could not ascertain whether it had been organised. I was rather inclined to think not, and to believe that the adhesion had been mechanical only. In truth, so firm are the mechanical adhesions



of this kind in certain cases, that the fact of adhesion must never be accepted alone as a sign of connexion by organisation.]

III. THE BLOOD AS A LOOSE CLOT—SEMI-COAGULATED.

The cases in which the blood is found semi-coagulated, as though its contractile force were lost, and where there is little or no tendency to a separation of fibrin, occur, in the first place, in instances where death has taken place from a lingering arrest of the process of respiration. In forty experiments in which I destroyed life in the inferior animals (dogs and cats chiefly), by making them slowly inhale some narcotic vapour, this condition of blood was usually met with. The results, however, were slightly different, according to the period after death at which the autopsy took place. In instances where the body was opened within two hours after death, I found in several cases that the blood still remained fluid, this state being most marked in cases where the process of death had been most prolonged. In each of these latter cases, the blood commenced to coagulate soon after its removal from the body; and whenever more than two hours was allowed to elapse before the performance of the autopsy, the coagulating process had always commenced.

I found, also, that the character of the gas inhaled made less difference, as regarded the state of the blood, than the mode of administration. If life were cut short in a few seconds by the inhalation of a large dose of the vapour of prussic acid, the process of coagulation, even if the blood were found fluid, was rarely delayed beyond eight or ten minutes after exposure. If, on the other hand, the gas was largely diluted and inhaled

slowly, so as to produce narcotism, convulsions, and prolonged death, the blood would retain its fluidity from one to two hours if allowed to remain in the body, and would only slowly become a semi-coagulated mass when exposed to the air.

The following experiments will illustrate this part of the argument.

EXPERIMENT IV. *Chloroform.* A pig, four months old, was made to breathe slowly the vapour of chloroform. From the difficulty with which the agent was exhibited, the exact amount of vapour breathed could not be ascertained. It was, however, exhibited so slowly, that a full half hour elapsed before the animal was narcotised; and when narcotism had commenced, it was kept up for half an hour longer before death took place. The heart then stopped suddenly; and quickly afterwards the respiration abruptly ceased. A large catheter was inserted into the trachea, and artificial respiration with pure oxygen was set up and continued for another half hour, but without any result.

The body was now laid open. The right side of the heart and the large veins were filled with blood, completely fluid, a portion of which showed no disposition to coagulate till after the lapse of an hour; it then formed a feeble clot, from which eventually no serum exuded.

Another portion of this blood, weighing about four ounces, was placed in a bottle containing some small angular bits of lead; and briskly shaken for a long time. A few traces of moist fibrin, amounting altogether to less than two grains, were obtained; the residue of blood remained permanently fluid.

EXPERIMENT V. *Fumes of Tobacco.* A dog was placed in a large chamber with glass walls. Into the chamber,

through an aperture in the bottom, a free amount of tobacco smoke was driven. The introduction of the smoke was steadily kept up for half an hour, when the animal became intoxicated, reeled about, and essayed to vomit. Soon afterwards he fell down insensible, and continued breathing with difficulty for twenty minutes longer, when both respiration and the beat of the heart finally ceased. The body was opened after the lapse of half-an-hour. It was then quite cold. The lungs were found slightly congested; the right side of the heart and the large veins were filled with blood, which was quite fluid. The blood was received into a test tube and retained. At the end of six hours it commenced to coagulate, and formed a loose coagulum, without any separation of serum.

In both this and the previous case, cadaveric rigidity did not occur for thirty hours; it passed off quickly.

EXPERIMENT VI. *Fumes of Lycoperdon giganteum, or common Puff-Ball.* I found, from several experiments, that if an animal were so exposed to the fumes of burning puff-ball that the fumes were inhaled very slowly, and if the narcotism, when induced, were kept up for a long time before death occurred, the coagulation of the blood was much retarded, and eventually was only imperfectly performed.*

[* The fact that the smoke of the puff-ball possesses anæsthetic properties was first discovered by myself in 1853. It is as yet an open question, what the agent is which produces the narcotism from fumes of puff ball. Dr. Snow is of opinion that it is a compound of cyanogen; but Mr. T. Herapath has more recently urged, with great amount of probability, that carbonic oxide is the narcotic principle. For my own part, I do not know what it is; but this is certain, that for physiological experiments on animals, puff-ball smoke is much cheaper and safer than chloroform. Its safety depends on the fact, that its influence in arresting the power of the heart is secondary. In extreme narcotism from puff-ball smoke, the circulation always outlives the respiration; so that life is safe as long as there is any respiration.]

The following single experiment will represent in full the rest. A full grown healthy dog was placed in a box charged with the fumes of puff-ball. It was not fairly narcotised until a lapse of twelve minutes had taken place. The animal was then quite insensible to pain. He was retained in the fumes for five minutes longer. The respirations were now reduced to ten per minute; the heart-beats were sixty. A portion of the fumes was at this time allowed to escape from the box, and the creature was thus left breathing a very diluted dose of the smoke. The respirations gradually fell to four in a minute, and after a period of half an hour ceased altogether; the heart-beats continued for seven minutes later.

The body of this animal was opened twenty minutes after the action of the heart had ceased. The blood throughout the right side of the circulation was quite fluid, although the animal temperature had well nigh departed. This blood remained fluid in a test tube for ten minutes, and eventually formed only a loose semi-coagulated clot.

EXPERIMENT VII. *Hydrocyanic Acid*. A full grown guinea pig was exposed to an atmosphere containing hydrocyanic acid much diluted. Death did not take place for five minutes. Fifteen minutes after death the body was opened. The right side of the heart was filled with fluid blood, which coagulated feebly in fifteen minutes after removal into a test-tube, and did not separate eventually into serum and clot.

EXPERIMENT VIII. *Hydrocyanic Acid*. In another guinea pig, which was killed instantaneously by being made to breathe a larger dose of the vapour of this acid, the blood was found firmly coagulated in the right side of the heart, within fifteen minutes after death.

EXPERIMENT IX. *Vapour of Ammonia.* A dog, placed in a large glass chamber, was made to inhale the vapour of ammonia for one hour and a quarter. The amount of the ammonia vapour inhaled could not be satisfactorily ascertained. The inhalation at first caused some considerable irritation, but in the end was borne pretty well. The vapour was driven into the chamber from a test-tube containing liquid ammonia, to which heat was applied. At the end of the hour and a quarter the animal fell on its side quite insensible. He was now removed from the chamber. The heart beats numbered sixty per minute, the respirations sixteen. The external jugular vein of the left side was laid bare, and six drachms of blood were drawn. The blood coagulated slightly in two and a half minutes; and in the course of six hours separated more decidedly into clot and serum, than in any of the preceding experiments. He evinced no sign of pain during the operation.

This blood unmistakeably evolved ammonia, for ammonia could be smelt. The animal, after lying senseless for the long period of one hour and three quarters, rallied, walked about for a while in a drunken staggering manner, and ultimately recovered.

I believe this is the first decisive experiment in which it has been shown that the vapour of ammonia can be made to produce anæsthetic effects.

EXPERIMENT X. *Carbonic Acid.* A guinea pig was made slowly to inhale an atmosphere impregnated with carbonic acid. The introduction of the gas into the chamber was occasionally suspended, that life might be longer sustained. The animal was thus made to survive for an hour. Half an hour after death the blood in the heart was still fluid, and was exceedingly dark.

It coagulated feebly on exposure to the air, and ultimately showed no disposition to separate into serum and clot.

EXPERIMENT XI. *Effects of Cold.* A large rat was placed in a glass chamber open at the top. The chamber was then completely surrounded by ice and salt; and the temperature of the air inside was reduced below freezing point. The intensity of the cold was kept up by relays of ice and salt. After exposure to the cold for two hours, the animal was evidently sleepy; the respirations were 100 per minute; and the tail was insensible to pain when pricked. Two hours later, the animal was still drowsy, but not absolutely comatose. Upon the floor of the chamber was now introduced a layer of ice and salt, on which the animal was obliged to recline. In forty minutes afterwards it was profoundly comatose, and was not excited by being pricked in various parts of the body. It reclined on its side, breathing gently, the head nodding, as is common in heavy sleep. The feet were quite frozen. An hour after this it remained the same. It was now left six hours, when it was found dead and rigid.

The animal was opened quickly afterwards. The eye was remarkably bright, and was unsunken. The brain and spinal cord were carefully laid open, and presented no trace of congestion, nor of any other lesion. The lungs were of a bright red colour, and free from congestion; but, on exposure to the air, the colour became paler: they floated in water. The heart was flaccid, and contained a small quantity of fluid blood on both sides. The veins were filled with blood. The blood on removal was quite fluid; but on its exposure to the atmosphere, at the temperature of the room, 60° Fahr.,

it formed a feeble coagulum. The bladder was filled with urine, which was found to be albuminous.

EXPERIMENT XII. *Electricity*. [For this experiment I am indebted to my friend Dr. Thudichum, who performed it, and most generously gave the history of the experiment to me.] A large bitch was the subject of the experiment. The wires from the poles of the powerful hydroelectric machine at the Polytechnic Institution were fixed to the animal by simple hoops; one round the neck, the other round the loins. The battery was now charged, and, on a given signal, discharged. The animal made a start, as if she were stretching all her muscles, and voided urine with great force; she fell on her left side, drawing the hind legs in trembling motions to the belly, stretching the fore legs straight from the body, and raising the nose so that the head and neck were in the same axis with the spine. The respiration ceased with the stroke. The heart beat at the rate of not less than 160 in a minute, became then interrupted for periods of two, five, and six seconds, made a stop of about ten seconds, and, beginning again to beat slowly, gradually recovered. The cornea and conjunctiva remained irritable. Respiration returned; the animal sat up; and was soon on her legs again.

The wires were again fastened, and a second shock of electricity was given. The animal started and fell in the same manner as before, and voided fæces while lying on her side. Immediately after the battery had been filled she got a third shock, which told very little upon the muscles. There was now no respiration; the heart's action could not be felt. The cornea and conjunctiva were not irritable; and the only muscles which acted were the respiratory muscles of the face. The

dog opened her mouth widely as if gasping for air; but, there being no motion of either thorax or heart, the efforts naturally proved unsuccessful, and, after having been repeated at longer intervals with decreasing intensity about five times, they ceased altogether.

The dog, being quite dead, was placed in a warm room. The animal had received the mortal stroke at twenty minutes past two. At ten minutes before three there were evident signs of *rigor mortis*; which, notwithstanding that the animal was handled in order to ascertain in what succession the muscles became rigid, went on increasing to such an extent that, at half-past seven (five hours and ten minutes after death), the dog appeared as if frozen hard or carved of wood, being quite stiff and inflexible.

After the outer muscles of the chest and abdomen had been dissected, the body was opened, to ascertain the state of the blood. All the veins were full of fluid blood, which, on being let out, presented no appearance of coagulation, but was of more consistency than venous blood in the living body.

In this case, it will be observed that the development of the coagulating process was much less marked than in any of the foregoing experiments.

[EXPERIMENT XIII. *Effects of sudden Exposure to heated Air.* The temperature of the day was 70° Fahr. I placed a large glass bell, open at the top and bottom, in a common washing tub. A young and healthy cat was put under the glass bell; a little straw was arranged at the bottom, on which she could recline or sit. The opening at the top of the jar was four inches in diameter; and she had ample room for moving in all directions within. When she was composed, I surrounded the jar

externally with a wall of sand, previously heated up to a temperature of 170° Fahr. The temperature of the air in the glass bell, and in which the animal was respiring, rose at once to 120° , and continued to rise till it reached 140° . Additional sand was added at intervals to sustain the temperature. At first the animal seemed to suffer nothing from the increase of warmth in the air surrounding it. She sat for five minutes quietly; then, as if she had received a sudden alarm or blow, she in a moment became startled. The breathing ran up so rapidly that it could hardly be counted; and the tongue became unnaturally red. Ten minutes later she lay on her side, convulsed, frothing at the mouth, and purged. The pupils were widely dilated, but she was not insensible: she dropped dead in an instant. Five minutes after death the body was removed and opened. The viscera felt to the fingers unusually warm, and the thermometer introduced into the folds of the viscera rose to 100° Fahr. The lungs were quite free from congestion, and inflated; the brain was pale, and free from congestion; the liver and kidneys were natural; the blood in the large veins, and on the right side of the heart, was bright red in colour, and of the thinnest quality I have ever seen. There was a little blood also on the left side of the heart: it resembled in colour that on the right so closely that it was impossible, by mere appearance, to detect any difference. The blood from each side was collected and left at rest, exposed to the air. It gained gradually in consistency, and after a time formed a soft clot, very bright in colour. The heart was flaccid. Cadaveric rigidity was strongly marked on the following day.]

EXPERIMENT XIV. *Ligature of the Vessels of the Kidney.* I cut down to the left kidney of a full grown dog, and

passed a ligature round all its vessels. The ligature was firmly tied so as to stop all circulation through the organ; about three fluid drachms of blood were lost during the experiment. The wound was neatly closed with four sutures. The temperature of the mouth of the animal was 96° . The dog seemed pretty well until twelve hours after the operation, when he was seized with severe rigors. He had passed a small quantity of urine once since the experiment. When the rigors passed off, he reclined in a sleepy inactive state; the temperature of the mouth and rectum was 102° Fahrenheit; the respiration varied from 30 to 40 in a minute, and was short; the heart-beats were from 140 to 160 in a minute, and feeble. He now refused food; and when roused seemed inclined to vomit. Six hours from this time he was still in a semisomnolent state. The action of the heart was feeble and most irregular; the respirations were reduced to 30 in a minute; the temperature of the mouth and rectum was still 102° ; the heat of the external surface was much increased. After another interval of twelve hours the following results were noted. He had been somewhat more lively, but took no food; the external wound was closed, and seemed healing kindly; there did not appear to be the slightest tenderness of the abdomen; the bowels had acted once, and a small portion of urine had been passed; the breathing was most irregular, it numbered, on an average, 35 respirations per minute, but an interval of ten seconds often elapsed without an inspiration, and then several hurried ones were taken; the heart-beats were also irregular; the temperature of the mouth was 97° , of the rectum, 100° . During the succeeding six hours the animal became very exhausted,

walked with a weak, tottering gait, and refused food, but took freely of water. The respirations continued to fail, and were more decidedly irregular; the heart-beat was feeble. When the animal was left quiet, he laid himself down in a drowsy condition. An hour and a half later he was found dead, but flaccid, and not quite cold.

The body was now opened. The lungs were collapsed and in no way congested. The blood of the right side of the heart, and of the large veins, all of which were filled, was fluid as water, without a trace of coagulum. The left side of the heart and the arteries were empty. The kidney operated on was dark, congested, and offensive. The pelvis of this organ was filled with loosely coagulated blood. There was no trace of peritoneal inflammation, nor was there any effused blood in the peritoneum. The opposite kidney was congested. The blood drawn from the heart and veins, when set aside, commenced to coagulate slightly after an hour, but formed only a feeble clot, without any separation of serum.

[EXPERIMENT XV. *Inhalation of the Fumes of Tobacco.* A young cat was placed in a glass chamber capable of holding 3,000 cubic inches. The smoke from some ignited tobacco was now driven gently through the chamber with air, so as to keep up a steady current. The symptoms of the poison commenced in about five minutes, with twitchings of the limbs and attempts to vomit. The twitchings soon passed into convulsions, with partial opisthotonos. There was no coma. At the end of twenty minutes the heart had ceased to beat; the breathing continued for some seconds afterwards.

Five minutes after death the body was opened. The lungs were collapsed, and peculiarly white in appear-

ance; they were quite free from congestion. The heart was still feebly contracting on both sides; and on both sides it was full of blood. The aorta was also filled with blood; the arterial blood was of a very bright red, contrasting strikingly with the venous, which was unusually dark. Fifteen minutes after this blood had been set aside, freely exposed to the air, it commenced to coagulate; but the coagulation was feeble and loose, without any ultimate separation of serum. All the vascular organs were free from congestion, and paler than natural. The brain was free from congestion. Cadaveric rigidity was well marked.

EXPERIMENT XVI. *Effects of Tobacco smoking.* I made a great number of experiments on the blood of a gentleman who was addicted to constant smoking. He was naturally stout, and at this time was anæmic, but was otherwise in moderate health, and pursued his daily labours with passable vigour. His appetite varied, and at times he suffered from dyspepsia. The state of his blood varied under special circumstances. In the morning, after rising, and previously to smoking, it coagulated in two minutes with moderate firmness, and the corpuscles were natural in shape generally: some, however, were always irregular. When two or three pipes had been smoked, a distinct change occurred in the blood; it retained its brightness, but flowed freely and coagulated slowly and feebly. After a long day of smoking,—from fifteen to twenty-five pipes having been taken,—the blood, though still retaining its bright colour, flowed much more readily, and would sometimes refuse to coagulate altogether. Left for a time in the cup of a microscope-glass, it would thicken from a sort of drying process, but would not healthily coagulate. Examined

with the microscope, when freshly drawn, the red corpuscles were irregular; some of them were oval; the central spot, or depression, was absent; and they did not run together in coin groups, but lay scattered irregularly, with but feeble indication of mutual attraction. During this condition the breath of the man always yielded freely the volatile alkali, and he was feeble, disinclined for any kind of exertion, and irritable; the skin was dry, the pulse quick and feeble. A night's rest would, in a great measure, dissipate these symptoms, and restore to the blood its plasticity and health. In these experiments the blood was drawn by puncture, and was therefore of the mixed kind. Capillary blood, I shall henceforth call it when thus obtained.

EXPERIMENT XVII. *Blood in a jaundiced Patient.* A man presented himself to me, for advice, whose skin was jaundiced from head to foot. I drew a little blood from this man with the artificial leech. The blood was of a dingy or dirty hue, and thin. It remained fluid, on exposure, for twenty minutes, and then feebly coagulated. The corpuscles, as in the previous cases, were irregular, ovoid, transparent, and some stellate. They were also loose and scattered. The fibrous network was ill developed. As the man recovered, these appearances subsided, the blood regained its plasticity, and the red corpuscles their normal characters. It coagulated, on exposure to the air, in from one and a half to two minutes, and the clot was firm.

The microscopical examination of the blood-corpuscles was conducted with scrupulous care, and the appearances were proved decisively correct by repeated observations.*

* In these, as in all succeeding experiments, where small quantities of blood were employed, the time of coagulation was determined by receiving the blood in

EXPERIMENT XVIII. *Blood in a jaundiced Patient.* In another man, who presented himself to me with well-marked jaundice, I conducted an observation similar to the last described. This man had an enlarged liver and some ascites: the yellowness of skin was universal. His blood, drawn with the artificial leech as before, presented the same dingy appearance when exposed to the air on the microscope glass. It had also a peculiar sticky, treacle-like consistence. It coagulated very slowly, as though drying rather than coagulating. However, it did eventually coagulate, but feebly. The red blood-corpuscles, though scattered, were of natural shape; but there was an abundance of white corpuscles. The fibrous network was but indifferently developed. The case is one which has obstinately resisted treatment, and I am unable to follow out the blood-characters further.

EXPERIMENT XIX. *Poisoning with Opium: Pseudo-hydrophobia: Rapid Death from Chloroform.* On Wednesday, July 1st, I administered to a young and apparently healthy cat seven drachms of Battley's solution of opium. She swallowed the dose freely; but within three minutes commenced to salivate profusely. On the following morning she was in a drowsy state, but ran about when called to, purred, took a little milk, and ate some animal food. After this I administered ten grains of morphia: she swallowed it all, but afterwards had the same symptoms of profuse salivation; this salivation continued during the whole of the day, with occasional slight vomiting. In the evening she was

the cup of a microscope glass, and then cautiously testing its time of coagulability by gently moving it with a fine needle. The times specified indicate a period extending from the moment when the blood escaped to the first appearance of coagulation.

only semi-narcotised. I now administered a scruple of morphia, without difficulty, but with the production of an increased salivation. She took food and drink on this occasion. On the following morning she was in a half-sleepy, intoxicated state, purring and rolling about and rubbing herself against anything in her way, in a playful manner. On Saturday, July 4th, she had a distaste for drinks, but she took three or four grains more morphia in some mutton; each dose, however small, reproduced the salivation. In the evening she continued in the same sleepy, half-intoxicated state; but in addition she had a peculiar snap with her jaw, and a further distaste for fluids. She was at the same time very gentle, and fussy; but, thinking that there were at least doubtful symptoms of hydrophobia, I brought matters to a close by destroying her rapidly with chloroform.

The body was examined twelve hours after death. On laying open the chest the lungs were found greatly congested on both sides, especially on the left. On both sides there were evidences of pleural adhesions. The right side of the heart was intensely congested, and was charged with blood resembling very thin black currant jelly; here and there were very small coagulated clots. On being removed from the ventricle the blood was found to contain bubbles of gas, and it evolved ammonia very freely. A little of the blood (three drachms) received into an evaporating dish was left exposed to the atmosphere; it coagulated with moderate firmness in six hours, the temperature of the atmosphere being 80°. The left side of the heart contained but little blood, and that dark and congealed. The kidneys were congested. The bladder was empty. The stomach was very vascu-

lar. The brain was congested, and presented bloody points in its structure. Morphia was chemically detected in the contents of the stomach.

EXPERIMENT XX. *Poisoning with Opium: Inhalation of Oxygen.* I diverge slightly from the present series of experiments to narrate one, where, under a modified plan, the blood was found with some portions of its fibrin separated. It occurred to me, that it would be worth trial to ascertain whether an animal profoundly narcotised with opium, could be rallied from that state by exposing it to oxygen.

I gave to a full grown healthy terrier ten grains of solid opium. The dose produced stupor for several hours; but no complete insensibility. The animal recovered. On the following day twenty-five grains were given, which in six hours brought on profound coma, coldness of the surface, and entire prostration. I now placed the animal in the oxygen chamber, and subjected him for two hours to the inhalation of oxygen. The temperature of his body rose, but there was no return of sensibility. In four hours after being removed from the chamber, he died, in the continuance of sleep.

The body was opened about two hours after death. The muscles were remarkably rigid. The blood throughout the body was bright red and firmly coagulated. The right auricle contained a large bulbous fibrinous concretion, which sent a prolongation into the ventricle and upwards to the pulmonary artery. The brain, liver, and kidneys were congested. Morphia was chemically detected in the stomach, the blood, and the urine.

EXPERIMENT XXI. *Poisoning with Arnica Montana.* Two drachms of the tincture of arnica montana were

administered to a large healthy cat. There was difficulty in getting it swallowed ; and afterwards vomiting came on, so that some of the poison was lost. The dose took but little effect. Two hours later, four drachms of the tincture were given ; the greater part was swallowed, and was retained. The animal soon became very feeble, and at the end of three hours the hinder extremities were paralysed, and the pupils were widely dilated. The half-ounce dose was now repeated and was retained. The symptoms of prostration and paralysis became more intensely marked, and in two hours she died partly comatose. The fore extremities were also paralysed, but never so fully as the hinder ones.

The *post mortem* examination was made twelve hours after death. There was some cadaveric rigidity, but not intensely marked. The lungs were rather red in colour and mottled, but well inflated ; on incision they presented no sign of congestion. There was no effusion in the pleural cavity. At some points in the upper part of the lungs there was some emphysema. The pericardium contained at least a drachm of dark bloody looking serum. The venæ cavæ, and the right auricle and ventricle, were distended to the last degree with blood. The blood was semi-coagulated, of the consistence of thick treacle, but presenting no definite firm clot. The pulmonary veins contained a little blood. The left auricle contained blood of the same character as that on the right side ; a little was also found in the left ventricle. The aorta contained blood exactly similar in character. The gall-bladder was not distended, but the surface of the liver was deeply tinged with bile. The liver presented many bloody points : the blood which exuded from it was fluid. The

kidneys were throughout intensely congested, the vessels on the surface forming a beautiful arborescent appearance: the spleen was slightly dark and congested: the bladder was empty but not contracted. The stomach contained a quantity of pinkish frothy mucus; the mucous surface was raised in deep folds, which were intensely vascular and had a dark velvety appearance; these folds extended nearly the whole length of the stomach, running in ten parallel lines: the rest of the surface of the stomach was of a cream colour. The duodenum contained a yellow fluid, but was not otherwise unnatural. The brain was considerably congested externally, but presented no bloody speck on the inner surface. The blood, left exposed to the air, underwent no further coagulation. The corpuscles were shrivelled, assumed different shapes, and were congregated in irregular patches; but not a perfect corpuscle could be found.

EXPERIMENT XXII. *Poisoning by Belladonna.* Two drachms of tincture of belladonna were given to a large cat. The dose was vomited. An hour afterwards, the same dose was repeated, and was retained. In the course of the succeeding hour the pupils were widely dilated, and there was paralysis of the hinder extremities. Two drachms more of the tincture were now given. General paralysis succeeded, partial coma, and death in four hours.

The body was examined sixteen hours after death. There was some cadaveric rigidity, but not strongly marked. The lungs externally were slightly dark and congested, but were filled with air; they were darker on the right side than on the left. The pericardium contained a drachm of bloody serum. The right side

of the heart was immensely distended and ingested: the right auricle was filled almost to bursting. The blood was very feebly coagulated, and of a tarry like consistence. The left side of the heart contained a little blood, of the same loose consistence and dark colour as the right. The liver externally had a peculiar nutmeg appearance, and was congested, giving forth fluid blood when incised. The kidneys were intensely congested externally, presenting a beautiful arborescent appearance; they were also congested internally. The blood in the inferior vena cava was completely fluid, showing no trace of coagulum. The bladder was empty and healthy. The spleen was healthy. The stomach was white, generally, with several pink patches on its inner surface. The blood set aside did not further coagulate; the corpuscles presented the same irregular and shrivelled characters as were observed in the arnica experiment. The actions of the two poisons seem, indeed, both in symptoms and pathology, to be almost identical.

EXPERIMENT XXIII. *Poisoning with Bichloride of Mercury.* A grain of bichloride of mercury was given in the evening to a rabbit. It quickly produced severe purging and prostration. On the following morning these effects had passed off. Two grains more were now given, with the repetition of the previous symptoms in a more severe form. The animal sank in a few hours.

The body was examined twenty hours after death. There was little cadaveric rigidity; the lungs were pale, almost to whiteness, and entirely free from congestion externally, but internally presenting bloody spots; the blood on the right side of the heart was dark and feebly coagulated, filling the auricle and ventricle; some blood

of a similar character was found on the left side. The liver was soft and dark, not congested; the kidneys were healthy, and free of congestion. There was perforation of the mucous and muscular coats of the stomach at two points, and at these points the peritoneum was inflated outwards, giving a peculiar, bladder-like appearance to the stomach externally; the stomach was filled with green food, and its mucous surface, though perforated, as if from ulceration, was pale. The blood set aside coagulated with moderate firmness; the corpuscles were irregular in shape, greatly contracted, and closely congregated. Mercury was chemically detected in the stomach, blood, and liver.

EXPERIMENT XXIV. *Death by Strangulation.* A dog, which its owner had destroyed by strangulation, was brought into the Grosvenor Place Medical School. I learned that the execution had been most unskilfully done, and that the animal had died very slowly, having been nearly twenty minutes insensible, and violently convulsed. I rescued him from ignominious burial to devote him to the cause of pathological science.

The *post-mortem* examination was made about two hours after death. Slight cadaveric rigidity had commenced; the brain, the lungs, the liver, and the kidneys, were all deeply congested; the right side of the heart was filled with blood, which was dark and uncoagulated. Set aside, and exposed to the air, it underwent a semi-coagulation, becoming thicker, and containing some small coagulated masses.

EXPERIMENT XXV. *Slow Poisoning with Liquor Potassæ.* A large dog was the subject of the experiment. On Tuesday, July 7, at 12, noon, two drachms of liquor potassæ, P.L., with a little water, were administered. He

swallowed it without hesitation; but it produced no effect. Two hours after, half an ounce was administered in the same way, which caused, after a short time, the vomiting of a little mucus tinged slightly with blood. The vomiting soon ceased, and was succeeded by symptoms of prostration and unintermitting thirst, with quickness and great irregularity of pulse. On the following day the symptoms were a little relieved. He took all liquid substances greedily, drinking water with the same avidity as on the day before. Another half ounce of liquor potassæ was administered. The administration was followed, in a few minutes, by the ejection of a small quantity of mucus. During the rest of the day he lay in a prostrate semi-comatose condition; the respiration was quick and feeble; the circulation quick and irregular to the last degree; the body was sometimes hot, sometimes cold, with occasional rigors; there was no purging; the urine was passed with moderate freedom. When placed on his legs he staggered, walked a few paces, and reclined on his side as soon as possible. The symptoms were so imminent, that the further administration of liquor potassæ was postponed this day. On Friday he seemed somewhat relieved. An ounce of the potash water, diluted, was administered *per anum*. Throughout the day he continued the same; nor was there much modification of symptoms on Saturday. On Saturday two ounces of diluted liquor potassæ were injected *per anum*. This was followed by the exaggeration of the symptoms of prostration. During Saturday night he lay breathing irregularly, and semi-comatose; and in this state he gradually sank; on Sunday morning he died, without any considerable manifestation of pain. The pupils throughout were widely dilated.

The *post-mortem* examination was made forty-eight hours after death, in the presence of Drs. Snow, G. Hewitt, Snow Beck, F. Webb, Rogers, Mr. Spencer Wells, and others. There was but little cadaveric rigidity, and such as appeared passed quickly off; the muscles were rather darker than usual, less so than in some other cases where I have seen death take place from the alkalies. The teeth were covered with dark sordes; the tongue was dry and black,—this black appearance extending to a point immediately below the pharynx, where it terminated almost in an even line, leaving the surface of the œsophagus of natural colour through its whole length; the stomach was free from congestion, blotch, or ulceration; the intestines, examined throughout, were generally healthy, but contained here and there slight vascular points; the liver was thickly covered with petechial blotches, and was softer than natural; the brain was healthy in appearance. The right lung contained some tuberculous masses of the size of small peas; the left lung was collapsed; neither lung was especially congested. The blood throughout the body generally was uncoagulated, thick, and treacly; it could be poured as a fluid from one vessel to another. In the right auricle there was a loose fibrinous clot, modeled to the auricle, and sending tubular prolongations into the superior and inferior cavæ; a small fibrinous cord ran into the pulmonary artery; the ventricles were distended with the fluid blood, and the muscular structure of the heart was dark. The blood-corpuscles were so entirely broken up, that no perfect corpuscle could be found, and but few irregular ones; the blood underwent no further coagulation on exposure to the air for many hours.

EXPERIMENT XXVI. *Slow Poisoning with Liquor Pot-*

assæ. I kept a guinea-pig for three months on a diet of milk and bread. It fattened on this diet, and remained in perfectly good health. On May 29th, I commenced to add two grains of potassa, in solution, to the milk; repeating the dose night and morning. This was continued for a week, the animal taking the milk, after a day or two, without hesitation, and seeming to suffer nothing. At the end of the week, I took some blood from a vessel at the base of the ear. The blood, when received in the glass, had a dusky dirty appearance; and its corpuscles were irregular, some being stellate, and others many sided. They had but little mutual attraction: and coagulation proceeded slowly. I now doubled the dose of potash, and continued its administration for another week. At the end of this time, the excreta from the bowels, which in health had been dark, were firm and of a clayey whiteness. The blood presented the same peculiarities as before. During the third week, I carried the administration of the potash to the extent of ten grains a day: but the animal began to refuse to take it, though it never failed to receive from three to four ounces of milk each day, and, when milk alone was given to it, it drank freely; the avidity for food seeming greater than it had been previously to the experiment. I continued the same administration for another week, with similar results. At the end of this time, I injected twelve grains of potash, in solution, into the stomach, by means of a small tube. This took decisive effect. On the following day, the animal suffered from incessant rigors and tremor; its heart-beat was feeble and irregular; it drank its milk freely, and was conscious. The next day, it was in a semi-comatose condition, avoided the light, and was in a constant state

of jactitation ; the ears seemed never to be at rest : it still took food. The next day, it was still semi-comatose ; and in the evening it sank and died, without any convulsion, but with constant tremor and jactitation of the limbs. The blood was examined frequently, and presented the same deficiency in coagulating power, and irregularity in the corpuscles.

The body was examined ten hours after death. There was slight cadaveric rigidity. The muscles throughout the body were of a deep dark colour. The lungs were shrunk, dark (like the other organs), but not congested. The heart was filled on both sides with black semi-coagulated blood ; the corpuscles of which were, as during life, irregular and disintegrated. I could not find a perfect corpuscle. The whole alimentary canal was pale on its mucous surface ; it presented no ulceration. The liver was dark, covered with petechial spots, and soft in structure. The spleen and kidneys were dark, and softer than natural. The vessels of the brain contained dark semi-coagulated blood ; the organ seemed otherwise healthy.

EXPERIMENT XXVII. *Administration of Ammonia.* At my request, Dr. Barker of Bedford poisoned a bitch with the strong liquid ammonia of the Pharmacopœia. He gave to her ten minims of the liquor, diluted in half an ounce of water. After the dose she fell on her side, but rallied, vomited freely, and recovered. On the following day, Dr. Barker gave twenty minims of the liquor, diluted in two ounces of water. It was swallowed readily. The bitch soon fell on her side, became convulsed, and died in a few minutes, with marked opisthotonos.

The body was sent to me for examination. The

cadaveric rigidity was feebly marked. The lungs were pale, and free from congestion. The stomach was slightly vascular on its inner surface. The kidneys were dark and congested. The bladder contained clear urine, which was not albuminous. The muscles of the body were darker in colour than natural. The heart was filled with blood on both sides. The blood was of dark colour, and resembled in point of consistence thin raspberry jam, being so generally fluid that it admitted of being poured like water from one vessel to another, but having scattered throughout it little semi-coagulated masses. This blood evolved ammonia. After it had remained a few hours exposed to the air, it coagulated so firmly as to become one loose clot, from which a little serum separated. The blood-corpuscles were irregular in shape, some oval, others many sided, others stellate; the central spot was absent in all.

EXPERIMENT XXVIII. *Continued Administration of the Bicarbonate of Ammonia.* I am again indebted to Dr. Barker for carrying out for me the following carefully conducted experiment. On November 29th, 1856, Dr. Barker extracted a little blood, by an incision in the nose, from a large and healthy dog. The blood coagulated in a few seconds; the red corpuscles were well defined, natural in size and appearance, and closely aggregated. The animal was made to breathe also on a little hydrochloric acid on a rod, but with no marked evidence of white fumes.

These observations made, five grains of bicarbonate of ammonia were administered, diluted in water; and this dose was repeated every day until December 3rd. On December 4th, the same dose was given twice daily, and was so continued until the 8th. Before administering

the first dose on the 8th, the breath was tested by the hydrochloric acid rod test, and yielded distinct white fumes. The dose was repeated in the course of the day.

On December 9th, after the usual dose had been given, blood was drawn from the ear, and examined. It coagulated slowly and imperfectly; the corpuscles were scattered and entirely modified, some collapsed, and all more or less irregular in shape, being oval or many sided. The animal, too, was unwell, was thirsty, and inactive; yet he took his food, as he had done all through, without hesitation. In the evening he vomited, bringing up a little viscid mucus. Although he had eaten heartily all through the experiment, he was now thinner than he was at first.

In the course of the 10th and 11th days of December, the animal received four five-grain doses of the bicarbonate. On December 12th, two doses of eight grains each were given. On the morning of December 13th, before any dose was administered, the breath was examined, and found markedly ammoniacal. The blood-corpuscles were much more generally modified; there were none perfect. Some were oval, some many sided, some star-like. The dark central point was absent in all.

On December 14th, an eight-grain dose was administered in the morning; on December 15th and 16th, the same; on December 17th and 18th, ten grains were given each forenoon. On this latter date, a little blood was extracted, and was watched for twenty minutes, during which time it did not coagulate.

On December 19th, 20th, and 21st, ten-grain doses were given each day. On December 21st, the breath was strongly ammoniacal, as before.

Dr. Barker now gave the animal a respite for seven

days. On December 28th, he recommenced by giving a scruple dose of the bicarbonate in the morning, and a second dose of the same size in the evening. These doses produced vomiting and a staggering gait; but the effects passed off in a few minutes.

On December 29th, one scruple dose was given in the morning. On December 30th, a little blood was drawn, which did not coagulate for nearly an hour. After this observation, another scruple dose was administered. On December 31st, a scruple dose was given in the morning and in the evening.

On January 1, 1857, a scruple dose was given; but none on the 2nd. The breath continued markedly ammoniacal on January 1st, 2nd, and 3rd. On the 3rd, a scruple dose was given; two scruple doses on January 4th, and three scruple doses on the 5th. At this point, the animal became decidedly ill; his appetite fell off, and he was prostrated and drowsy. On January 6th and 7th, two scruple doses were given each day; on January 8th, three similar doses; on the 9th, two; and on the 10th, three. During this time, the disease symptoms above described became more evident; the breath was more strongly ammoniacal, the blood coagulated slowly and feebly, and the red corpuscles underwent remarkable modifications. They assumed various shapes; stellate, many sided, and oval. Some were entirely disintegrated. All were free from central opacity. They sometimes aggregated loosely in circular groups, lying out flattened, not surface to surface like coins. They continued long in motion, and had but little mutual attraction. On January 11th, a dose of half a drachm of the bicarbonate was given, and proved final. A few minutes afterwards, the animal rolled on his side,

became convulsed with opisthotonos, and died. Directly after death, Dr. Barker sent him to me for examination.

At the *post mortem* examination, Dr. Fuller was present. The animal had been dead about thirty hours, but was quite fresh. There was slight cadaveric rigidity. On reflecting back the chest muscles, they were found remarkably dark in colour, an appearance which extended through the whole muscular system, and indeed through all the soft parts. The muscles were soft in structure, and easily torn. Fluid blood exuded from the divided parts. The lungs, the liver, and the kidneys, were dark, and intensely congested with fluid blood. The liver and kidneys were soft in structure, and blood exuded from incisions made into them. The bladder was charged with urine, which evolved ammonia freely, and which, subjected to heat and nitric acid, was found to be highly albuminous. The specific gravity of urine was 1035. The brain was congested with dark fluid blood. The stomach was vascular on its inner surface. Along the alimentary canal, vascular spots were here and there met with. There was no effusion in any of the serous cavities. The lungs were congested, and the bronchial mucous membrane injected in points, but everywhere lined with secretion. The heart was filled with blood on both sides. The blood was entirely fluid; and evolved ammonia so freely, that by holding over it, at a slight distance, a surface of glass moistened with a little pure dilute hydrochloric acid, the glass, on drying, was frosted with crystals of chloride of ammonium. The blood on both sides of the heart was dark in colour. Each variety was exposed to the air in a small evaporating cup, at a temperature of 65° Fahr. Thus exposed, the specimens continued fluid for thirty hours, and then

commenced to coagulate, eventually coagulating so far as to become modeled to the containing cup, and to admit of being turned out of it as a shaped mass. There was, however, no separation of serum. The blood-corpuscles presented the same modifications as were observed during life. They were stellate, many-sided, or collapsed; none were perfect.

EXPERIMENT XXIX. *Iodide of Ammonium*. Thirty grains of iodide of ammonium were given to a rabbit. The salt produced rapid and violent effects, great excitement, convulsions, and death in six minutes. The cadaveric rigidity was very feebly marked. At the *post mortem* examination, the brain was found natural. The lungs were peculiarly pale, almost white. There was no mark whatever of congestion of lungs. Both sides of the heart were filled with dark blood, having the consistence of thin jelly. The left side of the heart was fully distended with blood, but this blood was rather more firmly coagulated than that on the right side. The stomach was filled with vegetable substance; its mucous coat presented no sign of congestion. The kidneys were congested. The liver was dark, but not particularly congested. A little of the blood from each side of the heart was left exposed to the air in a test-tube. It set into a soft mass, from which serum exuded in twelve hours. The blood-corpuscles presented the same irregularity of character as in the two preceding experiments.

EXPERIMENT XXX. *Long continued Inhalation of Ammonia Vapour*. On Jan. 19th, 1857, I placed a fine large healthy guinea-pig in a glass chamber, of the same size and make as that described at page 71. The chamber was capable of containing 3,350 cubic inches. It

had a false bottom perforated in a few places. Beneath the perforated bottom and resting on the true bottom of the chamber, a half drachm of the strong liquid ammonia was placed in an evaporating dish. The chamber was then closed for an hour, so that the ammonia vapour might diffuse through the air contained. After an hour a small stream of air was permitted to flow through for eleven hours; then the ammonia was repeated as before. The air of the chamber was thus kept more or less charged with the ammonia vapour. It had the smell of a menagerie. Before the animal was placed in the chamber, I made a lancet incision in her ear, and collected six or seven drops of blood. The blood coagulated in one minute and twenty seconds. The corpuscles were perfectly regular and natural, running together in coin piles in the usual way. After the experiment commenced, the animal was fed as before; milk, green stuff, and bread formed her staple commodities.

The experiment was continued until January 21st. Meantime the animal continued moderately well; the only peculiarity was, that her cravings for food increased, and that she devoured ravenously all her vegetable matter. On the evening of the 21st I removed her from her chamber. She was warm and lively. A little blood drawn from her nose was rather more dusky than natural, and the corpuscles were irregular in form, some being serrated at the edge, others many sided. They continued for a long time in motion between the glasses, and their force of aggregation was feeble. The blood coagulated in two minutes.

The animal was again placed in the chamber. The times of supplying the ammonia were made the same; but the amount of ammonia was made a drachm each

time. At first the vapour excited some irritation of the nostrils, but this effect soon wore off.

On January 23rd, the animal became restless, and her breathing was quick and feeble. She took her food ravenously, and seemed as if she wished to be constantly eating; the instinctive desire for vegetable food was predominant. The blood examined to day showed further modification of the corpuscles. A perfect corpuscle was not to be met with. The blood rather dried on the glass than coagulated; and the fibrous net-work was scantily developed. The experiment was rigidly carried on for several days; the ravenous appetite continued, the animal slept well, and there was little variation in the other signs until January 30th. At this date she became very feeble; she reclined on the side in part, and was for the first time unusually sensitive to sounds. The merest noise, a scratch on the side of the chamber, or any rustling sound, at once startled her and made her uneasy. This day she refused milk, but sought more ravenously after green food. In the evening of this day her sight also must have become disturbed; for when food was put into the chamber, instead of going to it at once in her usual way, she sought about for it, without being able to find it. When it was placed under her nose, she ate cabbage leaf with great eagerness. Left quiet, but watched at a little distance, she was seen to recline a little on the left side, and to remain for several hours in a half comatose state with the ears involuntarily twitching, the limbs occasionally starting, and the breathing sharp and spasmodic, as in singultus. On removing her from the box, I found the tongue dry, the breathing hurried, and the heart-beat feeble, quick, and irregular. When the hand was placed over the back, all the

muscles were felt to be tremulous, and now and then the body was momentarily drawn up by a feeble spasmodic movement.

The blood-corpuscles were now so much modified, that it seemed a marvel to me how the animal could exist. On the ammonia vapour being removed, however, the serious symptoms quickly passed off. I now gave the ammonia less frequently, but occasionally repeated it in full dose for two or three days, and always with a repetition of the same train of symptoms. Once I carried on the administration till complete coma was produced, and afterwards exposed the animal freely to air. About the end of two hours signs of recovery recommenced.

On February 28th, I withdrew the administration altogether, and let the animal run about as usual, watching the process of recovery from day to day. The desire for food, especially for green food, was most extraordinary. In a week she seemed as lively and as well as ever, but the blood-corpuscles did not lose their irregularity for several weeks. It was as curious as instructive to watch the process of repair in those little floating cells. Their restoration was coincident with, if not dependent on, a restoration of the plasticity of the liquor sanguinis. Towards the end of April, but not until then, the blood assumed its normal attributes. The corpuscles were natural in size, shape, and power of aggregation, the colour of the blood was bright on exposure to air, and the fibrous net-work was well defined.

EXPERIMENT XXXI. *Inhalation of Sulphide of Ammonium.* In an experiment on a guinea-pig, conducted in the same manner as the last, I substituted the sulphide of ammonium for ammonia. The experiment extended over three weeks; and the results are summed up in say-

ing that the symptoms produced were identical with those related in the last experiment as occurring from ammonia simply. The effects on the blood were also the same.

EXPERIMENT XXXII. *Effects of Ammonia given as a Medicine.* I saw a case of inflammatory disease, which in its last stages was treated with five-grain doses of the bicarbonate of ammonia, given every two hours, in decoction of cinchona. The administration was continued for nearly three days. The girl was sinking and partly comatose before the ammonia was given; and the excreting processes were very much diminished. She gradually continued to sink until her death. At the *post mortem* examination, twenty hours after death, the odour of ammonia was distinct in the blood. The blood was dark and thick, but uncoagulated. I collected half an ounce of it from the right side of the heart. Upon exposure to the air for three days, it underwent feeble coagulation. The blood-corpuscles were all modified in the same manner as described in the last experiment.

The modifications which the blood-corpuscles undergo, as referred to in the preceding experiments, are depicted

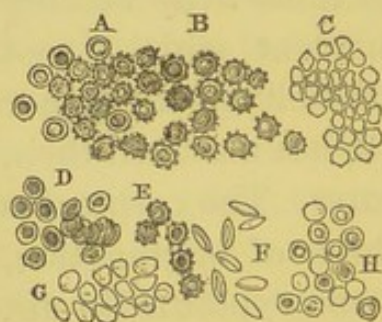


Fig.
D. Corpuscles healthy, before the administration of the alkali.
A, B, C, E, F, G, H. Corpuscles as modified by the administration of the alkali.

in the side sketches. These have all been taken by the artist from blood newly drawn from the animals that were subjected to the alkalies. I would repeat that the modifications here delineated were definitely due to the administration of the various agents

given to the animals subjected to experiment, and not to the accidents which sometimes occur from the manner in which microscopical observations are conducted. To

exclude all such false deduction, the observations were repeated over and over again, with the strictest regard to accuracy.

By mixing freshly drawn blood with weak solutions of the alkalies, modifications of the corpuscles, exactly similar in character, may be observed. The effects of the alkalies on living blood-corpuscles is, indeed, direct; and is, I believe, purely chemical. There is a pitch of alkalinity, exposed to which blood-corpuscles melt up altogether.]

FŒTAL BLOOD. It has been observed by many writers that a deficiency of fibrin is common to the blood of the fœtus. On this point I have made numerous observations, which all tend to support the truth of the statement, in so far as a want of coagulable power proves the absence of fibrin.

EXPERIMENT XXXIII. I placed two ligatures on the umbilical cord, about two inches from the abdomen of a healthy fœtus, in the usual way after birth. I now firmly compressed the placenta with the hand, and thus forced a considerable quantity of blood into the cord. I then nipped the cord firmly at its placental end between the thumb and finger, and, carrying them in this way in the direction of the ligatured end, made the cord congested with blood for the space of four inches. Another ligature was applied at the spot compressed by the fingers. The vein and arteries were next separately punctured with a lancet, and the blood from each (about three drachms) was received in separate tubes. The blood from the vein was less dark than that from the artery; but, on exposure to air, the artery blood soon assumed a bright colour. There was no coagulation for twenty minutes in either specimen; at the end of that

time a feeble clot formed, unattended with the separation of serum.

EXPERIMENT XXXIV. I placed a placenta in a wash-hand basin, the cord being tied, and observed the period of coagulation, by pricking the placental vessels with a lancet at different intervals of time. The first instance in which the blood was coagulated was in fifteen minutes. This occurred in a large vessel, which stood out prominently among the rest near the root of the cord. Five minutes later, the blood in all the vessels exposed to the air had slightly coagulated; but on turning the organ over, I found that several other vessels, which had been lying in contact with the basin beneath, contained blood still quite fluid. The blood generally did not coagulate firmly. It is well to observe that, immediately after the birth of this placenta, a little blood flowed from the vagina of the woman and was received in a teacup. This blood set into a firm clot in two minutes.

[EXPERIMENT XXXV. I opened the body of a child, born at the full period of utero-gestation, and which was stated to have lived an hour after birth. The body of the child had attained a natural development, was well nourished, and shewed no external evidence of injury. Internally, the following peculiarities presented themselves. Each pleural cavity contained from five to six drachms of bloody serous fluid; and the pericardium contained two drachms of a similar fluid, by which the membrane had been distended. The fœtal openings in the heart were still patent. The pulmonary veins and the left side of the heart were filled with blood. A small portion of lung floated readily, with and without pressure; the right lung, at its lower part, had, how-

ever, a dark mottled appearance. The blood generally was fluid, and slightly tarry in consistency, but with no trace of clot in any part. When a portion of it was mixed with a solution of potash, ammonia was distinctly evolved. The blood was dark in colour, and its corpuscles were irregular in shape and larger than natural, but not disintegrated. A little of this foetal blood was set aside, exposed to the air. It became in twelve hours a little thicker in consistence, but underwent no perfect coagulation.]

In a large number of further dissections of the foetus in various animals (amounting in all to forty-three), I have never found the blood firmly coagulated, and have never met with anything like a separation of fibrin. In a case where the head of a child was very large and where there was such severe compression that the death of the foetus occurred during parturition, I found a large loose clot of blood between the scalp and the cranium. In three foetal lambs, all from one ewe, which had been killed by the knife, I found a loose clot of blood in the abdominal cavity below the liver. Morgagni observed the same kind of clot in foetal calves, where the cows had been killed at an early stage of impregnation. In three instances in the human foetus, where there were evidences of syphilitic eruption on the skin, the blood was scarcely to be called coagulable at all, being only of a sticky, tarry consistence, like cholera blood, without even a trace of clot.

I have before referred to some cases recorded by Morgagni, in which patients dying from difficulty in respiration were found to have the blood on the right side of the heart in a state completely fluid, when the

body was opened many hours after death. I have never met with absolute fluidity of blood in such cases; but I have met with a few cases of the kind, in which only a form of semi-coagulation was present, there being no distinct clot.

I found this semi-coagulated condition, also, in an almost unique case of death from sheer starvation. The patient in this instance was a gentleman of considerable fortune, who suffered from a monomania, and became led away by a delusion that he had no stomach. He absolutely refused all food; and the efforts to force it on him at last caused such serious exhaustion, that the attempt became absolutely dangerous. Ultimately, after having passed several days without taking any food at all, he died, persisting in his delusion to the end. A more emaciated body it is almost impossible to conceive. I could find but few traces of organic lesion; but the stomach was darker than usual, and rather softened. The blood in the veins was a thickened, uncoagulable, sticky substance, with no trace of clot in any part.

[In two instances of death from cancerous disease, one being a case of epithelial cancer of the vagina, the other of scirrhus of the stomach, both in women of the lower class, and past the meridian of life, I found the same condition of blood—no evident clot, the whole a mere grumous fluid. In a thoracic case, where the right side of the heart was very much thinned and softened, where the breathing in the last days of life was most irregular, and the whole of the voluntary muscles were in a state of partial paralysis, the same condition of the blood presented itself.]

Lastly, in a case of leucocythæmia, with softened condition of the heart, hepatisation of the right lung,

and pleural adhesions of the left, the blood in both arteries and veins was found quite fluid at the *post mortem* examination, conducted twenty-four hours after death. This blood coagulated feebly on exposure to the air.

IV. ABSOLUTE FLUIDITY OF BLOOD.

[Until the latter part of last year (1856), I had never met with a case in which the blood after death from natural disease, was not only perfectly fluid in the body, but remained permanently fluid on exposure to the air. At last a child came before me at the Metropolitan Dispensary, suffering from cyanosis, together with tuberculous deposit in both lungs. This child died from deficient oxidation and exhaustion; the body was quite blue at death, but on the following day it assumed a natural, and, indeed, florid colour, especially in parts where it had been exposed to the air. When I opened the body, I found the blood in every part fluid, of a thickish consistence, dark in colour, and of a peculiar odour. This blood was feebly disengaging ammonia, as I proved by after experiment. I retained a few drachms of it for observation: it never fairly coagulated, but eventually became offensive, and more liquid than before. The corpuscles of this blood were all modified; some were oval, others many sided, others were stellate, others disintegrated.]

In examining the bodies of the inferior animals, I have never found the blood capable of remaining permanently fluid in any case where death has occurred from natural causes. But I have succeeded in inducing such a condition of blood experimentally, as I now proceed to describe.

EXPERIMENT XXXVI. *Injection of Water into the Peritoneum.* A dog, weighing twenty-three pounds, was bled to the extent of two drachms by making an incision into the ear. The blood coagulated firmly in two minutes. A small opening was now made into the peritoneal cavity with a lancet, and, a catheter being carefully introduced, four pounds of distilled water, at the temperature of 90° Fahr., were thrown slowly into the peritoneal sac. After the operation, by which the abdomen was much distended, the animal lay down quietly, and, in the course of four hours, was in a semi-comatose state. At this time the distension from the fluid had disappeared, but no fluid had escaped from the wound. The dog was carefully watched for eight hours more, during which time he once or twice got up and walked about, but with a tottering and exhausted gait. Finally he became more decidedly somnolent, and gradually sank and died.

On opening the body, an hour after death, no trace of the fluid could be found in the peritoneum; but the venous system was engorged with blood which was as fluid as water itself, and showed no tendency to coagulate. I kept some of this blood for many weeks, until it was offensive, but the fluidity remained. From another portion of this blood I endeavoured to extract fibrin, by agitation, without success. The blood-corpuscles were unusually large. When heat to boiling point was applied to some of the blood in a test-tube, only a feeble tendency to coagulation of albumen was witnessed.

EXPERIMENT XXXVII. *Injection of Water into the Peritoneum.* I injected into the peritoneal cavity of another dog as much water as was equal in weight

to a fifth part of his whole body.* Death took place with symptoms differing in no material point from those described in the last experiment. I found, on *post mortem* inquiry, the same marked fluidity of blood. The lungs were engorged with this watery blood; there was an effusion of two ounces of red coloured serum in the left pleural cavity, and one ounce in the right. The blood on both the arterial and venous sides of the circulation did not coagulate when exposed to the air.

EXPERIMENT XXXVIII. *Injection of Water into the Peritoneum.* Into the peritoneal cavity of another dog I injected the same proportion of water as in the last named instance. The symptoms were in all essential points the same. The blood was again found fluid after death, but the lungs were not unusually engorged. On exposure to air, the blood did not coagulate; nor could any traces of fibrin be obtained from it by agitation with pieces of lead.

EXPERIMENT XXXIX. *Injection of Water into the*

[* It is worthy of observation, that an amount of fluid, equal to a fifth part of his weight, is ordinarily fatal to a dog, when injected into the peritoneal cavity. Less than this, on the contrary, rarely proves fatal; but the animal is feeble for a few days, takes little food, drinks nothing, passes a good deal of urine, staggers when he first begins to walk, is generally cold over the whole surface of the body, and has an anæmic bruit in the neck. If a little of his blood is drawn, it is thin, bright red, and feebly coagulable; it flows from the wound freely, and is in no hurry to stop. The corpuscles are modified, being larger than natural, and often irregular in shape. The first sign of convalescence is a desire for food, and a returning warmth in the body. At least three days must elapse before the animal begins to run about again briskly; but, when he does begin to recover, he recovers quickly and perfectly. In one instance I saw anasarca supervene; but this soon passed away. I had one dog whose peritoneum I injected with water on three occasions, at intervals of twenty days. He showed the same symptoms of disease and of recovery each time. I meant to have continued this much longer, in order to see what ultimate change or degeneration of the blood and tissues would accrue from keeping the blood in this diluted condition. Unfortunately, the dog one day gnawed through his tether, vanished, and became a pathological wonder, wandering about the earth, with the only claims he ever had to notoriety unrecognised, and lost for good.]

Peritoneum. In a further experiment, I threw into the peritoneal cavity of a dog, weighing twenty-six pounds, three pounds of water. I also threw one pound of water into the cellular tissue. For a short time the animal was pretty well; and the fluid injected seemed to have been entirely absorbed in the course of four hours. Shortly after this he became exhausted, and died in eleven hours. On opening the body, I found in the peritoneal cavity no trace of water, but in the sac there lay about a pound of semi-coagulated blood, which had escaped from an artery that had been wounded by the trocar. This blood contrasted strongly with that in the heart and veins; the latter was like water itself as regards fluidity, and on exposure showed no tendency to coagulation. I shall be able to explain the cause of the different states of the blood in the sequel. Distilled water, at a temperature of 96° , was always used in these experiments.*

[EXPERIMENT XL. *Effects of copious Water-drinking.*
Bearing on the subject of the effect of dilution of

[* These experiments were devised in connexion with a plan suggested by me for the treatment of cholera. My paper on this subject will be found in the *Association Medical Journal* for August 1854, and in *Ranking's Abstract* for 1854, vol. ii. Thinking on the fact that in natural dropsy the most active purgation with elaterium (artificial cholera) removed the effused fluid, but did not destroy the patient, it occurred to me to reverse this order of things, and in natural cholera to produce artificial dropsy, either of the peritoneum or of the cellular tissue. My experiments were, as far as experimental inquiry can guide to practice, strongly in favour of the plan of injecting the peritoneal sac; and they entirely supported the view that the main point in cholera practice, is to throw as much fluid as possible into the body, so that the loss in the flux may be restored in the new supply. I have since, however, modified the plan of throwing water into the drained body by injecting the *bladder* with water, instead of the peritoneum. That water injected into the empty and contracted bladder of an animal exhausted by purging or loss of blood, is rapidly absorbed by the mucous surface of that viscus and is taken into the circulation, admits of direct experimental demonstration. It would lead me too far from the matter of the text, to dwell at the present moment on this subject: I therefore only state the fact as it is.]

blood with water, I had the opportunity of making some interesting observations on the human subject. On November 29th, 1856, a boy, aged 16, came before me with diabetes. He passed about seven quarts of urine in the twenty-four hours, but much the greater part in the night-half of the time. The amount of fluids which he took averaged also about seven quarts, but he was always thirsty. The urine yielded abundant evidence of sugar. I made it a point in this case to get the patient to do without drinking water, as long as it was possible. He could manage to abstain three hours. In this state I drew from his hand a few drops of capillary blood, and watched the process of coagulation. The blood was dense, rather dark, and coagulated in thirty seconds. The blood from the puncture ceased to flow in nearly the same time. When this observation was concluded, I allowed him to drink water freely. He took off two quarts greedily, in half-pint draughts, at intervals of two minutes. Five minutes after the last draught, I made a new incision, and drew off in the same way as before a few drops of blood. There could be no doubt as to the physical differences between this and the blood previously drawn. It was more fluid, it remained fluid for five minutes, and ultimately rather dried than coagulated. The wound last made continued to give out blood; and the wound previously made recommenced to bleed. Both wounds continued bleeding for several minutes, the fluid retaining its liquid character; at last I stopped the flow by pressure. I examined the red corpuscles in each specimen of blood. The difference here again was well marked. There was not much variation in size, but important variations in shape; those of the

latter or watery blood being irregular, some oval, others many sided, and a few stellate. These also continued in motion for a much longer time.

This experiment, as illustrating the rapid absorption of water by the exhausted body, and the effects of the water on the blood, throws much light on the cause of death in instances where fatal effects have occurred in exhausted persons, after the drinking of fluids too copiously. I may remark that this patient always showed symptoms of faintness on replenishing himself overmuch with water upon a prolonged abstinence. He exhaled ammonia freely by the breath at all times.

EXPERIMENT XLI. *Inhalation of Antimonuretted Hydrogen.* In cases of antimonial poisoning, according to my observations, the blood is found after death loosely coagulated; while in some extreme cases it is quite uncoagulable, even after exposure to the air.

A young dog was placed in a chamber capable of holding 3350 cubic inches. The chamber and its arrangements were the same as in the experiment No. 1, described at page 71. After the animal had become quiet in the chamber, I drove into it 100 cubic inches of antimonuretted hydrogen; and this operation was repeated every twenty minutes so long as the experiment continued, 100 cubic inches of air being driven through with each dose of the gas. In the atmosphere thus empoisoned the animal lived three hours and forty minutes, in the course of which time 1000 cubic inches of the gas, with the same quantity of fresh air, were driven through the chamber. The current was kept up so steadily that complication from carbonic acid was entirely excluded.

The symptoms arising from antimony were soon

elicited. At the end of an hour and forty minutes there was copious purging, and ten minutes later there was free vomiting. The excreted matters thus thrown off yielded abundant evidence of antimony. The death was not preceded by coma, but by increasing feebleness and simple failure of the circulation. In this case the breathing organs outlived the heart.

Forty-one hours after death, I examined the body with Dr. Snow. There was intense congestion of all the viscera. The heart was charged with blood on both sides, and the aorta was full of blood. The blood was so fluid that it could be poured out freely; and on exposure to the air for two days it underwent no solidification whatever. In the pleural cavity of this animal there were about six drachms of a pinkish fluid, which, being collected in a test-tube, coagulated on exposure to air into a jelly-like clot from which clear serum exuded. This was obviously an exudation of simple liquor sanguinis: it resembled in every way the fluid which can be skimmed off the surface of inflammatory blood before the fibrin separates.

EXPERIMENT XLII. *Antimony injected into the Jugular Vein.* Dr. Barker, of Bedford, was kind enough to send me a dog, which he, together with Dr. Thudichum, had destroyed by injecting into the jugular vein one scruple of tartar emetic, dissolved in two ounces of water. As the solution came into contact with the blood, the colour of the blood became suddenly of a bright scarlet. The animal soon exhibited the symptoms of prostration common to antimonial poisoning. There was, however, no purging, nor vomiting; but at times there seemed to be attempts to vomit. The prostration terminated in death about three hours after the operation. On

opening the body, I found the heart on both sides, as well as the veins and large arteries, full of blood, which was entirely fluid, and remained so permanently on exposure to the air.

EXPERIMENT XLIII. *Antimony injected into the Peritoneum.* Into the peritoneum of a healthy bitch, one scruple of tartar emetic was injected, dissolved in two ounces of water. The symptoms of poisoning commenced within an hour, and the animal died, entirely prostrated, at the end of the third hour. The *post mortem* appearances were those common to antimony, as I have described elsewhere.* The heart on both sides, and the large vessels, were all filled with perfectly fluid blood, which remained permanently fluid on exposure to the air.

EXPERIMENT XLIV. *Antimony administered by the Mouth.* On the 24th of April, 1856, Dr. Barker, of Bedford, commenced to administer to a dog two grains of tartar emetic, with his food, twice daily. After the twelfth dose, the animal died, without having previously exhibited such serious symptoms as usually precede death from this poison. With the ordinary pathological signs, there was the same entire and permanent fluidity of the blood.

It may be remarked, that in all these experiments, the signs of cadaveric rigidity were very feebly manifested; that the blood always gave free evidence of the presence of antimony; that the corpuscles were disintegrated; and that fibrin could not be extracted by agitation with lead. I have retained specimens of these bloods for months, and they have undergone no obvious change.

I have thus adduced numerous illustrations of the

* See *Lancet* for May 10, 1856, and *Brit. and For. Medico-Chir. Review* for October 1856.

four general conditions of blood found after death. I could have added the details of many more cases ; but to have done so would have implied the turning of this chapter into a book of itself. Some authors have described certain conditions of blood, in which that fluid is visibly charged with bubbles of gas ; the blood being, under such circumstances, decomposed. I have not met with any approach to this extreme condition, except in the instance described under experiment XIX, at p. 104.

There are, however, one or two other facts which require to be referred to generally, before this chapter is closed.

In many cases, the condition of the blood found in the body after death is modified by the circumstance, whether the circulatory canals have or have not been opened at or immediately after death. For example, let two animals be killed by drowning at the same period of time. As soon as death has occurred, lay open the jugular vein and the carotid artery, or any other large artery and vein, in one of the animals ; and fix in each vessel an open tube, bent upwards at right angles, so that the blood shall not escape, and yet the circulatory canals on both the venous and the arterial sides shall be laid open. Let the body of the other animal remain entire. At the end of ten minutes, lay open the body of the animal whose circulatory canals have been opened ; the blood generally will be found coagulated. Let the second animal, whose body has been left entire, remain untouched for half an hour, then open the body ; the blood will be found fluid, but will soon coagulate when it has been exposed to the air.

I have observed, again, on many occasions (and I doubt not that other pathologists have made the same

observation), that when, on opening the dead body, the right side of the heart is found filled with blood, and the left side contains but a small quantity, the aorta also being empty, the blood on the right side is often feebly coagulated, or in part fluid; while the small portion of blood on the left side is condensed into a firm clot.

Further, in opening the body of an animal soon after death, it is common to observe that, if the knife in an early step of the operation divides a large vein (say the subclavian), the blood will flow out in the fluid state; but that, by the time the heart is laid bare, the blood found in it, as well as the blood in the *venæ cavæ*, will show distinct evidence of coagulation.

It has often been observed, that blood effused into the areolar tissue, or locked up closely in small cavities, remains fluid for a considerable period; so long, in fact, as it is sealed up from the air. My friend, Mr. Henry Lee, informs me of a case in which a bursa was filled, for many months, with blood which flowed out in a state of perfect fluidity when the bursa was opened. Another important observation has been made also by Mr. Lee, which I can fully confirm, though it had escaped my attention until he pointed it out. It is, that on removing the calvarium in the dead subject there is almost invariably an escape of fluid blood, however firmly the blood may be coagulated in some other parts of the body.

On the other hand, when comparatively small quantities of blood are effused into large and distensible cavities, as the pericardium or peritoneum, such blood is usually found after death in the form of a firm red clot; and not infrequently, with exuded serum surrounding the clot. I have found such clots both in the

pericardial and the peritoneal sacs. In an interesting case of dissecting aneurism of the aorta, which I examined with my friends Drs. Hawksley, Cockle, and Webb, a clot of this character was found in the pericardium; and a thin layer of coagulated blood extended for several inches along the course of the aorta, between the external and middle coats of that vessel.

After various forms of death in which the last act has been sudden, and in which the blood has been fluid at the moment of death, as in death by shock, the blood remains fluid for a long time afterwards, if the circulatory canals are entire. But such blood coagulates readily enough, after it is exposed to the air. It is not, however, true, as some have presumed, that blood after death from simple shock remains fluid in the unopened body. The following experiments definitely negative such supposition as a general thesis.

EXPERIMENT XLV. *The Blood after Death by Shock.* A kitten was killed by a sharp blow on the head. It died almost instantaneously, and without a struggle. Eight hours after death I opened the body. There was blood on each side of the heart, and in all the large veins. This blood was dark and everywhere coagulated, but not firmly. There was no cadaveric rigidity.

EXPERIMENT XLVI. *The Blood after Death by Shock.* Another kitten from the same litter was killed by the same mode, and died as instantaneously. Twenty-four hours after death the body was opened. The heart contained blood on both sides, and the large veins were filled. The blood everywhere was dark, but firmly coagulated. There was no cadaveric rigidity.

EXPERIMENT XLVII. *The Blood after Death by Shock.* A third kitten of the same litter was killed in a similar

manner, and died as instantaneously. Forty-eight hours after death, I opened the body. The heart and large veins were filled with blood which, as before, was dark and firmly coagulated. There was in this case also no cadaveric rigidity.

In the slaughter-house I have observed in oxen the effects of shock, from the blow on the head with a pole-axe, more than two hundred times; but I could never find that the shock administered before the blood was drawn, in any way prolonged the process of coagulation in the blood afterwards abstracted by the knife. From the fact that the butcher is anxious, the moment that a beast is prostrated by the axe, to lay open the throat, in order, as he says, "to empty the body" completely (an act which cannot be effected if time is lost), I thought once that some partial coagulation might occur in the body directly after the blow is struck, inasmuch as the blood flows with difficulty in proportion to the time that is lost. But I soon learned that the expedition is called for, in order that the heart may retain sufficient force to pump out the blood from the divided vessels, and that coagulation is not the primary obstacle to the "emptying process."]

The observations recorded in this chapter have all important bearings in regard to the phenomenon of coagulation, as I shall have frequent occasion to point out in the sequel. The immediate inferences to be deduced from them are:—

1. That in cases of immediately sudden death (death by electricity excepted) the blood coagulates, as a general rule, with moderate firmness; and in the ordinary mode, that is, by separating into two parts—simple red clot and serum: [but that this process is

quickenened or delayed according as the circulatory canals are opened early, or left unopened.]

2. That in states of the body in which the blood is superfibrinised, either from active hyperinosis, or from relative increase of fibrin, there is often a modified form of coagulation, consisting of a separation of blood into three parts; viz., *fibrin* isolated, *blood-corpuscles* isolated or mixed up and held together by fibrin, and *serum*.

3. That in instances where life is destroyed by gradual arrest of respiration, the phenomenon of coagulation is only feebly exhibited; [and that the same law obtains in cases where death is induced by electricity, sudden exposure to intense heat or cold, the narcotics, and the alkalies.]

4. That an enfeebled movement of the blood in any part of the circulatory system is favourable to coagulation, and this especially if the respiration continue free.

5. That by throwing into the circulation a large quantity of water, the process of coagulation may be prevented. [That antimony produces a similar effect in many cases; that the like result may follow death from certain natural causes, as from cyanosis; and that the same effect has been observed by various authors to follow deaths from poisoning by phosphorus, arsenic, and amylene; as well as deaths from cholera, yellow fever, typhus, and uræmia.

6. That the cause of imperfect coagulability of blood would appear to be due to one of two causes—to a positive deficiency in the elaboration of fibrin, or to the fact that the fibrin, being elaborated, is held in an abnormal state of solution in the liquor sanguinis.

7. That such absence or unusual fluidity of the fibrin is attended, as a general rule, with a modification, consisting possibly of a partial solution, of the red corpuscles.]

CHAPTER IV.

EXPERIMENTAL INQUIRY INTO THE PHYSICAL AGENCIES INFLUENCING THE COAGULATION OF THE BLOOD.

"There are few, if any, physical hypotheses, which afford the only way of explaining the phenomena to which they are applied : and therefore, admitting them to be perfectly consistent with all the known facts, they leave us in the same state of uncertainty in which the decypherer would find himself, if he should discover a variety of keys to the same cypher."—DUGALD STEWART.

I. EFFECTS OF TEMPERATURE.

It has been shown in a preceding chapter that Hewson, Magendie, Scudamore, and other distinguished physiologists, have investigated very closely the effects of temperature on drawn blood ; and that the results of these inquiries have been to show, that the phenomenon of coagulation is not in any way to be attributed to the loss of heat as the ancients supposed, but, on the other hand, that an increased temperature tends the more decisively and rapidly to bring about the process of coagulation. I have myself instituted a long continued and repeated series of inquiries into this question, all of which have but led to a confirmation of this foregone conclusion. Some experimenters, as it is known, have inferred that temperature has no effect on the coagulation of blood ; but this is widely different from any inference, that could be deduced from my experiments ; for I

have found, without exception, that a well marked difference in the period of coagulation may be produced by exposure of blood to extremes of temperature, to wit, exposure at freezing point and at 140° Fahr. Between these points, experiments on the mere process of coagulation are, in some measure, limited; since above 140° Fahr. coagulation of the albumen is imminent; while below 32°, the physical change of freezing is probable, by which change coagulation is temporarily suspended.

[Before proceeding to the details of experiments, I think it right to point out, as a guide to future inquirers, and as an indication of some of the causes of the differences which are to be met with in the history of past inquiries, certain difficulties which beset the question of the influence of temperature on the process of coagulation.

In the first place, it is necessary rigidly to observe the rule of drawing no *comparative* deductions regarding the effects of temperature from experiments made on the blood of *different* animals, inasmuch as there are constant variations in the period of coagulation according to the animal from which the blood is taken, and independently altogether of the temperature. For example, the blood of man, of the ox, and of the pig, coagulates, under the same conditions, much more slowly than the blood of lambs, and the blood of lambs more slowly than the blood of sheep. The blood of an animal that is heated by exercise coagulates more quickly than that of one that is cold or exhausted. Again, in animals of the same kind, and under the same conditions, the period of the coagulation of their blood varies, possibly from modifications in the condition of such blood itself. For

example, I have repeatedly been present in the slaughter-house when six sheep of the same breed, and all apparently healthy, have been slaughtered one after the other. I have received blood from each victim in the same cup, in the same quantity, and in the same temperature, and have observed variations in the periods of coagulation, ranging from fifty seconds to four minutes; nor can I, indeed, recall any two cases of this kind in which there was absolute uniformity of result. To take the same point of temperature, therefore, and to draw deductions as to the effects of such temperature on the period of coagulation in the blood of different animals is, of necessity, to make a false inference.

In the second place, in exposing the blood of the same animal to different points of temperature at the same time, it is of absolute necessity so to use the thermometer as to obtain the absolute temperature of the blood itself, and not merely of the medium in which the cup containing the blood is placed. Take, for instance, two cups of blood drawn at the same moment; place them in different conditions; place one cup in water at a temperature of 60° , and the other in water at a temperature of 100° ; and, if the heat of the medium only be considered, the inference, in nine cases out of ten, will be that there is no appreciable difference as regards the period of coagulation. To show, however, that this inference is incorrect, it is only necessary to remove the thermometers from the water, at the moment when the cups for containing the blood are filled, and to immerse the bulbs of the thermometers into the blood itself. It will then be proved that the mercury in the thermometer from the cold medium, as soon as the bulb is immersed in the blood, runs up quickly towards the

point of the temperature of the blood, *i.e.*, to 90° , or a degree or two more ; while the mercury which has been exposed to the higher temperature will, on the thermometer being immersed in the blood, sink down to the temperature of the blood. Thus the two bloods, although placed under such different circumstances, are in fact, within a degree or two, of the same heat ; and as the period of coagulation is one sometimes of seconds, and at most of minutes, and as the blood is a fluid which yields up its caloric slowly, and absorbs caloric slowly, the effects of temperature are often too refined to become manifested at first sight. In order, therefore, to obviate the difficulties here described, it is positively necessary, in testing the effects of temperature, firstly, to employ extremes of temperature, and, secondly, to take the point of temperature from the blood itself. Any inference deduced without attention to these details is necessarily delusive.

Thirdly, the temperature of the surrounding atmosphere must be taken into account. In all animals the blood coagulates, as a general rule, more rapidly in very hot than in very cold weather ; and, as one surface of the blood exposed in a cup is open to the influence of the external air, this influence has its effects, despite the temperature of the medium in which the containing cup is immersed. Blood, for instance, received in an open cup, and placed in water at a temperature of 120° , will coagulate more quickly if the external temperature is at 70° , than if it were at 35° , and *vice versá* ; a fact which can only be proved by performing the same experiment in winter and in summer. This may seem a truism ; but it requires to be stated to secure accuracy.

Lastly, in performing comparative experiments on

the effects of temperature, cups of the same size and shape for containing the blood must be used, otherwise an error from another source will spring up, as will be fully shown in a succeeding page.]

EXPERIMENT XLVIII. *Exposure of Blood to a temperature of 70° Fahr.* An ounce of fluid blood was drawn direct from the throat of an ox, and was received into a test-tube. It was allowed to coagulate at the ordinary temperature of the day, viz., 70° Fahr. The temperature of the blood on being drawn, as ascertained by a fine hair-bulb thermometer, was 98.5° Fahr. The blood coagulated in three minutes.

EXPERIMENT XLIX. *Exposure of Blood to a temperature of 98° Fahr.* At the same moment a similar quantity of the same blood was received into a test-tube, of the same size and shape as in the last experiment. This tube was now placed in water at 98° Fahr.; the blood it contained coagulated, as in the former instance, in three minutes.

EXPERIMENT L. *Exposure of Blood to a temperature of 32° Fahr.* Another portion of blood was received in a similar manner (in a test-tube) at the same time and from the same animal. The test-tube was then immersed in water at a temperature of 32°. The blood coagulated in four minutes and two seconds.

EXPERIMENT LI. *Exposure of Blood to a temperature of 10° above Zero.* The same amount of blood was received in a similar manner (in a test-tube) at the same time and from the same animal. The test-tube was then plunged into a mixture of ice and salt, in which the thermometer stood at 10° above zero. In four minutes the blood became rather firmer in consistency; but it did not coagulate for six minutes and ten seconds.

[In the preceding experiments, as will be seen, I observed only the temperature of the medium in which the blood was placed. In those immediately succeeding, the temperature of the blood itself was taken, after it had been placed in the cups intended for its reception. These experiments illustrate the importance of the precautions laid down at the commencement of this chapter.

EXPERIMENT LII. *Effects of Temperature.* I took three thermometers, which kept tune together, when tested at different temperatures. I also fitted up three glass cups, so that each cup should inclose a second cup for holding blood. I then surrounded one of the inner cups with water at 56° Fahr. : a second cup I placed in water at 140° Fahr. The temperature of the external air was 72° Fahr.

After taking the exact temperatures of the hot and cold waters, as noted above, I removed the thermometers from the fluids in which they had been immersed, and placed them upright in the two empty cups intended to receive the blood. The mercury in each thermometer at once changed its position. That in the cup surrounded by cold water rose to 65° ; that in the cup surrounded by the heated water fell to 126° . At this moment an assistant received blood from the neck of a sheep, and instantly filled the two cups; and also a third cup, of the same size and shape, which was simply exposed to the temperature of the air, and in which the thermometer stood at 72° Fahr. As soon as the blood enveloped the thermometers, the mercury changed position in all of them; the two thermometers, which had stood respectively at 65° and 72° , rose to 92° ; the thermometer, which in the cup surrounded by hot water had stood at 126° , fell to 95° , and did not reascend until after

coagulation had occurred. The blood in each cup coagulated in fifty seconds. I was unable to notice any difference at all in the period of coagulation ; but the clot, at the end of one minute, was decidedly firmest in the blood which had been placed at the highest temperature.

EXPERIMENT LIII. *Effects of Temperature.* I performed on the same day a similar experiment on the blood of a lamb, modifying it slightly by employing water at other temperatures. The cool water was brought down by ice to 50° , the warm water was raised to 150° . The thermometers were placed in the empty cups, and surrounded with newly drawn blood. Before coagulation, each thermometer came to the same temperature, within two degrees : the first rose to 91° , the other fell to 93° ; and at these points they stood when the blood coagulated, which it did in each case in forty-six seconds after reaching the cups. As before, the blood that had been poured into the warm cup was firmest, as a clot, at the end of a minute.

EXPERIMENT LIV. *Effects of Temperature.* I performed a similar experiment, on the same day, with the blood of a sheep ; the only modification being, that the water surrounding the blood was, in one vessel, at 60° , in the other, at 120° : the results were the same. The thermometers approached the same point, and coagulation took place in each cup at the end of one minute and three seconds. The blood exposed to the warm cup did possibly coagulate more quickly by the space of one or two seconds ; but the determination of this delicate point being doubtful, it would not be fair to press it as a fact.

EXPERIMENT LV. *Effects of Temperature.* The temperature of the external air was 72° Fahrenheit. I

placed an eight-ounce thin glass cup in a freezing mixture of ice and salt, and a second glass cup, of the same size and shape, in water at 130° Fahr.; I then put a thermometer into each empty cup which was to receive blood. These preparations made, I received blood from the throat of an ox, and instantly filled both cups, together with another similar cup, which was simply exposed to the ordinary temperature of the day. When the blood was first poured into the cups in which the thermometers stood, the mercury of the thermometer in the cold cup rose to 91° ; while the mercury in the thermometer in the warm cup fell to 95° . After a lapse of fifty seconds, the mercury in each thermometer again underwent change, the blood being still fluid in both cases. The thermometer in the cold cup gradually fell, and in the course of another fifty seconds stood at 68° , which position it retained. The thermometer in the warm cup, on the contrary, rose to 104° , at which point it stood at the moment of coagulation, which occurred precisely in two minutes. The blood which had been set aside, at the ordinary temperature, coagulated thirty seconds later. The blood, the temperature of which was 68° , was, at this time, entirely fluid, and conveyed a distinct impression of cold to the finger; it was, in fact, chilled throughout its entire mass. At the end of four minutes and a half it was still perfectly fluid; at five minutes it commenced to thicken; and at five minutes and thirty seconds it was coagulated. The blood which had been exposed to a high temperature, set in a firm and dark clot; that exposed to a low temperature retained its bright red colour, but the clot was less firm so long as it remained surrounded by the cold.

I remarked in this experiment the interesting fact,

that the blood in the warm cup commenced to coagulate from below upwards; while that in the cold cup commenced to coagulate at the top, the process extending gradually downwards.

I shall show, in a succeeding section, the effects which arise from the addition of water to blood. I must anticipate the results of these observations at this point to say that, at ordinary temperatures, the addition of water to blood, in quantities not exceeding the quantity of blood used, does not materially affect the coagulating process. I took advantage of this fact to ascertain the effects of temperature on coagulation, by mixing blood, newly drawn, with water at different degrees of temperature. By this intermixture I raised or reduced the temperature of the blood at once, and was thus enabled to compare the periods of coagulation at different points of the thermometer. The following experiments will illustrate this plan of research.

EXPERIMENT LVI. *Effects of Water at different Temperatures on the Process of Coagulation.* I placed in one glass cup a fluid ounce of water at a temperature of 135° Fahr. In another cup I placed an ounce of water at a temperature of 40° Fahr. I now received from the neck of a sheep four fluid ounces of blood, and at once transferred two ounces of the blood to the cold water, and the other two ounces to the warm water. After the blood, which was added to the warm water, was fully commingled with the water, a thermometer placed in the mixed fluid rose to 100° : this blood coagulated in fifty-seven seconds, the clot being firm and dark. After the blood, which was added to the cold water, was commingled with the water, a thermometer placed in the mixed fluids rose to 63° : this blood coa-

gulated in one minute and twenty-five seconds, the clot retaining its red colour, but being much looser in texture than the other clot.

EXPERIMENT LVII. *Effects of Water at different Temperatures.* I received two ounces of blood, freshly drawn from the neck of a sheep, into a glass cup containing one ounce of water, at a temperature of 45° Fahr. Instantly afterwards, I received two ounces more blood, from the same source, into a cup containing one ounce of water, heated to 130° Fahr. The blood received into the warm water coagulated in a firm and perfect, but dark looking clot, in forty-four seconds. The blood mixed with the cold water commenced to coagulate in one minute and thirteen seconds. The clot, though not dark, was very loose, and, at the end of ten minutes, was less firm than that in the other cup at its first formation.

EXPERIMENT LVIII. *Effects of Water at different Temperatures.* I placed in one glass cup two ounces of water, the temperature of which was 50° Fahr.; in another cup I placed two ounces of water at a temperature of 120° Fahr.; the temperature of the external air was 70°. When all was ready, I received from the neck of a sheep six ounces of blood. I transferred two ounces of this blood instantly into the cup containing the cold water, and two other ounces into the cup containing the warm water; the remaining two ounces were left to coagulate naturally. The period of natural coagulation was one minute and forty seconds. After the blood added to the cold water was commingled with the water, the thermometer immersed in the common fluid rose to 68°; the blood became dark, and coagulation did not commence for three minutes, and was never

firm. After the blood was added to the warm water, the thermometer fell to 111° . This blood coagulated in one minute; the clot was dark, but firm.

EXPERIMENT LIX. *Effects of Water at different Temperatures.* I placed in one glass cup two ounces of water at a temperature of 56° Fahr.; in another cup I placed two ounces of water at a temperature of 125° ; the temperature of the air was 71° . I now received from the neck of a sheep six ounces of blood: two ounces were at once poured into the cup containing the cold water; two other ounces into the cup containing the warm water; and two ounces were left exposed to the external air. After thirty seconds, the thermometer in the colder cup rose to 70° ; that in the warmer cup fell to 115° ; another thermometer placed in the natural blood rose to 93° . The order of coagulation was as follows: The blood at 115° coagulated in fifty seconds, with a firm but dark clot; the blood at 93° in one minute and three seconds, with a red and firm clot; the blood at 72° coagulated in one minute and twenty-six seconds, with the clot loose and dark. Serous fluid exuded freely from all these specimens, but most so from those with which water had been mixed.

I one day observed that some blood that had been poured into a hollow part of a block of ice (the temperature of the air around being 50° Fahr.) was not frozen, but was chilled generally, and was prevented from coagulating for several minutes. Taking advantage of this observation, I had suggested to hand a variety of pretty experiments for illustrating this part of my subject. I ask special attention to such of these experiments as are about to be given; because they are so simple, and the results are so uniform and broadly marked, that

any observer may at once perform and confirm them without expense, and with the slightest possible trouble incident to experiment.

EXPERIMENT LX. *Effect of receiving Blood in an Ice-cup.* The temperature of the day was 70° Fahr. I cut out of a block of ice a cup of the size and shape of a large watch-glass; I then received blood from the neck of a lamb, and instantly filled the ice-cup, as well as a glass cup of the same size, which was simply exposed to the external air. The blood in the glass cup coagulated in one minute and twenty-two seconds. The blood in the ice-cup remained perfectly fluid for fifteen minutes, being dark in colour. At the end of twenty minutes, coagulation commenced, and was more developed in five minutes, but the clot was not firm. Removed from the ice and exposed to the external air, the clot became firmer, and serum exuded from it.

EXPERIMENT LXI. *Effect of receiving Blood in an Ice-tube.* In a large block of ice I cautiously drilled a round bore, three inches deep and three-quarters of an inch in diameter. At the lower part of the bore I scooped out the ice more, so as to make a bulb at this point. I then cut a stopper out of a smaller block of ice, and made it fit as closely as possible into the upper part of the ice-tube. My plans thus arranged, I received blood from the neck of a sheep, filled the ice-tube with it instantly, and inserted the stopper. The blood of this animal, exposed to the external air, the temperature of which was 75° Fahr., coagulated firmly in one minute and fifty-three seconds. The blood inclosed in the ice was left alone for half an hour. The ice-stopper did not perfectly close its tube: by the side of the stopper small bubbles of gas were observed

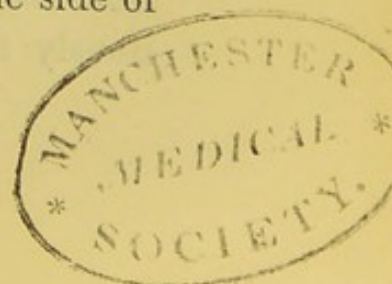
escaping. At the end of the half hour the stopper was removed, and the blood was found as fluid as at the moment when it was first drawn. At the termination of another half hour the blood was examined, and was found partly coagulated; and in fifteen minutes more it had formed generally a soft coagulum, having at its upper part a pale appearance. Replacing the stopper, I set the whole aside in a cold place. At the end of fifteen hours, the clot was still very loose and jelly-like, but was distinctly coated at its upper surface with a thin buff layer of fibrin.

EXPERIMENT LXII. *Effect of receiving Blood in an Ice-cup.* I carved in a block of ice a shallow cup, three inches in diameter at the upper and widest part. I then cut a rounded block, which fitted into the hollow cup and covered it externally, but did not quite fill up the whole concavity beneath. Thus prepared, I received half an ounce of blood from the throat of a lamb, and poured it into the ice-cup, instantly closing it in with the rounded block, and setting it aside. A little more blood from the same animal coagulated in one minute and five seconds in the outer air, the temperature of which was 75° Fahr. At the end of half an hour, the blood in the ice was examined, and found liquid, but commencing slightly to thicken. At the end of thirty-seven minutes it had formed a soft clot, covered at the upper surface with a fine, pale, striated coat.

EXPERIMENT LXIII. *Mixture of newly-drawn Blood with Ice-scrapings.* I scraped into a cup two teaspoonfuls of ice. I next received an ounce of blood from the neck of a lamb, into a cup of the same size and shape. As soon as the blood was in the cup, I transferred half of it into the cup holding the ice, and gently stirred the

ice and blood together. The blood left to coagulate naturally at the temperature of the air, 75° Fahr., was so firm a clot in one minute and twenty seconds, that it could be turned *en masse* on to the table. By this time, the ice in the other cup had dissolved in the blood, and the blood was quite fluid. The thermometer bulb being immersed in the cold fluid, the mercury fell down to 50°, and at this point it remained for seven minutes and a half, the blood meantime being entirely fluid. At this moment the mercury began to change its position, and slowly to rise. At the end of two minutes the blood was thickening; and this process continued until fourteen minutes had elapsed, when the thermometer stood at 60°, and the blood had become an uniform dark and soft coagulum.

EXPERIMENT LXIV. *Effect of Freezing Blood.* I had constructed a long eight-ounce vessel made of thin tin, and having a lid which could be slipped on air-tight. Having, on a day when the temperature was 35°, placed this vessel in a box surrounded with snow and salt, I received into it, direct from the neck of a sheep, as much blood as completely filled it. I then adjusted the lid, heaped above some more snow and salt, and set the whole aside for half an hour. Meanwhile, a little blood received into a teacup, exposed to the air, was found to coagulate in three minutes and twenty-six seconds. When the half hour had elapsed, I unclosed, in the open air, the tin vessel containing the blood which had been surrounded with the snow and salt. The blood was in two states. In the centre of the vessel there was a column of liquid blood, amounting, by measure, to ten drachms, which was poured off into a cup. The remainder of the blood was a frozen mass, adhering firmly to the side of the vessel.



EXPERIMENT LXV. *Observations on the Liquid portion of Blood.* Leaving the frozen blood, named above, in its vessel, still surrounded by the cold, I hastily divided the fluid portion into equal parts in two glass cups. Number one I left exposed to the open air, at 35° Fahr.; number two I carried into a room, the temperature of the air of which at the place of observation was 60° Fahr. This blood thus observed coagulated firmly in four minutes. At the end of this time, I returned out of doors to blood number one. This was still fluid. In one minute more it began to thicken, and in two minutes was firmly clotted. Serum did not exude from either specimen of blood-clot.

EXPERIMENT LXVI. *Observation on the Frozen Blood.* I now returned to the blood which remained frozen. The portions most central were crispy, and were easily removed with the handle of a scalpel. A portion of this kind of frozen blood was received into a shallow cup and taken into the warm air at 60°; it speedily became fluid, and immediately commenced to coagulate. It coagulated firmly, but no serum exuded from the clot.

EXPERIMENT LXVII. *Observation on the Frozen Blood.* A second portion of the frozen mass was put into a spoon, and suddenly placed at a temperature of 100°. It thawed first, and coagulated so quickly afterwards, that, although I could observe the transitions, I could not accurately note the intervals of time in which they occurred.

EXPERIMENT LXVIII. *Observation on the Frozen Blood.* I next removed a portion of the frozen mass nearest to the surface of the tin vessel. This was hard, bright, and glossy. I placed it in a test-tube, broke it (the frozen blood) gently with a glass rod, and very cautiously thawed it. When it was fluid, I immersed

the test-tube in ice and salt, and froze the liquid a second time. Again I gently dissolved it by heat, again froze it. Having once more dissolved it by heat, I poured it into a glass cup and carried it into the air at 60°. Thus exposed, it slowly coagulated, but the clot was dark in colour, feeble in consistency, and from it no serum exuded.

EXPERIMENT LXIX. *Observation on the Frozen Blood.* Lastly, I placed the tin vessel, containing the remaining part of the mass of frozen blood, in the air at 60°. Thus placed, the blood gradually thawed and then coagulated; but the stages of transition from fluidity to coagulation were not readily distinguishable, and the clot formed was dark and loose.

In performing the experiments of freezing, thawing, and coagulating blood, the utmost delicacy is required in the thawing part of the process; otherwise the blood will coagulate so quickly that the stage of fluidity will not be observed at all. I have only once been able to freeze and thaw blood three times successively, and that was in the instance detailed in the last experiment.

I do not think it necessary to introduce any further experiments on the effects of temperature on coagulation. Those above named have been modified in various ways, but with results tallying in essentials in every point. It is clear that the period and the force of coagulation are modified importantly by temperature; that extreme cold suspends this process altogether, while heat quickens and intensifies it. But to see this significant fact clearly and positively by experiment, it is requisite to provide for all modifying causes, to remember the laws by which heat is absorbed and radiated, and to consider how the mass of blood used is

acted on by the heat or the cold to which it is subjected. Recognizing the great truth, that "what is of the local is of the general", I could never observe the often repeated fact, that very intense cold prevents coagulation, without feeling that this fact was but a point in the scale of a general law. Now, with full experimental information to guide me, I am safe in concluding that the period of coagulation, under circumstances favourable to the process itself, and to the influence of heat on it, is quickened by the addition of every degree of heat, and suspended in the converse scale by the abstraction of the heat.

Experiment lxiii gives of all, perhaps, the best illustration of the influence of temperature. While the mass of blood was subjected to the cold, the thermometer fell and the blood remained fluid. When the heat was equalised, and the combined ice-water and blood began to absorb heat from the external air, the thermometer rose, and the blood slowly coagulated.]

This conclusion is in strict accordance with what occurs in regard to the abstraction of blood at various seasons of the year. In hot summer weather, in performing the operation of phlebotomy, I have seen the blood, even when drawn from a free opening, coagulate at once on reaching the basin, although drawn from a pneumonic patient. In performing the same operation in a similar case in the middle of winter, when the temperature of the room was itself 50° Fahr., I once saw the blood six minutes in coagulating; a result which was obviously due to temperature, since another portion of blood from the same patient, which had been placed in a cup floating on water at 120° Fahr., coagulated in three minutes.

The effects of heat and cold on the process of coagulation are well known in the slaughterhouse. In very hot weather, the coagulation is so rapid, that it is almost impossible to gain sufficient time for whipping out the fibrin from a mass of blood.

These results are, further, in accordance with the observations of Metcalfe; viz. that the period of coagulation varies with the animal from which it is drawn, being quickest in those which are endowed with the highest state of chemical activity, and *vice versâ*.

When animals are driven for a short distance immediately before slaughter, and are killed while they are yet warm, and respiring quickly from the exercise, the blood coagulates with remarkable rapidity. I have seen the blood of sheep thus drawn, even on a day when the temperature was at 50° Fahr., coagulate in twenty seconds when received into a test-tube; and any physiological butcher who may be questioned on this point, will confirm the observation. If, on the other hand, the animal has been kept quiet, and in a cool place, for a few hours previous to death, the blood coagulates with moderate slowness; while in instances where the animal has been driven for many miles, and is brought to the *abattoir* cold, breathless, and exhausted from the fatigue, the blood drawn shows a very feeble tendency to coagulate, and the clot formed is but loose after a lapse of from two to three hours. An animal in this condition is, indeed, in much the same state as is one that has long been breathing a narcotic vapour; for the force of the heart has been weakened; the respiratory muscles have been reduced to a minimum of power; and the chemical changes of respiration and circulation have, from this combined failure, become materially reduced in energy.

I do not enter into any inquiry regarding the evolution of caloric from coagulating blood; because this question has been thoroughly investigated by Dr. John Davy, and because it seems to be irrelevant at this moment to do more than refer to it. For, as the fact is now proved, that the addition of caloric favours coagulation, while its abstraction retards coagulation, it is illogical to refer this process to the absolute escape of heat.

The solution of the question, Why is the rapidity of the coagulating process increased by an increase of temperature? may be easily and correctly made by attributing the effect to a mere physical cause. It may be inferred, and we shall see how far succeeding observations will confirm this inference, that a high temperature exerts its well known physical effects of quickening evaporation and the extrication of gases.

[II. EFFECTS ARISING FROM THE ADDITION OF WATER TO
FRESH BLOOD.

I have pointed out in the first Chapter certain results which have been arrived at by different observers as to the effect of diluting blood with water; and in the second Chapter, in commenting on this historical point, I have indicated that the discrepancies which have arisen were possibly due to the fact, that water of different qualities was employed by different observers. It may be added in this place, after the experiments which have been detailed regarding the effects of water of different temperatures on blood, that modifications in the temperature of the water used, and of the surrounding air, may also have modified the observations which have been made. To obviate these probable mishaps, I took special care, in the performance

of the experiments now to be related, to use a pure water; to use the same kind of water every time; to note the temperature of the air and of the water at the period when the experiment was proceeding; and to alter the temperature of the water in the different series of inquiries. I believe, therefore, that the succeeding observations will convey to the reader a clear and correct idea of the influence of water in quickening or retarding the process of coagulation.

EXPERIMENT LXX. *Effect of Diluting Blood with Water. Temperature of the Water, 60° Fahr.; of the Air, 70° Fahr.* I placed *two* ounces of water at 60° in a glass measure; I then received into the same measure *two* ounces of blood direct from the neck of a sheep, and handed the cup to an assistant to note the time of coagulation. The blood coagulated in fifty-four seconds: the clot was dark and loose. A large quantity of water afterwards exuded from it, upon which the clot became much firmer.

EXPERIMENT LXXI. *Effect of Diluting Blood with Water. Temperature of the Water, 60°; of the Air, 70° Fahr.* From the same animal I received into another measure ready at hand, and containing *one* ounce of water at 60°, *two* ounces of blood, and passed it to another assistant to observe the period of coagulation. The blood coagulated firmly into a bright red clot in fifty seconds. From this clot much serum exuded: the clot itself was very firm, and retained its red colour.

EXPERIMENT LXXII. *Effect of Diluting Blood with Water. Temperature of the Water, 60°; of the Air, 70° Fahr.* From the same animal I received into another glass measure, in which there were already *two* fluid ounces of water at 60°, *one* fluid ounce of blood. This blood did not coagulate for one minute and fifty seconds. The clot formed was very dark in the lower

part, and very loose; but at the upper surface there were white flaky separations of fibrin. Set aside for an hour, a large quantity of watery matter exuded from the clot; the mass of the clot beneath continued loose and dark, but the upper surface was coated with a fine soft layer of fibrin, about a line in thickness, and firmly adherent to the clot beneath.

The blood of the animal used in these experiments coagulated in fifty seconds simply exposed to the surrounding air, in which the thermometer stood at 70° Fahrenheit.

EXPERIMENT LXXIII. *Effects of diluting Blood with Water. Temperature of the Water, 40° Fahr.; of the Air, 45° Fahr.* I mixed *six* fluid ounces of newly drawn sheep's blood, by measure, with *six* fluid ounces of water at 40°. In four minutes coagulation feebly commenced: the blood became many shades darker in colour as it commingled with the water, and the clot was never firm, though it could be turned out of the bason, *en masse*, and serum exuded from it freely.

Other blood taken at the same moment from the same animal coagulated firmly in one minute, exposed to the temperature of the air.

EXPERIMENT LXXIV. *Effects of diluting Blood with Water. Temperature of the Water, 40° Fahr.; of the Air, 45° Fahr.* I mixed *six* fluid ounces of fresh blood from the neck of another sheep, with *three* fluid ounces of water at 40°. The change of colour was very slight. The blood in this instance coagulated in one minute, and ultimately formed a moderately firm clot. The blood of this animal, exposed to the open air, was fully set in one minute into a very firm clot.

EXPERIMENT LXXV. *Effect of diluting Blood with Water. Temperature of the Water, 40° Fahr.; of the Air,*

45° *Fahr.* I mixed *three* fluid ounces, by measure, of another sheep's blood, freshly drawn, with *six* fluid ounces of water. The blood commenced to coagulate feebly in one minute, and the process continued for five minutes longer: the clot was dark and very loose. The blood of this animal, left to itself, coagulated firmly in one minute.

EXPERIMENT LXXVI. *Effect of diluting Blood with Water. Temperature of the Water, 40° Fahr.; of the Air, 45° Fahr.* I mixed *six* fluid ounces of fresh blood from the neck of another sheep, with *twenty-four* fluid ounces of water. At the end of four minutes the blood began feebly to coagulate, but the coagulation was modified. No uniform red clot was formed; but the fibrin separated in a pale jelly-like layer, which floated loosely to the top of the fluid: fully fifteen minutes elapsed before the separation was complete. The blood of this sheep, left exposed to the air, coagulated firmly into a red clot in one minute and a half.

EXPERIMENT LXXVII. *Effect of diluting Blood with Water. Temperature of the Water, 40° Fahr.; of the Air, 45° Fahr.* I mixed *six* fluid ounces of fresh blood from another sheep with *twenty-four* fluid ounces of water. The results were the same as in last experiment. There was a separation of the fibrin resembling pale jelly in appearance, which floated in loose flakes in the upper part of the general fluid. The separation was not complete for an hour; but when, fifteen hours afterwards, the serum was poured away, the fibrin contracted into a loose jelly-like pale mass. The blood of this animal, left to itself in the air, coagulated firmly in one minute.

I took from the neck of a sheep a pint of blood, and subjected portions of it to the following experiments.

EXPERIMENT LXXVIII. *Effect of diluting Blood with Water. Temperature of the Water, 96° Fahr.; of the Air, 75° Fahr.* I poured *two* fluid ounces of the blood separately into three cups, each of which contained *two* ounces of water at 96°. The period of coagulation was noted by an assistant: it took place in all simultaneously in thirty seconds, the clots being firm and dark. The clot in one of these cups was turned out, *en masse*, before the blood left exposed to the air at 75° had begun to coagulate.

EXPERIMENT LXXIX. *Effect of diluting Blood with Water. Temperature of the Water, 96°; of the Air, 75°.* The instant after the third measure of two ounces had been poured into the third cup, *one* fluid ounce of the same animal's blood was poured into a cup holding *two* fluid ounces of water, also at 96°: this blood was watched by another observer. Although it had been longest drawn, before reaching the water, it did not begin to coagulate for fifty seconds, and was not a general clot for a minute and a half: it set into a dark and loose mass as compared with the clots in the other cups.

EXPERIMENT LXXX. *Effect of diluting Blood with Water. Temperature of the Water, 96°; of the Air, 75°.* Of the same animal's blood, I poured a fluid *half-ounce* into a cup containing *two* ounces of water at 96°. This blood, on commingling with the water, remained a thin fluid for a full minute; then it began slowly to come together in the centre, and in two minutes it had formed into a loose rounded clot, floating in the fluid, and coated above with a fine pale fibrous network. This clot was slightly cupped.

The blood of the animal used in this series of experiments coagulated firmly in forty seconds when exposed to the air (temperature 75°).

EXPERIMENT LXXXI. *Effect of diluting Blood with Water. Temperature of the Water, 96° Fahr.; of the Air, 72° Fahr.* I poured *two* fluid ounces of blood from the neck of a sheep into a cup containing *two* fluid ounces of water at 96°: the period of coagulation was noted by an assistant. The process was complete in thirty-five seconds; the clot was dark but firm.

EXPERIMENT LXXXII. *Effect of diluting Blood with Water. Temperature of the Water, 96°; of the Air, 72°.* *Two* fluid ounces of the same animal's blood were poured into *four* fluid ounces of water at 96°. Coagulation occurred in forty seconds, the clot being dark and loose.

EXPERIMENT LXXXIII. *Effect of diluting Blood with Water. Temperature of the Water, 96°; of the Air, 72°.* *Two* fluid ounces of the same animal's blood were poured into *six* fluid ounces of water at 96°. Coagulation commenced at the end of fifty-five seconds, the clot being not fully formed for two minutes, and being dark beneath and very loose, with a pale surface above.

EXPERIMENT LXXXIV. *Effect of diluting Blood with Water. Temperature of the Water, 96°; of the Air, 72°.* *Two* ounces of the same animal's blood were poured into *eight* ounces of water at 96°. In one minute and ten seconds thickening began to occur in the centre of the liquid; and in four minutes there was a loose coagulum, coated at its upper surface with a pale fibrous layer; beneath, the colour was dark.

The blood used in this series of experiments coagulated firmly in fifty seconds on exposure to the air (temperature 72°).

I received four ounces of blood from the neck of a sheep, and subjected it to the following experiments.

EXPERIMENT LXXXV. *Effects of diluting Blood with Water. Temperature of the Water, 60° Fahr.; of the Air, 71° Fahr.* Two fluid drachms of the blood were mixed with two fluid drachms of the water. Coagulation occurred in two minutes and twenty seconds: the clot was loose and dark, but could be turned out as a general coagulum.

EXPERIMENT LXXXVI. *Effect of diluting Blood with Water. Temperature of the Water, 60°; of the Air, 71°.* Two drachms of the blood were mixed with two ounces of water (temperature 60°). The blood commenced to form a loose gelatinous mass at the end of six minutes: at the termination of half an hour, a large gelatinous semi-transparent clot floated in an abundance of fluid: a pale film lined the clot on its upper surface. The clot, on being poured into a basin, broke up into soft fragments, resembling thin red currant jelly.

EXPERIMENT LXXXVII. *Effect of diluting Blood with Water. Temperature of the Water, 60°; of the Air, 71°.* Two drachms of the blood were mixed with four ounces of the water at 60°. A process of gelatinisation commenced at the end of ten minutes. At the end of half an hour there was no definite clot, but a general soft, semi-transparent gelatinous mass, coated at the top with delicate, pale lymph flakes.

EXPERIMENT LXXXVIII. *Effect of diluting Blood with Water. Temperature of the Water, 60°; of the Air, 71°.* Two drachms of the blood were mixed with eight ounces of water at 60°. Gelatinisation slowly commenced at the end of thirteen minutes. At the end of half an hour, there was a feeble gelatinous mass floating in the water,

coated at the upper surface with light lymphous membranous-like shreds. The soft mass broke up completely on being turned into a basin, but the lymph shreds floated again quickly to the surface.

EXPERIMENT LXXXIX. *Effect of diluting Blood with Water. Temperature of the Water, 60°; of the Air, 71°. Two drachms of the blood were mixed with sixteen ounces of water. Gelatinisation commenced at the end of twenty-two minutes: at the end of half an hour there was a very feeble gelatinous mass floating loosely in the water, and coated at its upper surface with white lymphous shreds. When the lymph was skimmed off, the soft mass, with the water surrounding it, flowed in a uniform current, into a receiving basin.*

The period of coagulation of the blood used in this series of experiments, when exposed simply to the air, was one minute and twenty-five seconds.

These experiments on the effects of dilution of blood with water were repeated in various ways, but the results were the same. I believe I am quite safe in deducing from them altogether,

1. That dilution of blood with water does not materially modify the period of coagulation, if the amount of water employed be not greater than the amount of blood, but that the clot thus produced is loose in structure and uniformly dark.

2. That when the amount of water added to blood is greater than the amount of blood itself, the process of coagulation is retarded and modified. That when the dilution is considerable,—as one of blood to sixty-four of water,—a mere gelatinous coagulum is formed, with a feeble separation of fibrin superiorly; and that when the dilution is extreme,—say one of blood to a

hundred and twenty-eight of water,—the attempt at coagulation consists mainly in a slow and simple separation of the fibrin, which rises, as it separates, to the surface of the fluid.

III. EFFECTS OF MIXING BLOOD WITH OTHER FLUIDS OF DIFFERENT DENSITIES.

I received eight ounces of blood from the neck of a lamb. A portion of this blood, exposed to the external air, the temperature of which was 70° Fahr., coagulated firmly in forty seconds.

EXPERIMENT XC. *Admixture of Blood with Water at 60° Fahr.* Two ounces of the blood were mixed with two ounces of the water. Coagulation was firm in one minute, the clot being very dark, almost black.

EXPERIMENT XCI. *Admixture of Blood with Albumen.* One fluid ounce of the blood was mixed with one-half ounce of white of egg, specific gravity 1.040. Coagulation commenced in two minutes and thirty seconds. The clot retained its red colour and was firm; it was mottled with white on its upper surface.

EXPERIMENT XCII. *Admixture of Blood with Syrup.* Two fluid ounces of blood were mixed with two fluid ounces of syrup, of a specific gravity of 1.060. Coagulation commenced in two minutes and five seconds. The clot formed was very firm and retained its red colour: there was no paleness of surface above.

I drew direct from the neck of a sheep six ounces of blood. The natural period of coagulation of this blood, at the temperature of the external air (65° Fahr.), was two minutes.

EXPERIMENT XCIII. *Admixture of Blood with Water.* One ounce of the blood was mixed with one ounce of

water at a temperature of 60° Fahr. The blood coagulated feebly in two minutes: there was a firm but very dark clot in two minutes and ten seconds.

EXPERIMENT XCIV. *Admixture of Blood with Albumen.* One ounce of the blood was mixed with one ounce of albumen, the temperature of which was 60° Fahr., the specific gravity 1.040. The blood commenced feebly to gelatinise at the end of six minutes. There was no distinct coagulation until the end of twenty-six minutes, when there was a feeble clot of a bright red colour, free from buff colour at the upper surface.

EXPERIMENT XCV. *Admixture of Blood with Syrup and Mucilage.* One ounce of the blood was mixed with one ounce of a mixture of simple syrup and mucilage, the temperature of which was 60° Fahr., the specific gravity 1.050. Coagulation commenced feebly in seven minutes and twenty seconds: at the end of sixteen minutes there was a general but loose clot of a bright red colour.

I took from the neck of a sheep six ounces of blood. The natural period of coagulation of a portion of this blood, as exposed to the air, was one minute and fifteen seconds. The temperature of the air was 65° Fahr.

EXPERIMENT XCVI. *Admixture of Blood with Water.* One ounce of the blood was mixed with one ounce of water at 60° Fahr. Coagulation commenced in one minute and forty seconds: the clot formed was firm and dark. The blood darkened immediately after its admixture with the water.

EXPERIMENT XCVII. *Admixture of Blood with Albumen.* One ounce of the blood was mixed with one ounce of albumen, at a temperature of 60°, and a specific gravity of 1.040. The blood commenced feebly to gelatinise in two minutes and twenty seconds. There was no dis-

tinct coagulation for eight minutes: at that time the clot was very loose and was easily broken up; and in this condition it remained. The blood retained its bright red colour.

EXPERIMENT XCVIII. *Admixture of Blood with Syrup.* One ounce of the blood was mixed with one ounce of simple syrup at a temperature of 60° , and of a specific gravity of 1.200. The blood commenced to gelatinise at two minutes and a half, but it had not fully coagulated for eight minutes and ten seconds, when the clot formed was very loose, but of a bright red colour.

EXPERIMENT XCIX. *Admixture of Blood with Syrup.* Two ounces of the blood were mixed with one ounce of syrup at 60° , and of a specific gravity of 1.200. Coagulation occurred in one minute and twenty seconds, the clot being firm and of a bright red colour.

I took from the neck of a sheep six ounces of blood. A portion of this blood exposed to the air, the temperature of which was 65° , coagulated firmly in one minute and forty seconds.

EXPERIMENT C. *Admixture of Blood with Water.* One ounce of the blood was mixed with one ounce of water at 60° . Coagulation occurred in two minutes and five seconds, the clot being firm and dark.

EXPERIMENT CI. *Admixture of Blood with Syrup.* Two ounces of the blood were mixed with two ounces of simple syrup at a temperature of 60° , and of a specific gravity of 1.300. Coagulation commenced in seven minutes and ten seconds: at the end of ten minutes the clot was uniform, but loose. The colour remained of a natural bright red.

EXPERIMENT CII. *Admixture of Blood with Albumen.* One ounce of the blood was mixed with one ounce of

albumen at 60°, and of a specific gravity of 1·040. The blood feebly coagulated at the end of five minutes: the clot remained very loose, but of a bright red colour.

I received from the neck of a sheep six ounces of blood. A portion of this blood, exposed to the air at 65°, coagulated in fifty seconds.

EXPERIMENT CIII. *Admixture of Blood with Water.* One ounce of the blood was mixed with one ounce of water at a temperature of 60°. Coagulation was perfect in one minute, the clot being firm, but dark.

EXPERIMENT CIV. *Admixture of Blood with Syrup.* Half a fluid ounce of the blood was mixed with a quarter of a fluid ounce of syrup at a temperature of 60°, and of a specific gravity of 1·300. This blood coagulated feebly in two minutes; the clot remained loose, but of a bright red colour.

EXPERIMENT CV. *Admixture of Blood with Albumen.* Half a fluid ounce of the blood was mixed with a quarter fluid ounce of albumen at a temperature of 60°, and of a specific gravity of 1·040. Coagulation occurred feebly in two minutes and ten seconds: the clot remained loose, but of a red colour.

EXPERIMENT CVI. *Admixture of Blood with Albumen.* A quarter fluid ounce of the blood was mixed with half a fluid ounce of the albumen. At the end of five minutes there was commencement of coagulation; but the clot, though red in colour, was very loose.

EXPERIMENT CVII. *Admixture of Blood with Gum-water.* Two ounces of blood were taken from the neck of a sheep. One ounce set aside, exposed to the open air at 65° Fahr., coagulated firmly in two minutes. The other ounce was mixed with one ounce of gum-water (gum arabic) at a temperature of 60°, and of a specific

gravity of 1.050. Coagulation had not set in at the end of half an hour; but at the end of two hours there was a very loose flaky coagulum, floating in abundance of liquid. The blood retained its bright red colour.

EXPERIMENT CVIII. *Admixture of Blood with Gum-water.* Two fluid ounces of blood were taken from the neck of a sheep: one ounce set aside, exposed to the air at 65°, coagulated firmly in one minute and forty seconds: the remaining one ounce of blood was mixed with one ounce of gum-water of specific gravity 1.050, and of a temperature of 60°. This blood remained perfectly fluid for half an hour, and at the end of an hour was only a little thicker than before; in two hours, it was separated into a very feeble clot, which floated, in a flaky-like condition, in abundance of liquid, and retained its red colour.

I drew from the jugular vein of an ox four ounces of blood. A portion of this blood, exposed to the air at 68°, coagulated firmly in a red clot in three minutes and a half.

EXPERIMENT CIX. *Admixture of Blood with Water at 60°.* One fluid ounce of the blood was mixed with one ounce of the water: the admixture produced a general dark colour. Coagulation was perfect in six minutes, so that the clot could be turned out of the cup in one mass.

EXPERIMENT CX. *Admixture of Blood with Syrup.* One fluid ounce of the blood was mixed the next moment with one ounce of syrup of a specific gravity 1.300, and a temperature of 60°. No change of colour followed the admixture: at the end of six minutes there was no indication of coagulation; but, one minute later, feeble gelatinisation commenced; at ten minutes the upper surface of the clot was paler than before; and

at the end of fifteen minutes the whole was a feeble coagulum, with a marked, pale fibrinous coat at the upper surface. The remaining part of the blood used in these experiments, exposed to the air at 60°, coagulated firmly into a bright red clot in three minutes and a half.

It is clear from these experiments that, by increasing the specific gravity of blood, or by mixing it equally with a fluid of, or near, its own specific gravity (1.055), the process of coagulation is markedly retarded and modified. It is clear, too, that this retardation is not due to mere fluid admixture, according to quantities, nor yet to special chemical action exerted by the added fluid, but to the physical modification. If the mere addition of fluid were the cause of retardation, then the equal addition of water ought equally to effect the retarding process. If, again, the effect were chemical, the retardation would not be common with different agents; whereas it occurs whether gum-water, albumen, or syrup be the fluids employed in the way of experiment.

If two drops of blood be taken from the hand, and placed on the microscope glass at different points; if the one be mixed with a drop of albumen, and the other be left free, a modification in the process of coagulation will be readily observed. The blood mixed with the albumen will remain fluid between the glasses, and the corpuscles in motion for double, or even quadruple, the time of the blood left naturally. The corpuscles of the blood admixed with albumen will be seen also shrunken and stellate, much in the same conditions as obtain in super-alkaline blood, while the fibrous network will be but slowly and feebly developed. Experiments thus conducted, with drops of blood and solutions of different

densities, give a good general demonstration of the facts above stated; but to obtain a positive and correct knowledge of this part of the subject of coagulation, larger portions, both of fluid and of blood, are necessary, so that the exact densities of the fluids may be obtained at the temperature of 60° Fahrenheit.

The fact, that the addition of distilled water to blood produces a general darkness of that fluid, while a fluid of greater specific gravity—though added in the same quantity—produces no such effect, is a curious circumstance, having some indirect bearing, perchance, on the cause of the colour of blood. I leave this for future research.]

IV. EFFECTS OF EXPOSING BLOOD TO, OR EXCLUDING IT FROM, THE AIR.

That free exposure of blood to air hastens coagulation, and that exclusion of newly drawn blood from air retards the process, are facts well ascertained by many writers. These results are well brought out in the following series of experiments.

Coagulation of Dog's Blood in vessels of different kinds. The jugular vein of a large dog was laid bare for the space of an inch and a half. The vein was now placed under the control of an assistant, who, with a pair of strong forceps, was enabled completely to manage the current.

EXPERIMENT CXI. *Coagulation in a three-inch Dish.* When ready for operation, a free opening was made in the vein, and six drachms of blood were drawn into a common evaporating dish, *three* inches in diameter at the top and *one* inch deep at the centre. The blood thus placed coagulated in two minutes and sixteen seconds.

EXPERIMENT CXII. *Coagulation in a half-inch Tube.*

When the vein had discharged the first six drachms of blood already mentioned, the current was stopped until the blood could be removed and handed to an assistant, who was specially employed to observe the period of coagulation. The vein was then again loosened, and another six drachms were received into a *half-inch* tube, measuring eight inches in length: this blood did not coagulate for five minutes and three seconds.

EXPERIMENT CXIII. *Coagulation in a Closed Tube.* A fluid draught of blood, the same as the preceding, was received into a half-inch tube, which was immediately closed at the top. This blood showed no inclination to coagulate for seven minutes; it then coagulated, but the coagulum was darker and less firm in consistence than in the former case, and it did not so readily separate into serum and clot. The vein was now tied with a ligature, and the animal did well.

Coagulation of Ox's Blood in vessels of different kinds. Three vessels of the same size and shape were procured; the mouth of one was free, leaving an exposed surface of two and a half inches diameter: the mouth of the second was reduced to half an inch: the third vessel was provided with a stopper which closed it. One pint of blood was now received direct from the throat of an ox; it was drawn all at once into a tin spouted vessel, and treated as follows.

EXPERIMENT CXIV. *Coagulation in a Closed Vessel.* A third part of the blood was poured into the vessel which was to be closed; as soon as the blood was in the vessel, the stopper was firmly inserted. This blood was quite fluid at the end of six minutes, when the stopper was temporarily removed; at the end of nine minutes and twenty seconds the stopper was again withdrawn, and the blood was found feebly coagulated.

EXPERIMENT CXV. *Coagulation in the half-inch Vessel.* Another third part of the blood was poured into the vessel the mouth of which was half an inch: coagulation took place in four minutes and fifteen seconds.

EXPERIMENT CXVI. *Coagulation in the Open Vessel.* The last third of the blood was poured into the open-mouthed vessel: coagulation occurred in three minutes and twenty seconds, the clot being very firm.

In these experiments the period of coagulation dates, as in all previous and after ones, from the moment when the blood escaped from the animal.

Coagulation of Blood in Tubes of different diameters and lengths. I made four tubes of glass: the first was straight, was closed at the lower end like a test-tube, was an inch in diameter, and, when full, held exactly four fluid drachms of blood: we will call this the one-inch tube. I made a second tube, of a similar kind, half an inch in diameter, but so much longer that it held exactly the same amount of fluid as the other tube: we will term this the half-inch tube. I made a third tube, one-eighth of an inch in the bore, but extended in length so as to hold the same amount of fluid as the two previous tubes. That this tube might be filled the more easily, instead of closing it at one end I left both ends open, but bent the tube in the middle with an easy curve, making it in shape like a Marsh's apparatus without the bulb. The tubes being arranged in a line with each other, a few ounces of blood were drawn from the jugular vein of an ox, and subjected to the following experiments and observations. The temperature of the air was 70° Fahrenheit.

EXPERIMENT CXVII. *Coagulation in a three and a half-inch Cup.* Half an ounce of the blood was poured into

a cup having a diameter of *three inches and a half*: this blood was a firm clot in three minutes and twenty-five seconds.

EXPERIMENT CXVIII. *Coagulation in the one-inch Tube.* Half an ounce of the blood was poured into the *one-inch tube*; this blood commenced to coagulate in four minutes, and was a firm clot in four minutes and a half.

EXPERIMENT CXIX. *Coagulation in the half-inch Tube.* Half an ounce of the blood was poured into the *half-inch tube*; at the end of five minutes the blood could be poured out of the tube in a semi-coagulated state: after being exposed to a wider surface in a cup, it formed, in a minute, a uniform coagulum like the others.

EXPERIMENT CXX. *Coagulation in the eighth of an inch Tube.* The *eighth of an inch* long bent tube was filled with blood; it was filled last of the series, and at least four or five seconds later than the first (since moments fly fast, however quick may be the hands); when six minutes had elapsed, the blood was examined. At each open end of the tube there was a firm seal of blood-clot, and this extended down the tube for the space of an inch on each side. I drew out these coagula, and then, putting my mouth to one end of the tube, blew through it, placing the other end over a cup. As I blew, the blood in the tube flowed out in a thick stream, and looked like broken up black currant jam, as it fell into the cup: exposed widely to the air, the coagulation quickened, and, in two minutes, the blood could be turned on the table, a uniform and moderately firm coagulum.

Coagulation of Blood under diminished Atmospheric Pressure. Scudamore has shown that blood placed in

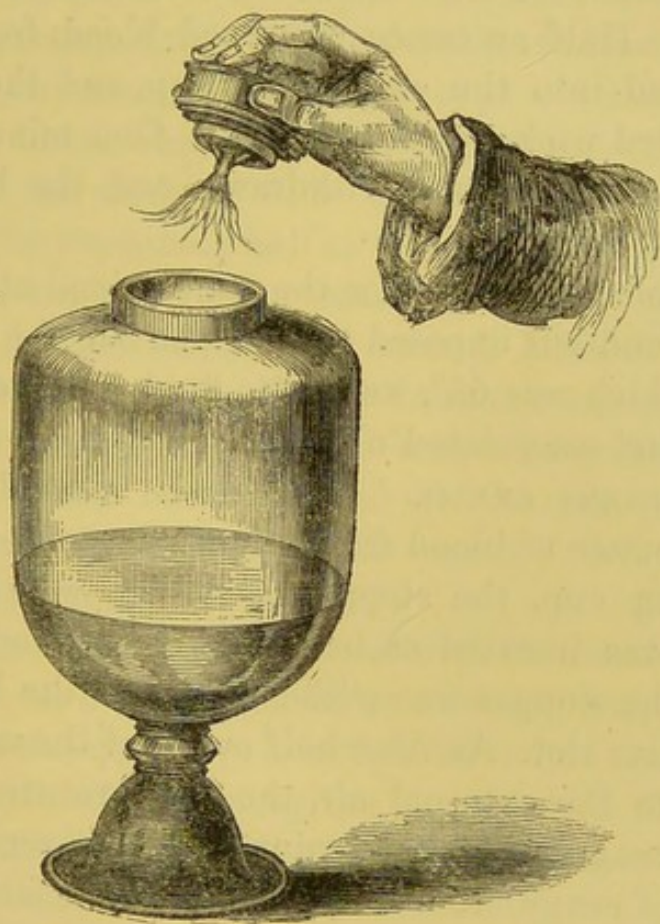
vacuo coagulates more quickly than when it is exposed to the ordinary pressure of the atmosphere. A variety of experiments have confirmed to me the truth of this position, as the succeeding illustrations verify.

EXPERIMENT CXXI. *Blood under diminished Pressure.* Two watch-glasses were filled with freshly drawn blood, taken from an ox: one was exposed to the ordinary atmosphere (temperature 55° Fahr.); the other was placed in the bell of an air-pump, and the air was extracted as rapidly and as completely as possible. The blood in the ordinary atmosphere began to coagulate in a minute and a half; that under the air-pump coagulated rapidly, with a free evolution of vapour. Removed from the bell of the air-pump at the end of a minute, this blood was found as a firm and consistent clot; while the blood in the air was still entirely fluid. At the end of six minutes, the blood exposed simply to the air was less firm than the previous blood had been at the moment when it was taken from the bell.

[In experimenting on the effects of placing blood under a diminished atmospheric pressure, it is better to use the blood of the ox than that of the sheep; for the blood of the sheep coagulates so quickly, and the steps of the operation are, comparatively, so slow, that it is difficult, even with two assistants at hand, to detect well marked differences, as regards periods of coagulation, under the ordinary and the reduced pressures. It is requisite, also, to take the first gush of blood, and, when possible, to draw it from the jugular vein before the animal is felled; since coagulation is proportionately rapid as the current of blood is slow. Moreover, I found, practically, that the air-pump is a tedious and even difficult instrument to use in this inquiry.

In using it, time is lost in placing the cup of blood under the bell, as well as in pumping out the air afterwards. I therefore adopted a simple and more ready plan.

I had made and fixed on a stand a strong glass vessel, like a cupping glass inverted, and having a firm and narrow neck. For the neck a movable stopper was made, from which a small tube depended for holding a bit of cotton wick. The form of this exhausting cup, with mode of using it, are given in the drawing below.



When the instrument was being used, the wick, charged with spirit for ignition, was held ready at hand by an assistant. The portion of blood required was

then received from the animal, and at once poured into the glass, immediately upon which the assistant inserted the stopper with the wick ignited, but slowly, so that the enclosed air could escape. When the stopper required to be taken out, a turn of the little stop-cock at the top let in air, and allowed its easy removal.

Although by this exhausting cup less air is removed than by a good air-pump, the simplicity and directness of the experiment are so well marked, that the disadvantage is more than counterbalanced.

EXPERIMENT CXXII. *Blood under reduced Atmospheric Pressure.* Half an ounce of mixed blood from an ox was poured into the exhausting cup, and the stopper with ignited wick was introduced. One minute afterwards the stopper was withdrawn, and the blood was found coagulated.

Other blood, drawn from the same animal at the same moment, and left exposed to the open air the temperature of which was 65° , was quite fluid at the end of the minute, and coagulated ultimately in three minutes.

EXPERIMENT CXXIII. *Blood under reduced Pressure.* Half an ounce of blood from an ox was poured into the exhausting cup, the stopper of which, with the wick ignited, was inserted as before. At the end of forty seconds the stopper was withdrawn, and the blood was found a firm clot. Another half ounce of the same blood, exposed to the external air, the temperature of which was 65° , coagulated in one minute and ten seconds. The rapidity of coagulation was here due to the fact, that the blood had been caught while flowing in a languid current.

EXPERIMENT CXXIV. *Blood under reduced Pressure.* I received an ounce of mixed blood from the neck of a lamb. One half of it was poured into the exhausting cup. The other half was set aside in an open cup, ex-

posed to the temperature of the external air at 65° Fahr. As soon as the blood had reached the exhausting cup, the stopper, with the wick ignited, was inserted. At the end of one minute I removed the stopper, and found the blood not fully coagulated. I therefore relighted the wick, and again introduced it. After forty seconds had elapsed, I once more withdrew the stopper, and removed the blood in a firm and uniform coagulum. Turning now to the blood in the cup, I found it still fluid. It coagulated thirty seconds later, the clot being firm and uniform.

EXPERIMENT CXXV. *Blood under reduced Pressure.* I caught an ounce of blood from the neck of a sheep. Half this blood was at once poured into the exhausting cup, and the stopper, with the wick ignited, was inserted. The remaining half of the blood was placed in an open cup, exposed to the external air, at a temperature of 65°. At the end of forty seconds I raised the stopper, and turned out the blood from the exhausting cup in a firm coagulum. At the end of one minute, the blood that had been exposed to the air coagulated loosely; and, in twenty seconds more, it had become a firm coagulum.

EXPERIMENT CXXVI. *Blood under reduced Pressure.* I received an ounce of blood by measure from the neck of another sheep, and poured half of it into the exhausting cup, instantly inserting the stopper with the lighted wick; the remaining half ounce of blood was left exposed to the air (temperature 65°), as before. At the end of half a minute I removed the stopper of the exhausting cup, and turned out its contained blood in a firm coagulum. Turning next to the blood exposed to the air, I found it so fluid that I could pour it in an unbroken liquid

current into another vessel. It did not begin to coagulate for fifty-five seconds, and then formed quickly into a firm clot.

EXPERIMENT CXXVII. *Blood under diminished Pressure.* One ounce of sheep's blood, freshly drawn, was used as before. Half an ounce was poured into the exhausting cup; and the remainder was left in the open cup, at a temperature of 65°. After forty-five seconds I removed the stopper of the exhausting cup, and turned out its contained blood in a firm clot. The blood in the open cup was still perfectly fluid, and could be poured from one vessel into another; it remained fluid thirty seconds longer. It then set into a firm clot.

It would be needless repetition to illustrate this section further, by the detailing of similar observations. There are no experiments more easy or satisfactory to perform than those with the exhausting cup. Of course a little manipulative practice is required; but this achieved, the stopper of the exhausting cup well fitted, the blood received in the *first* gush from the animal, and a competent assistant at hand to note and indicate time, and every experiment becomes a success; *i. e.* the blood in the exhausting cup may be turned out each time a coagulated mass, while the blood in the open cup is yet fluid. In some instances, the blood of the sheep coagulated so quickly on the introduction of the stopper and lighted wick, that, on removing the stopper, after counting twenty seconds, I found the blood fully coagulated. The rapidity in these cases occurred from the more perfect abstraction of the air. Indeed, if a portion of blood from the sheep could, by any possibility, be introduced suddenly into a perfect vacuum, its coagulation would, I believe, be the act almost of a moment.

The effect of the vacuum on coagulation is nowhere better shewn than in the ordinary operation of drawing blood by cupping. In this operation, the blood which escapes into the glass coagulates with remarkable activity. I once observed blood thus extracted coagulate at the depending part of the glass in twenty seconds; whilst other blood, drawn at the same time, from a lancet puncture in a free part of the back, did not coagulate for a full minute. Indeed, the success of the operation of cupping depends upon the expedition with which a free quantity of blood can be drawn into a glass placed as *lightly* as is possible on the flesh. If too great a portion of air is extracted from the glass when it is applied to the skin—in other words, if too perfect a vacuum is produced—the blood coagulates immediately, and the incised wounds becoming quickly filled with clotted blood, the operation in great part fails.]

EXPERIMENT CXXVIII. *Effects of drawing Blood through Pointed Tubes.* I drew out six tubes, from a piece of glass tubing of the quarter-inch bore, into tapering points, as shewn in the drawing. I dipped one end of



each tube into ox's blood, freshly drawn, and then drew up from the other end by my mouth. As each tube filled, I handed it to an assistant, for the purpose of his sealing it up hermetically at both ends with the spirit-lamp and blow-pipe. To my momentary surprise (for I was not at that time prepared for such an event, and had, indeed, another object in view), the blood thus treated coagu-

lated much more quickly than did some blood from the same animal, which was exposed to the air; indeed, the blood had coagulated in the tubes before their fine ends could be annealed. I learned afterwards that this rapidity of coagulation arose from my having drawn the blood into the tubes by the vacuum process. This observation led to several special experiments.

[EXPERIMENT CXXIX. *Blood drawn through a Pointed Tube.* I drew out a quarter-inch tube three inches long into tapering points. The opening at each extremity was the twentieth of an inch in diameter. I caught a little blood from the neck of an ox in a cup, immersed one end of the tube into the blood, and drew blood from the other end very slowly through it with my mouth. As soon as the tube was filled I withdrew it from the blood; but coagulation was so far commenced that the fluid would not flow out of either end when the tube was held upright. The blood in the vessel, from which the supply to the tube was taken, did not coagulate for two minutes later.

EXPERIMENT CXXX. *Blood drawn through a Pointed Tube.* I drew out a quarter-inch tube to six inches long, the ends tapering: the one end was brought out to a diameter of the twentieth of an inch; the other end was drawn out to a point into which a fine sewing needle, number eight, could only be introduced. I now dipped the wider end into a little blood drawn from an ox, and drew up strongly from the finer end of the tube. I succeeded in filling the tube with blood; but on removing it, instantly, its contained blood was found firmly coagulated. The blood of this animal, exposed freely to the air, coagulated a full minute later than that in the tube.

EXPERIMENT CXXXI. *Blood drawn through a Pointed*

Tube. I drew out a glass tube of a quarter-inch bore into two fine ends, the diameter of each end being such as to admit only of the introduction of a fine needle, of number nine size. I immersed one end of this tube into a little blood freshly drawn from an ox, and then drew up strongly by my mouth. The blood rose at first; but I could not, with all my force, fill the tube completely. While making the suction effort, the blood coagulated, and was fixed in the tube. At that moment the blood in the cup, exposed to the air, at a temperature of 68° , was completely fluid, and remained so two minutes longer, when it set into a firm coagulum.

EXPERIMENT CXXXII. *Blood drawn through a Pointed Tube.* I drew out another tube, of the same length and central diameter as the last named. One end was drawn to the needle-point diameter; the other end was drawn to the twentieth of an inch in diameter. I immersed the finer end of this tube into half an ounce of blood, that moment drawn from the neck of a lamb, and then, with my mouth at the wider end, drew up the blood gently but continuously. In ten seconds the tube was full. When full, I gently blew downwards, and drove out for a moment a thin blood stream; but the current stopped almost instantly, from coagulation having occurred at the fine end of the tube, and in ten seconds more all the blood in the tube was firmly set. The blood left in the cup, from which the tube was filled, remained perfectly fluid for a minute and a half, as it lay exposed to the air (the temperature of which was 70° Fahr.), but it had coagulated firmly at the end of two minutes.

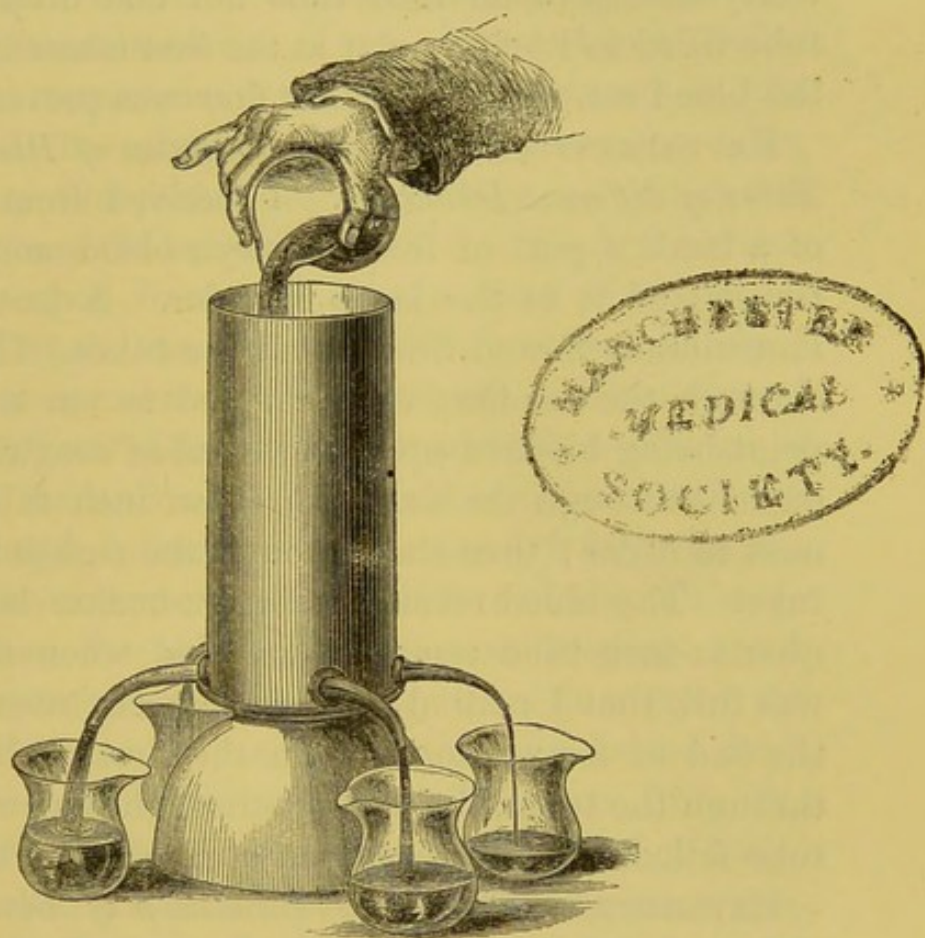
These experiments, very simple to perform, need not be multiplied; they are, in fact, but modifications of the exhausting cup and air-pump processes. By pro-

longing the fine extremity of one of these tubes to the length of three or four inches, each minute drop of blood, as it is drawn through this capillary course, is so acted on by the exhausting force that it coagulates, and the passage of blood may thus be stopped at the outset.]

Coagulation of flowing Blood in Streams of different Diameters. The fact has been known for ages past, that if, in the operation of phlebotomy, the puncture in the vein be small, the thin blood-stream soon stops, from coagulation occurring at the wound; while such blood as it is caught coagulates with great rapidity. In bleeding, I have seen the blood, when the current has been slow and thin, coagulate as it trickled down the arm of the patient, or fell on my own hand. On the other side, when a full and free stream of blood is drawn, it continues in the current until it is stopped from failure in the force of the circulation; while the mass of blood received into the basin coagulates slowly in comparison.

By a very simple instrument I found myself able to imitate this occurrence, and to see at a *coup d'œil* the result of the thin and broad blood streams on coagulation. I had made a cylinder of tin, eight inches long and four inches in diameter. This cylinder was closed at the lower end, and open at the top. At the lower part in the side wall I inserted, at different points of the circumference, four tubes, which stood out at right angles from the vessel, and took a gentle spout curve. The ends of these tubes within the tin cylinder measured the same, viz. a quarter of an inch in diameter; but at the other or projecting ends, each tube was brought to a different diameter; one was left at the quarter-inch bore; another was drawn out to an eighth of an inch; the third

to the sixteenth of an inch; the fourth to the thirty-second of an inch. The instrument, when in use, was raised on a pedestal, so that a beaker could be placed beneath each spout; then the large tin cylinder was filled with freshly drawn blood, which discharged itself into the beakers in currents of different diameters, as shewn in the subjoined diagram.



EXPERIMENT CXXXIII. *Transmission of Blood through Tubes of different Diameters.* I received a quart of blood from the neck of a bullock, and from it filled the large cylinder. The blood ran out in a full stream from the quarter-inch tube, and coagulated in a firm clot in one minute after being received into the beaker. The cur-

rent through the eighth of an inch tube ran for a few seconds, then stopped altogether. The blood discharged by this tube coagulated almost instantly after reaching the beaker beneath. Through the sixteenth of an inch tube no current at all was set up. A few drops only escaped, when a drop at the end of the tube coagulated and sealed up the aperture altogether. Through the thirty-second of an inch tube not one drop fell; the tube filled to its fine point at the first moment, but here the blood set, and the further flow was prevented.

EXPERIMENT CXXXIV. *Transmission of Blood through Tubes of different Diameters.* I received from the neck of a lamb a pint of freshly drawn blood, and instantly transferred it to the large cylinder. A brisk current immediately flowed through all the tubes. The current through the smallest tube stopped in ten seconds, its point being blocked up with a bead of coagulum. The current through the sixteenth of an inch tube stopped next in order; then that through the eighth of an inch tube. The blood received into the beaker beneath the quarter-inch tube remained so fluid when the beaker was full, that I poured it back into the reservoir. At the end of forty seconds from the first gush of blood through the tubes, the current through the quarter-inch tube failed from the formation of clot in the tube.

EXPERIMENT CXXXV. *Transmission of Blood through Tubes of different Diameters.* I received a charge of blood from the neck of a sheep, and instantly filled the large cylinder or reservoir. At first there was a free spirt of blood from all the tubes; but the current through the smallest stopped in three seconds from coagulation at the point. The current through the sixteenth of an inch bore stopped from the same cause

at twenty seconds. When the beaker beneath the quarter-inch tube was full of blood, the blood it contained was perfectly fluid, and was thus returned to the reservoir. At the end of forty seconds, the currents through the eighth of an inch and quarter-inch tubes stopped flowing from coagulation, the smaller of the two stopping first by the matter of a few seconds.

EXPERIMENT CXXXVI. *Transmission of Blood through Tubes of different Diameters.* I experimented in a similar way to that recorded in the last experiment, on the blood of another sheep. The results were the same, with the one exception that a continuous current was not set up from the smaller tube. As the first portion of blood escaped from this tube, a bead of coagulum was formed at the mouth and sealed it up completely.

EXPERIMENT CXXXVII. *Transmission of Blood through Tubes of different Diameters.* I received a charge of blood from the neck of a sheep, and at once transferred it to the large cylinder or reservoir. I kept up the supply in the reservoir by the addition of a new charge of blood from the animal, an assistant keeping watch on the currents from the tubes. The flow from the smallest tube was only a few drops, and ceased from coagulation within five seconds. The flow from the second smallest tube ceased next in order, and quickly; while the currents in the two larger tubes were continuous for one minute, and stopped nearly at the same time, from the tubes becoming blocked up with red clot.

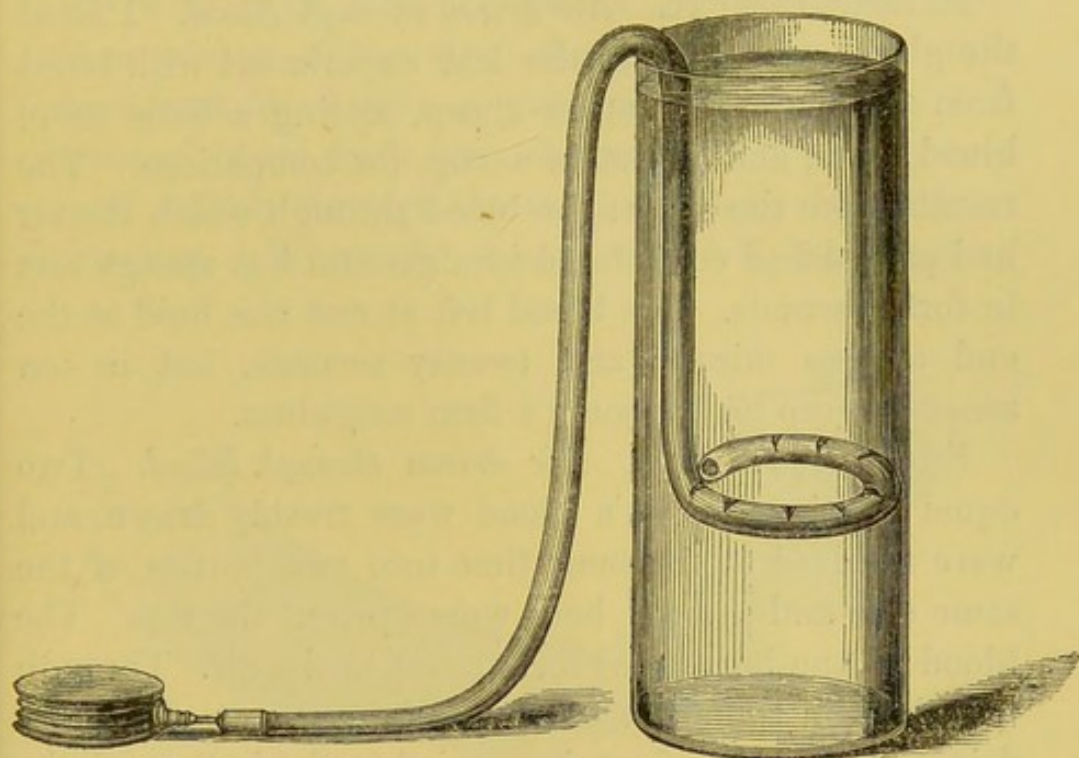
EXPERIMENT CXXXVIII. *Exposure of Blood to the Air in a Stream.* I caught in a spouted jug a pint of blood from the neck of a sheep. One half of this was decanted into a beaker. The other half I poured in a slow

stream from the jug into a another similar jug, repeating the process. In twenty-five seconds I felt a clot passing from one vessel to the other. At the end of fifty seconds, an assistant noted that the blood left at rest was coagulated. On examining the blood which had been poured out, I found that the mode of coagulation had been by simple separation of the fibrin, as obtains when blood is whipped with the hand. The separation of fibrin in this experiment was very perfect, as no coagulation whatever occurred when the fibrous mesh was removed from the fluid.

On the Effects of driving currents of Air through newly drawn Blood. The abstraction of air favours and hastens coagulation. The force of brisk currents of air through blood has precisely the same influence. I use the word air in this place, not because *air* only is implied, but because air was the compound gas usually employed in these inquiries, as being at once the readiest to hand and cheapest. The effects, however, are precisely the same, whether oxygen be the gas driven through, or nitrogen, or certain other gases, which I shall refer to further on, and which are negative in their chemical action on the blood when driven through it, but exert the ordinary physical effect of carrying with them other free gases with which they may come in contact in their course.

To be able to drive air through blood with equality of diffusion and freely, I constructed an apparatus, as shewn in the next drawing. It was simply a straight glass vessel, three inches in diameter, and eight inches in height; it was open at the top. A little below the middle part of this vessel was placed a circular tube, perforated with holes above, like a circular gas-burner;

from this a tube ascended, which, bending over the vessel, was connected with a pair of small bellows at its extreme end.



EXPERIMENT CXXXIX. *Air driven through Blood.* I received from the neck of a sheep as much blood as would fill the glass vessel above named. As soon as the vessel was filled, an assistant, who held the bellows, drove through the blood a brisk current of air. A separate portion of blood from the same animal was received in a cup, and left at rest exposed to air, for comparison. I took the periods of coagulation myself. The blood through which the air was passing was well coagulated in forty-five seconds. I now drew out the clot above the circular jet; it was a well made but spongy mass. The blood in the lower part of the glass, *i. e.* beneath the jets, was next turned out, and found half in clot, the rest quite fluid. The fluid part coagu-

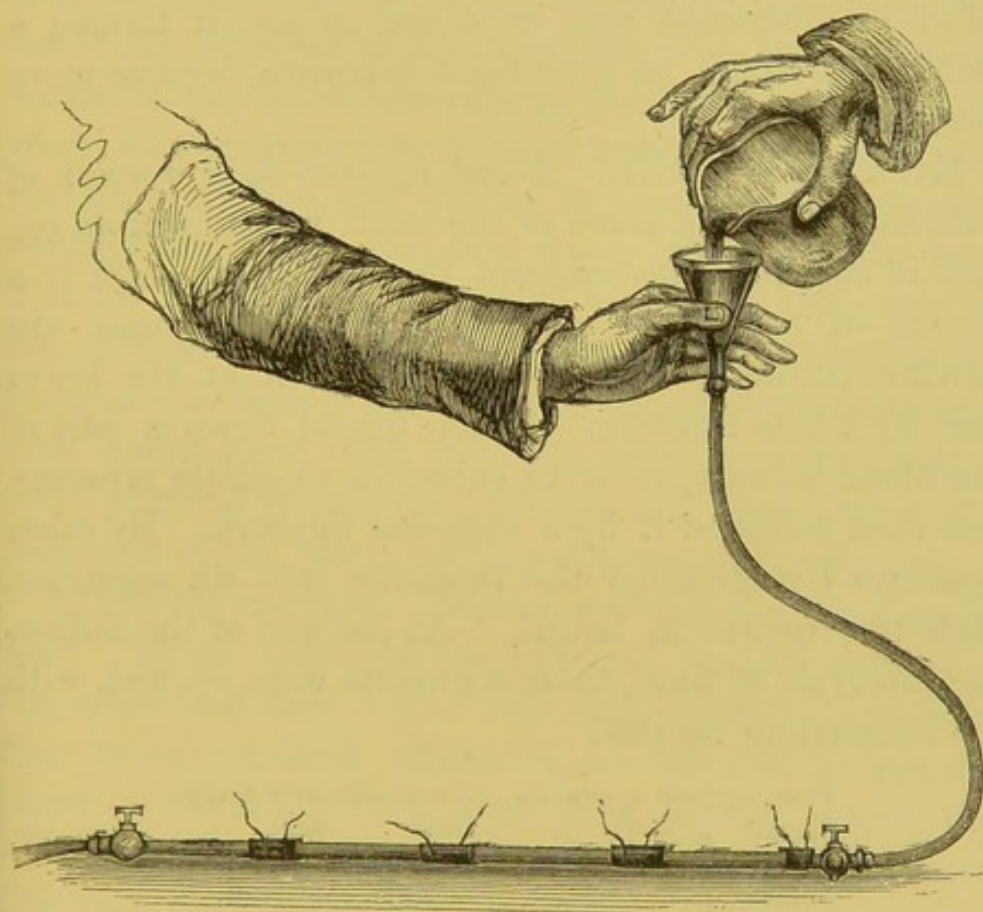
lated in one minute after removal. The blood left naturally at rest in the air did not coagulate for one minute and a half. It then set into a firm clot.

EXPERIMENT CXL. *Air driven through Blood.* I filled the glass vessel used in the last experiment with blood from the neck of another sheep, setting a little more blood aside, and at rest in a cup, for comparison. The results were the same: the blood through which the air had passed had coagulated in a general but spongy clot in forty seconds. The blood left at rest was fluid at the end of one minute and twenty seconds, but in ten seconds more had become a firm coagulum.

EXPERIMENT CXLI. *Air driven through Blood.* Two equal portions of ox's blood were freshly drawn, and were received at the same time into two bottles of the same size and shape; both were open at the top. The blood in one bottle was left at rest in the air. Through the blood in the other bottle a brisk current of air was driven, by means of a tube carried to the bottom of the blood, as in the common Wolf's bottle, and connected at its opposite end with the bellows. The blood thus treated coagulated in forty seconds. The blood at rest did not coagulate for two minutes, but it formed a less spongy coagulum.

On the Exclusion of Blood from Air, and the results in regard to Coagulation. In the preceding experiments it has been shewn, that the free exposure of blood to air, as well as the removal of atmospheric pressure, favour coagulation. In the ensuing series, the effects of simple exclusion from air and of increased pressure will be demonstrated. Some of these experiments are modifications or imitations from Hewson, others are original.

[EXPERIMENT CXLII. *Blood inclosed in a Tube.* I took four pieces of glass tubing, two inches in length, and a quarter of an inch in diameter. I connected these tubes firmly with each other by pieces of vulcanised India rubber tubing of the same diameter. The tube thus formed was fitted with a stop-cock at each end. A current of blood fresh from the neck of an ox was now poured briskly through the tube, as shewn in the next illustration. When the stream was full, both ends of



the tube were simultaneously closed by a turn of the stop-cocks, and a ligature was passed round the India rubber tubing between each piece of glass tube, in order that the blood inclosed in the segments might be

examined at different times. Unfortunately, the experiment was not quite so cleverly performed as it might have been, and a little air was admitted with the blood. However, the effects were well marked. A portion of the animal's blood, which had not passed through the tube, coagulated in three minutes. The blood inclosed in the upper and lower segments of the tube, examined in eight minutes, was found uncoagulated; while that in the two middle segments was found quite fluid when liberated, at the end of fifteen minutes. After its liberation and exposure to air, it formed a feeble clot, which, on prolonged exposure, became more consistent.

EXPERIMENT CXLIII. *Blood inclosed in a portion of Intestine.* I took a piece of the small intestine of an ox, had it carefully washed, and then drove through it a stream of newly drawn blood. As the current was flowing through, I suddenly arrested it at the lower part by a firm ligature. I then forced down a part of the blood column, so as to submit it to gentle pressure, and then confined it by a superior ligature. By other ligatures I partitioned the intestine into six segments, each two inches in length. At the end of the following intervals of time, these segments were opened, with the succeeding results:

First segment	4 minutes.	Blood coagulated firmly.
Second	„ 5 „	Ditto ditto.
Third	„ 6 „	Blood semi-coagulated.
Fourth	„ 7 „	Blood all coagulated.
Fifth	„ 8 „	Ditto ditto.
Sixth	„ 9 „	Ditto ditto.

The blood of the animal, as it flowed on the pavement, coagulated in two minutes. This experiment, though interesting, in that the blood in the middle

segment was but partly coagulated, was in great measure a failure, from the two circumstances that it is difficult to ligature a portion of intestine so as to make it air tight, and that intestine is easily distensible.

But I would speak of this experiment as important from another point of view. It was an experiment framed and carried out on the same principles as the one which immediately preceded it. The only difference between the two experiments consisted in the fact that, in the first, the tube containing the blood was made up of dead material—glass and India rubber; while, in the later experiment, the tube enclosing the blood was an animal membrane recently removed from its living position, and still by its warmth and occasional contraction giving proof that it was not absolutely dead. Yet the blood enclosed in this organised tube was retained fluid for less than half the period of that in the inorganised tube. And why? Clearly not from any vital endowment, but from the obvious and common sense physical reason that, in the first experiment, the occlusion of the blood was more thoroughly effected.

EXPERIMENT CXLIV. *Occlusion of Blood in the Jugular Vein.* Three inches of the external jugular vein of a dog were laid bare. The vein was carefully separated from its surrounding adhesions, for the full length exposed. Four ligatures were now passed round the vein, at intervals of half an inch, and were firmly tied. The vein was thus divided into three distinct segments, each one filled with blood. The operation took thirteen minutes to perform. A little blood (a drachm) was then drawn from a vein in the ear: it coagulated firmly in seventeen seconds. The edges of the wound in the neck were at this time brought temporarily

together, and the jugular vein was left alone for fifteen minutes. At the end of this period the vein was exposed, and the middle segment was punctured with a lancet; the blood it contained flowed out freely in the fluid state, and was caught in a watch-glass; it coagulated firmly in one minute after being thus drawn and exposed to the air. The wound was now again temporarily closed for fifteen minutes more; it was then reopened, and the blood in the upper segment was drawn: this blood was quite fluid, like the last, and coagulated in the watch-glass in one minute as before. For the third time the wound was closed for fifteen minutes, and then reopened; the remaining segment of vein was observed to be remarkably distended; on being punctured, a portion of semi-coagulated blood was turned out, followed by a little dark fluid blood. The wound in the neck was neatly closed with sutures, and the animal did well.

EXPERIMENT CXLV. *Occlusion of Blood in the Veins.* An animal (a dog) was dosed at night with a drachm of solid opium. He became partly comatose in a few hours, and in the morning was found conscious, but unable to move, cold, and very little alive to pain. A little blood drawn from the ear coagulated in six minutes. He had had given to him full doses of opium for several previous days. After the blood was drawn from the ear, he was slowly killed by being made to breathe a diluted dose of prussic acid vapour. The object in producing gradual death by narcotism, was to render the blood slowly coagulable, so that its period of coagulation in different parts might be observed systematically and deliberately in an animal newly dead. The instant the animal had ceased to breathe, the external

jugular vein was laid bare, tied in two sections, and recovered with the skin and soft parts. Next, the abdomen was laid quickly open, the intestines were turned aside, and the vena cava inferior was tied in two places, so as to leave an inch of space, between the ligatures, full of blood. The intestines were immediately afterwards replaced in exact position, and the wound in the abdominal walls was stitched up. The animal was now let alone for one hour; at the end of this time the jugular vein was examined, and the lower segment was punctured; the blood in it flowed out in the fluid state, and coagulated in seven minutes after removal. At the end of fifteen minutes, the blood in the upper segment was drawn: it, too, was fluid, but coagulated in seven minutes on exposure. The chest was then opened. The heart on the right side was distended with blood, and, when the cavity was laid open, this blood was found principally fluid; but in one or two points (in the auricula, for instance, and in the pulmonary artery) there were small loose coagula. Received in an evaporating dish and exposed to the air, this blood all coagulated in one firm clot in ten minutes. The blood in the left cavities of the heart was small in amount, and had fully coagulated.

After a lapse of time, amounting to two hours and a quarter, from the death of the animal, the inferior vena was now again exposed. By this time the blood in all the exposed and opened veins was coagulated; but on puncturing the segment of the cava which had been included in the ligatures, the blood it contained flowed out in a free fluid stream, and coagulated in ten minutes on exposure to the air.

EXPERIMENT CXLVI. *Occlusion of Blood in Veins.*

The external jugular vein of a living dog was laid bare, and the vein was tied in three sections. The blood in the lower section, fifteen minutes after the operation, was found perfectly fluid; but coagulated in four minutes on exposure to air. The blood in the upper section was found fluid, in the same manner, after a lapse of another fifteen minutes. On watching the remaining segment for five minutes, it was seen to become more than ordinarily distended; and, on puncture, it yielded a feeble coagulum. It is right to observe that, in this experiment, as in Experiment CXLIV, the animal made a speedy and good recovery.

EXPERIMENT CXLVII. *Blood effused into the Soft Parts.* By a subcutaneous section with a long fine bladed knife, I divided the femoral artery of a large strong dog; rapidly withdrawing the knife, I closed the external wound with a cross stitch, so that the blood effused could not escape. The result was a free infiltration of blood into the soft structures of the thigh. The effusion soon produced a soft doughy tumour. The animal was left for an hour; at the end of this time the tumour was more enlarged, was remarkably tense, and had some of the characters of a dissecting aneurism. No blood had escaped from the point where the knife had entered. The tumour, on being punctured with a lancet, gave out a free gush of perfectly fluid blood, which coagulated very rapidly on exposure; so rapidly, indeed, that there was barely sufficient time to catch it in a cup. The wound from which this blood was drawn was closed firmly with a cross stitch; and the tumour was, at various intervals in the course of two succeeding hours, punctured as before, but in different parts: the result invariably was the emission of blood, perfectly fluid, but which coagu-

lated quickly on exposure to the air. This animal, six hours later, was killed, and the thigh was examined. The blood effused had escaped freely into the inter-muscular spaces, and was found coagulated with moderate firmness.

[EXPERIMENT CXLVIII. *Occlusion of Blood in the Veins and Heart.* I narcotised a dog with the smoke of the *Lycoperdon giganteum*, until he ceased to breathe. I then laid bare the external jugular vein, placed on it two firm ligatures, and punctured it above the ligature. A half ounce of fluid blood was drawn off, which coagulated firmly in two minutes and a half. Fifteen minutes after this blood had set, I laid open the chest of the animal, and found the blood in the veins below the ligature, and the blood on the right side of the heart, entirely fluid: drawn off and exposed to the air, this blood coagulated firmly in two minutes and a half.

The experiments last narrated may all be strikingly confirmed, without the physiologist's hand or knife, by any one who will visit the slaughter-house, and make observations on the killing and dressing of animals. A large slaughter-house is a kind of physiological and pathological school, in which an attentive observer may learn a host of invaluable facts, and this, too, with the satisfaction of feeling that the animal is sacrificed to other than mere physiological necessities. In all experiments on the blood, the slaughter-house arena is an absolute necessity, since such experiments must be seen on the large scale, and must be repeated over and over again before any safe deduction can be made. I shall state one or two facts connected with the present part of my

theme, which may be accepted in the light of experiments observed and confirmed so many times as to be absolute as experimental data.

When a sheep is killed, from one and a half to three pints of blood escape from the wound before death takes place, sometimes more. The death is rapid ; the heart and respiration cease together, and a strong convulsive struggle finishes the scene. The blood drawn from the neck coagulates with great rapidity : to my recollection I have never seen it retain its fluidity for longer than four minutes, when the animal was in health. The period of coagulation is, in most cases, complete in one minute and twenty or thirty seconds. The blood is derived from the carotid arteries and the jugular veins. When the animal is quite dead, it is kept in the horizontal position until it is in part dressed. To complete the removal of the skin, the creature is raised by its hinder legs ; and a little blood flows afresh from the wound as the new position of the body is made ; but this flow soon stops. Next, the skin is altogether removed. About fifteen minutes usually elapses in these steps of the operation. Meantime, from the change of position from the horizontal to the perpendicular, the right side of the heart and the inferior cava become charged with blood from the veins below the heart ; this blood the butcher proceeds to remove. He makes a straight incision down the neck, and then plunges his knife into or near to the base of the heart : a gush of blood follows, amounting often to six or eight ounces. Caught in a basin, it is found entirely fluid ; subjected to experiment, it coagulates in the same way, and follows the same laws as the blood first drawn.

When several sheep have had to be killed on the

same occasion, I have often induced the butchers to do the killing part of their craft first, and have asked them to wait a few minutes in the steps of the dressing operation, in order to allow as much time to elapse as possible. Thus I have seen a full half hour intervene between the times of the abstraction of the first and second portions of blood; but, without exception, the second batch of blood has always come into my beaker or basin in the uncoagulated state, and has coagulated afterwards, like the first blood, on being exposed to the air.

Another fact is equally interesting. When an ox is slaughtered, the throat is cut as quickly as possible after the infliction of the blow from the poleaxe and the pithing process by the cane; for if the animal were to die outright from shock, the heart would not pour out its blood freely. The cut in the throat is carried deeply down to the great vessels, and a tremendous gush and flow of blood follows: the flow continues for four or five minutes, and the blood as it escapes coagulates in from three to four minutes after it has kissed the air. But the butcher knows practically that the spontaneous cessation of the hæmorrhage does not indicate that the body of his victim is emptied of its blood. To complete the emptying process, therefore, he and his assistant place their broad feet on the abdomen of the animal, and pump away with the utmost unconcern in life. Whence the new supply of blood comes, they have no idea, superficial or profound; but certain it is that new blood comes, and though the animal shall have been dead half an hour, the blood comes fluid, and does not coagulate till it gets plenty of air-space for coagulation.

The skin being in part removed, the animal is raised by the hinder legs till it hangs perpendicularly, with its head downwards; and it is then skinned, embowelled, and eviscerated completely. It is divided down the back with saw and cleaver, and one would say, that of uncoagulated blood there could be not a drop remaining,—a most unpractical and false inference. For when the body is hauled up, the large veins, coursing from the fore limbs to the shoulder, pointed towards the heart, still contain blood: and when the suspension is complete, the fore legs fall forcibly downwards towards the head from the shoulder-joint. In this act the vein is compressed above, and its contained blood is locked up. If the blood were left there, it would leave discoloration and clot about the soft parts of the joints: to remove it, therefore, the butcher seizes the fore limb, and, jerking it sharply upwards, makes a portion of confined blood, amounting often to several drachms, spirt out. Sometimes it comes out partly coagulated; but I have many times, a full hour after the death of the animal, caught it in my beaker, perfectly fluid, and have watched it coagulate on exposure to the air, as though it had been that moment drawn from the vessel of a living animal.

While experimenting on the effects of tying up blood in the veins, I took several opportunities of specially observing, through the semi-transparent vessel, certain changes which the fluid undergoes in that condition. The results, though of simple meaning, deserve mention. Two experiments will suffice for illustration.

EXPERIMENT CXLIX. *Blood enclosed in a portion of Vein.* I laid bare the external jugular vein of a cat, and placed on it two ligatures an inch and a half apart.

I took care not to distend with blood the portion of occluded vein. I watched the vein now for half an hour without observing any change; but, when a few minutes more had elapsed, it became obvious that in the occluded part of the vessel there was a degree of transparency in the uppermost position. This process of change continued, until at length the dark and the transparent parts were nearly equal in length. On changing the position of the animal, the dark and the transparent parts of the vein changed position also. It was clear, in fact, that the blood had yielded up some gaseous matter, and that the portion of enclosed tube was filled partly with gas and partly with blood. On puncturing the vein into a watch-glass, a portion of semi-coagulated blood escaped, on the surface of which there remained some small bubbles of gas.

EXPERIMENT CL. *Blood enclosed in portions of Vein.* I laid bare the external jugular vein of a dog, and tied it as before, but in two segments instead of one. In this case the change in the occluded vein, *i. e.* the spontaneous division into gaseous matter and blood, commenced in twenty minutes. It commenced simultaneously in the two segments, and was as well marked as in the cat experiment. After the extrication of gas seemed to have ceased altogether, I punctured the vein, and let out of each section a small soft clot of blood and a little coloured serum.

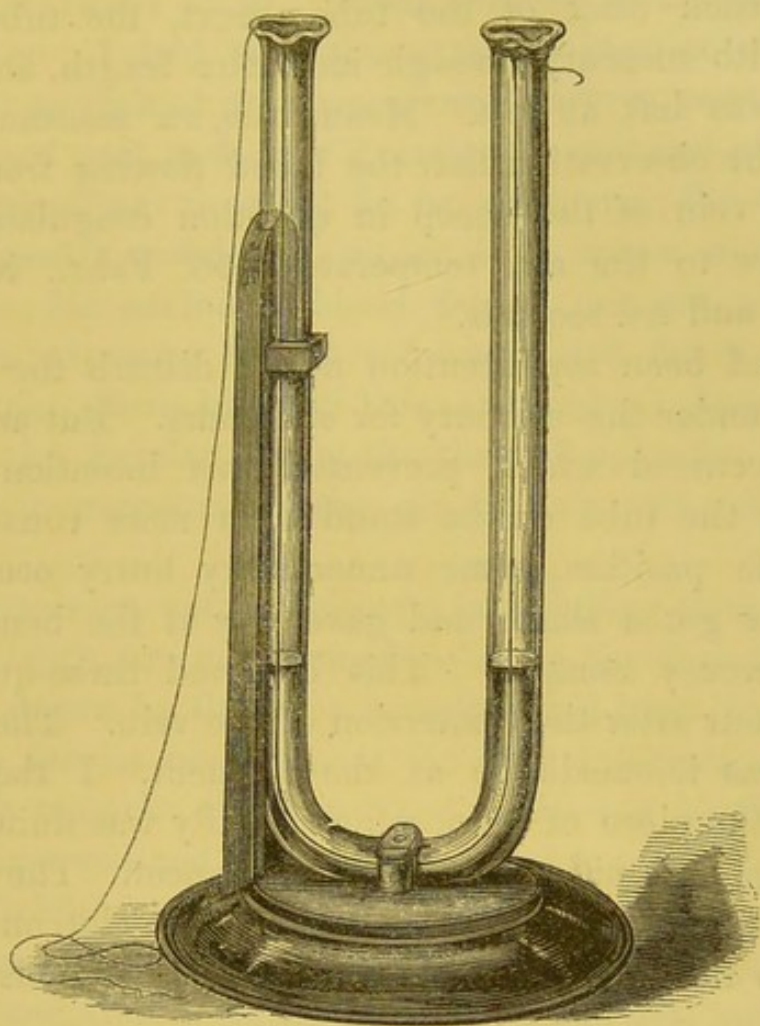
The above experiments and observations show, then, that when blood is arrested in its motion, and excluded from the air by being tied up in a segment of its vessels, its coagulation is arrested. I have referred here to the occlusion of blood in veins only, but the fact is even better developed when the arteries are subjected to the

same experiment, since the arteries are of firmer structure. Greater care, however, is required in the experiment; for, practically, it is a more difficult task than might be supposed, *à priori*, to enclose a column of blood in a portion of pulsating artery. Both ligatures must be tied at the same moment, and very firmly, and even then sometimes the occluded part of the vessel is afterwards found empty. But when blood is really entrapped in a piece of artery, the result is admirably effective: not hours in this case, but days will pass, during which the blood remains fluid, for the vessel contracts on the column of blood, and compression is added to occlusion.

It is clear, then, that complete occlusion from air has, under the circumstances named, the opposite effect on coagulation to that of exposing blood to air. But the objection may be urged, that in the experiments above narrated, the blood was enclosed and retained in the bodies of the animals. To remove this objection, I pursued the following course:

I made out of a piece of barometer tubing an instrument, as shown in the opposite drawing.

It consisted of a tube thirty-two inches long, and half an inch in the bore. At its middle the tube was bent in an easy curve, so as to have two equal upright limbs; thus formed, it was fixed on a stand, such as supports a Marsh's bulb apparatus. Prior to using the tube, a piece of ligature cord was passed through it. One end of the cord was affixed to the neck of one of the upright limbs; the other end was left long and free; next, the lower part of the tube was filled with mercury, as shown in the sketch. The further details are given in the succeeding experiments:



EXPERIMENT CLI. *Blood enclosed in a Vein under Mercury.* I laid bare the jugular vein of a sheep, and tied it firmly at two points: the lower ligature was left long; the upper ligature was taken from the long end of the string running through the tube. After the ligatures were attached firmly, the portion of vein included within the ligatures was removed altogether from the animal. By drawing out the string attached to the neck of the glass tube, the piece of vein was easily drawn under the mercury, and was there left lying in the bend of the tube. Here it was secured safely by a few turns of the loose ends of the string

round each neck of the tube: next, the tube was filled with mercury through its entire length, and the whole was left at rest. Meanwhile, an assistant had taken the observation that the blood flowing from the divided vein of the sheep in question coagulated on exposure to the air, temperature 66° Fahr., in one minute and ten seconds.

It had been my intention not to disturb the blood buried under the mercury for six hours. But an accident occurred which prevented this intention. In moving the tube on its stand to a more convenient and safe position, some unnecessary hurry occurred, the tube got a shake and gave way at the bend, and the mercury escaped. This occurred three-quarters of an hour after the immersion of the vein. The accident was irremediable at the moment. I therefore placed the piece of vein, which luckily was uninjured, in a cup, and punctured it with a lancet. The blood flowed out quite fluid, but set into a firm clot, on exposure to the air, one minute and twenty seconds afterwards.

EXPERIMENT CLII. *Blood enclosed in a Vein under Mercury.* I laid bare the external jugular vein of a dog, ligatured it as in last experiment, and drew it under mercury in an instrument precisely similar to the one already described. The vein thus placed was left at rest for nine hours: it was then gently removed, placed in a cup, and punctured with a lancet. Its contained blood flowed out in a perfectly fluid condition, but coagulated in four minutes on exposure to the air. A little blood, caught from the vein of this animal directly after the operation to which he had been subjected, coagulated firmly in three minutes on exposure to the air.

EXPERIMENT CLIII. *Blood enclosed in a Vein under Mercury.* I laid bare the external jugular of a cat, placed an inch of it between two ligatures, removed the ligatured part, and drew it under the mercury as before. This blood was thus left for twenty hours: the vein was then gently withdrawn, placed in a spoon, and punctured. Its contained blood flowed out entirely fluid, and on exposure to the air coagulated firmly in four minutes. Some blood of this same animal, derived also from the jugular vein at the time of operation, coagulated, on exposure to the air, in two minutes and a half.

Writers on natural history, in referring to the medicinal leech, are accustomed to state the fact, that the blood drawn by the leech remains fluid in its body, and serves for its nourishment for long intervals of time. Cuvier remarks, that the blood swallowed by the leech continues red and without alteration for several weeks; and Griffiths (*Animal Kingdom*, part 35, p. 129), says that in the leech the process of digestion is extremely slow, and that a single meal of blood will suffice for many months, during all which period "so much of the blood as remains undigested in the stomach continues in the fluid state and as if just taken in, notwithstanding the vast difference in the heat of the body of a mammiferous animal and that of a leech."

It is clear that in writing this passage, Mr. Griffiths laboured under the erroneous idea that this fluidity of blood is due to the presence of heat. The fact, however, about the leech is of interest, and the study of it has some points bearing on coagulation. If a leech is allowed to engorge itself, and is then removed and emptied of its blood by firm pressure with the finger

and thumb, the blood thus extracted will be found quite fluid, and its power of coagulation exceedingly feeble, and in some cases *nil*. I have seen slight coagulation in the blood thus obtained from leeches, but I have also seen the blood so obtained perfectly uncoagulable. I have observed also that leech-bites continue to bleed for a much longer period than do wounds from a lancet point made in the same individual at the same time; while the first blood which flows from the bite after the removal of the leech continues uncoagulable for a very long time, and is even in some cases also uncoagulable. This fact accounts for the difficulty which not unfrequently occurs in the stopping of the bleeding from leech-bites. It is not until the blood has flowed away for some minutes, that a coagulable current is supplied.

The cause of this simple but striking phenomenon is not very easily explained. The first inference on my mind was, that in the body of the leech the blood meets with some solvent secretion which holds it permanently fluid, or else that in the mechanical act of abstracting the blood some change occurs, some kind of defibrination. To follow these questions, I made a few simple experiments on leech-drawn blood.

EXPERIMENT CLIV. *Observation on Leech-drawn Blood.* I laid a leech on the arm of a gentleman who was in perfect health. The leech filled itself with blood, and fell off of its own accord. As soon as it removed itself, I emptied it of its contained blood by traction. The blood was dark and entirely fluid. This blood remained fluid on exposure to the air (temperature 65°) in a shallow cup, for nine hours; after this it became a little thicker and more glutinous, but it never underwent the proper process of coagulation.

EXPERIMENT CLV. *Observation on Leech-drawn Blood.* I laid another leech on the arm of the same gentleman, and allowed it to draw blood until it fell off of its own free will. As soon as this occurred, I removed its contained blood by laying its body freely open with a lancet. The blood was received into a spoon, into which it flowed freely. This blood was set aside, exposed to the air at a temperature of 65° Fahr., and closely observed. It remained fluid for nearly two hours, then became slightly glutinous, and at the end of four hours presented a few feebly formed clots. Eventually it formed a loose coagulum, resembling thin black currant jelly.

After the leech was removed from the arm, the wound it had produced continued to give out blood very freely. I caught the blood thus flowing at different intervals, allowing it to trickle into teaspoons of the same size and shape. The results were curious. The blood which was received into the first spoon, and which was collected immediately after the removal of the leech, was dark, and showed the same feebleness of coagulation as the blood taken from the leech itself. Another portion of blood received into a second spoon five minutes later, coagulated in twenty-five minutes with moderate firmness. A third portion of blood, caught ten minutes later still, coagulated in eight minutes; while at the end of half an hour the blood which still flowed from the wound coagulated firmly, and in fine red clots, in two minutes. Ultimately the blood coagulated as it slowly oozed from the wound, and so the wound itself was sealed up.

I laid two leeches on the arm of the same gentleman. They took hold nearly at the same moment, and filled to engorgement.

EXPERIMENT CLVI. *Observation on Leech-drawn Blood.*

I received one of the leeches as it fell off into a glass plate, and at once placed round it, a few lines from its mouth, a firm ligature. It was thus prevented from ejecting its contained blood; in this condition it was placed securely in an empty beaker, and left exposed to the air, the mean temperature of which, during the experiment, was 62° Fahr. For two days the leech, by its occasional movement, showed signs of life, and it was therefore left untouched. On the morning of the third day it was found quite dead, and its body stiffened and dry. I laid open the body with a scalpel, and found the contained blood universally coagulated. The clots were dark, but uniform and firm.

EXPERIMENT CLVII. *Observation on Leech-drawn Blood.*

The second of the leeches referred to above, after its removal from the arm, was ligatured as in the preceding case, so as to prevent the ejection of its contained blood. A second ligature was also carried round its body at its tail extremity. Thus fixed, the body of the leech was drawn under mercury in the heat tube instrument, delineated and described at pages 202-3, and was thus left for the space of nine clear days, during which the temperature of the room was never lower than 60° Fahr. All movement ceased almost instantly after the immersion in the mercury. On the morning of the tenth day the leech was withdrawn from the mercury, and its body was laid open. The body was filled with blood, which was entirely fluid. There was no trace or indication of coagulum. This blood, received into a small evaporating dish, and exposed to the air at a temperature of 65°, underwent slow coagulation, and at the end of six hours was in the form of broken

clot. Its coagulatory force after this was not further developed.

Blood under Oil. An experiment of receiving blood under oil was performed some years since by Dr. Babington. He immersed the head of a cock under oil, and in this position cut off the head and allowed the blood to sink to the bottom of the vessel. In these experiments Dr. Babington observed, as he informs me, a retardation in the process of coagulation, and in some instances the formation of a slight buffy coat.

Modifying Dr. Babington's process in some particulars, I went through a series of like experiments, the results of which were so uniform that one might be taken as the type of all. I shall give, however, examples to illustrate the modifications in the method of experiment.

EXPERIMENT CLVIII. *Coagulation under Oil.* I filled a tube eighteen inches long and one inch and a half in diameter, with sperm oil. A narrower but longer tube, with a funnel top, was carried to the bottom of the oil. One ounce of blood, that moment drawn from the neck of a sheep, was at once deposited beneath the column of oil through the smaller tube, which was then slowly withdrawn. An evolution of gaseous matter took place from the blood. After three minutes had passed, I found, by gently agitating the fluids, that the blood was liquid. Three minutes later still, from the solidity of the under stratum of blood, it was clear that coagulation had occurred. The oil and blood, in the same positions, were set aside for twelve hours in a warm room. At the end of this time, on observing the two fluids, a pale film or crust was seen to lie between them. I inferred that this was a buffy coat, but on decanting the oil carefully, it turned out that the pale

layer pertained to the oil only. The blood beneath was a dark, soft, but tolerably uniform coagulum.

The blood of the animal used in this experiment coagulated in a firm red clot in one minute and a half.

EXPERIMENT CLIX. *Coagulation under Oil.* I laid bare the external jugular vein of a healthy dog. An assistant seized with forceps the vein at the upper part of the wound. Meanwhile I made an opening into the vein, and inserted in it a small metal tube, tying the tube firmly in its place. Continuous with the metal tube was a small elastic tube, six inches in length. When all was complete, the free end of the elastic tube was immersed under oil, which was confined in a glass test-tube eighteen inches long and half an inch in diameter. The forceps were next removed from the vein, and a current of blood at once gushed into the oil. The elastic tube was then withdrawn; about half an ounce of blood having been thus caught under the oil. The blood sank very gradually to the bottom, giving off bubbles of gas, which rose freely in the oil. By gentle motion of the tube I was able to note that the blood under the oil had coagulated in from two and a half to three minutes. The oil and blood were set aside in the tube for twenty-four hours. Observed then, the same appearances were presented as in the previous experiment. There was a thin pale film between the blood and oil. When the oil was decanted off, the blood beneath was found free of buffy coat, dark and coagulated, but the clot was broken and very soft. A little blood of this animal, caught in a cup by my assistants, coagulated on exposure to the air, in a firm, red clot, within a few seconds of two minutes. The vein was left untied, and the animal recovered without a bad symptom.

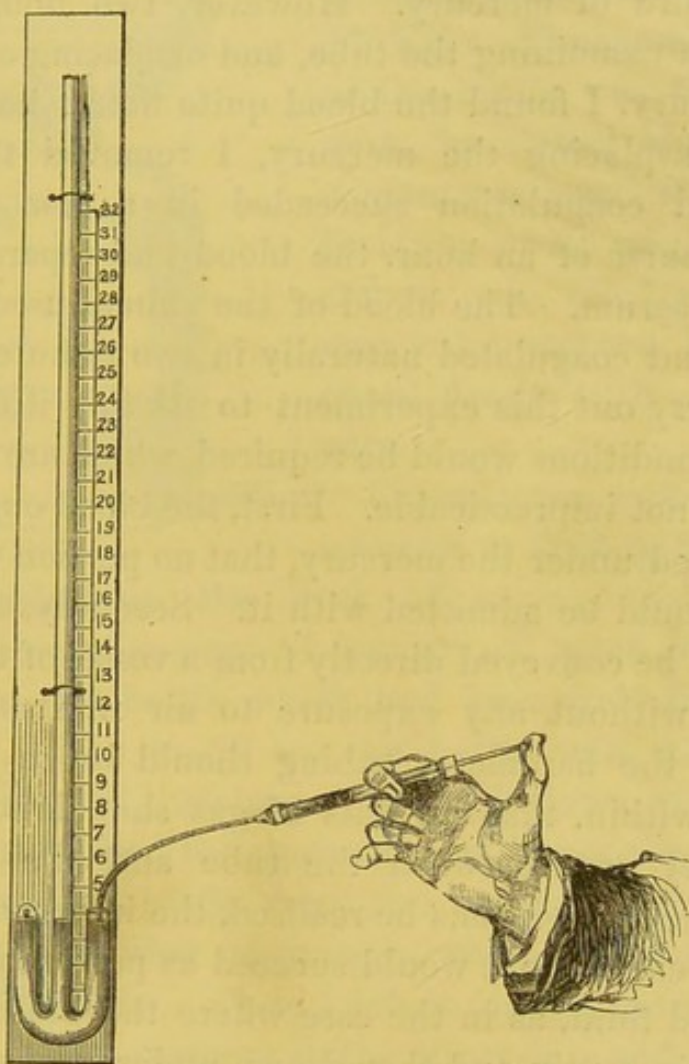
EXPERIMENT CLX. *Coagulation under Oil at a Low Temperature.* I took the glass tube delineated at page 203. I filled both limbs to within two inches of the top with oil, and then immersed the lower part of the tube in a mixture of ice and salt, in which the thermometer stood at 17° Fahr. I then poured through the long funnel tube, which had been carried through one column of the oil, one ounce of freshly drawn blood from the jugular vein of an ox. Four minutes afterwards, the blood under the oil was still fluid; but a few bubbles of gas rose on each surface of blood, and formed a froth. A few large bubbles also ascended very slowly through the oil. I now removed the tube from the cold mixture, and immersed it in water at 100° Fahr. There was at once a more liberal extrication of gases; and in two minutes the blood was an uniform coagulated column. On pouring off the oil, the blood escaped from the tube modeled to it, in a firm round cord. The blood of the animal coagulated naturally, on exposure to the air, temperature 63° , in two minutes and a half.

Experiments with Cold and Pressure. In the year 1851, I conducted several inquiries as to the effect of pressure on newly drawn blood. In those experiments, I employed the screw-piston syringe, invented by my friend Dr. James Arnott. To the lower part of this syringe I fixed a strong glass tube, closed at its further end. I then filled the syringe with blood from above, the piston being removed. When the barrel was nearly full of blood, the piston was replaced; and, by a few gentle turns of the screw, pressure was applied. The experiment was unsatisfactory: much time was lost in adapting the screw, and coagulation sometimes occurred before the experiment could be considered fully

commenced. On one occasion, my glass tube broke ; and the difficulties were so many, that I gave up the inquiry for the time. In the beginning of 1856, Mr. Wentworth Scott (whose kind assistance I have already acknowledged) suggested to me the propriety of placing blood under pressure, and devised for me a mercurial tube of a very ingenious kind. I tried Mr. Scott's plan with partial success, using first his tube, and then modifying it in various ways. The principle suggested was that of having a long barometer tube, bending slightly upwards at its lower part, and having the small arm removable, so that it could be filled with blood under mercury, and adapted to the long arm ; the long arm itself being afterwards filled to the extent of thirty-two inches with mercury. My ultimate modification of this apparatus is illustrated in the opposite sketch.

It consisted, as will be seen, of a central graduated long tube, connected by a curve with a shorter tube on each side at its lower part ; the tubes being all continuous. The short tube on the left was closed ; the long central tube open ; and the right-hand one open. A piece of elastic catheter was attached to a syringe by one end, and the other end was carried to the upper part of the left-hand small arm, as delineated. When these arrangements were finished, the two short tubes, and the long tube to the height of the short ones, were filled with mercury. Blood freshly drawn was then poured into the syringe from above, the piston being removed : next, the piston being replaced, the charge of blood was driven into the upper part of the left-hand closed tube, the displaced mercury flowing over from the open right-hand tube into a basin placed beneath. The blood being introduced, the elastic tube was with-

drawn, a firm screw stopper was placed on the right-hand tube, and the long tube was filled up with mercury to thirty-two inches.



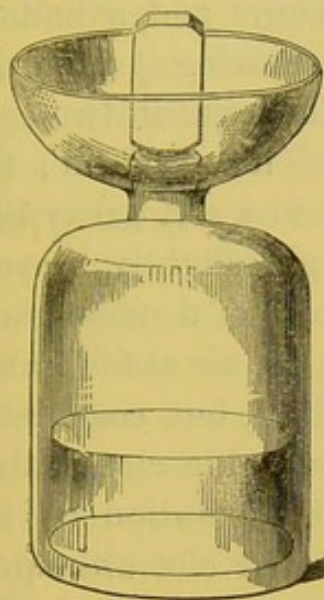
EXPERIMENT CLXI. *Blood under Mercurial Pressure.* I subjected some freshly drawn lamb's blood to the operation described above, and set it aside at a temperature of 60° Fahr. I found the experiment very difficult and complicated. With the elastic tube passing through the mercury, I could not prevent the admission of some air; while the column of air in the tube forced its way before the blood. When, therefore, the blood was

introduced, the stopper put on, and the long column filled with mercury, there were in the left-hand tube three strata; one of air, superiorly; another of blood; and a third of mercury. However, two hours afterwards, on examining the tube, and displacing a little of the mercury, I found the blood quite fluid: but, in the act of displacing the mercury, I removed the pressure, and coagulation succeeded in a few minutes. In the course of an hour, the blood had separated into clot and serum. The blood of the animal used in this experiment coagulated naturally in two minutes.

To carry out this experiment to its full illustration, several conditions would be required, which are very difficult, if not impracticable. First, the blood ought to be so received under the mercury, that no portion whatever of air should be admitted with it. Secondly, the blood ought to be conveyed directly from a vessel of the living animal, without any exposure to air in its progress. Thirdly, the barometer tubing should be so perfectly smooth within, that currents of gas should not by any possibility pass between the tube and the mercury. Could these conditions be realised, the inference is clear that the experiment would succeed as perfectly in keeping blood fluid, as in the case where the blood was entrapped in a vein and then drawn under mercurial pressure. The last experiment, in which blood was kept fluid two hours, affords a complete illustration of the truth of this inference.

A simpler mode of illustrating the effects above described afterwards suggested itself. Taking advantage of the fact that cold retards coagulation, I received blood from the throat of an ox into ice, then transferred it into a bottle sold in the shops under the name

of Turnbull's eye-glass, and depicted below. The bottle was first half filled with mercury, and immersed partly



in a mixture of ice and salt, in which a thermometer stood at 17° Fahr. The remaining part of the bottle was then filled with the chilled blood. The stopper was inserted; and the little cup which surrounds the stopper was filled with mercury, the stopper being secured firmly with a twist of wire.

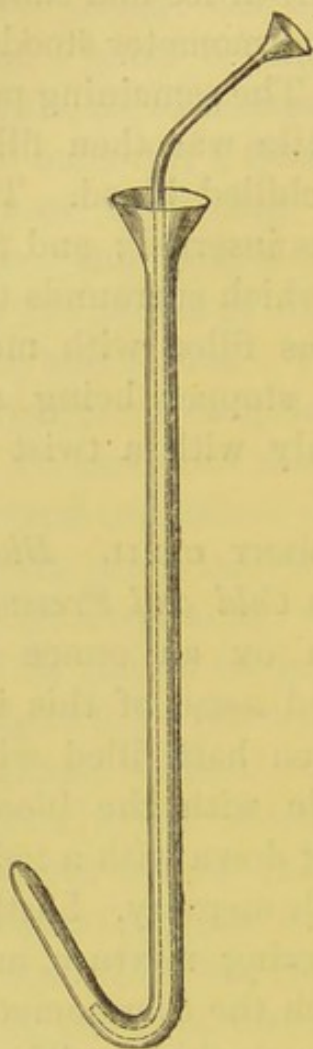
EXPERIMENT CLXII. *Blood subjected to Cold and Pressure.*

I received from the neck of an ox an ounce of blood into an ice-cup. I transferred some of this instantly to the bottle which had been half filled with mercury, so as to fill up the bottle with the blood. Next I inserted the stopper, bound it down with a twist of wire, and filled the upper cup with mercury. Lastly, I removed the bottle from the freezing mixture, and placed it in another mixture, in which the thermometer stood at 32° Fahr. Here I left it for one hour. Then, pouring off the mercury in the upper cup, and removing the stopper, I poured out the contents of the bottle into a wine-glass. The blood lay on the upper surface of the mercury in the glass completely fluid. The temperature of the air was 60° Fahr. Exposed to this, the blood coagulated, in a dark but firm clot, in four minutes and a half. The blood of the animal used in this experiment coagulated naturally in three minutes.

EXPERIMENT CLXIII. *Blood subjected to Cold and Pres-*

52^u

sure. I subjected the blood of another ox to the same experiment, taking exactly the same precaution, but allowing five hours and a half to elapse before removing it from the bottle. The blood was in two conditions; part of it was fluid; the other part was in a soft gritty-like state, as though slightly frozen. When poured into a wine-glass, and exposed to the air at 60° Fahr., it all became fluid, but coagulated afterwards in a feeble clot, with a slight fibrinous separation on the upper surface. The clot ultimately remained loose and feeble. The blood of the animal coagulated naturally, on exposure to the air at a temperature of 65° Fahr., in two minutes and a half.



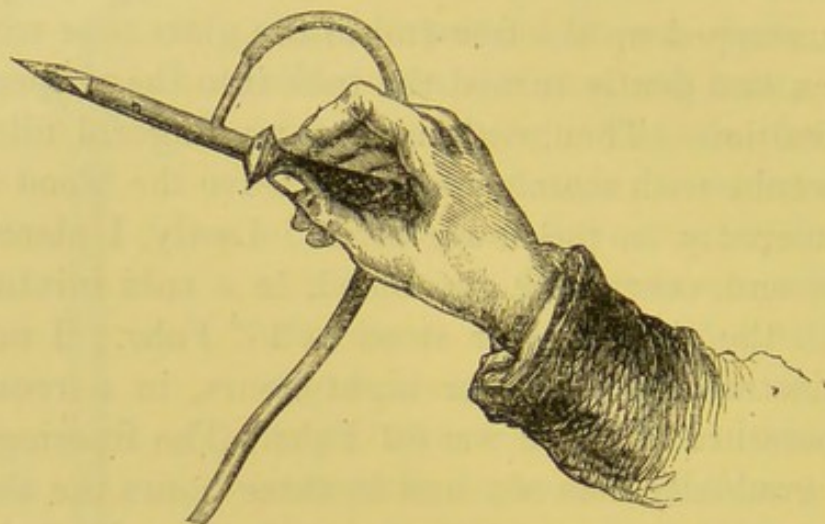
While this sheet was in press, I constructed a simple tubular instrument, as follows. I took a piece of barometer tubing, of half-inch bore, closed it at one end, and then bent it into the form represented in the drawing. The lower and closed part was bent upwards at an angle of 45° ; the upper part terminated in a wide funnel mouth. Through the tube a long gutta percha tube, one-eighth of an inch in diameter, was carried down to the beginning of the upward bend. The gutta percha tube ended superiorly in a small funnel.

EXPERIMENT CLXIV. *Blood subjected to Cold and Pressure.* I received from the neck of an ox a few

drachms of blood into ice, as before. First, holding the glass tube horizontally, and bending the gutta percha tube upwards, I poured in blood through the funnel of the gutta percha tube until the closed bent and depending end was filled. I next withdrew the gutta percha tube, stopped up the free end of the glass tube with my finger, and gently turned the tube into the perpendicular position. Then, withdrawing my finger, I filled the glass tube with mercury, so as to leave the blood above the mercury in the lower bend. Lastly, I placed the lower end, containing the blood, in a cold mixture, in which the thermometer stood at 17° Fahr. I now set the instrument aside for eight hours, in a room the temperature of which was 60° Fahr. The freezing mixture gradually thawed; and in three hours the thermometer stood in it at 55° , and remained at this point till the end of the experiment. At the end of the eight hours the mercury was poured off, and the blood flowed out in a dark, rather thick, but fluid current. It was poured into a shallow cup, became of a brighter colour, and coagulated, in the course of an hour, in several loose clots. The blood of the animal used in this experiment coagulated naturally in two minutes, in the air, at a temperature of 60° .

In the course of this chapter, I have sometimes spoken of drawing blood direct from the veins of animals. For effecting this purpose, I used a trocar, modified slightly, as shewn in the drawing. From the canula, a small tube stood out at a right angle; and to it was attached a piece of elastic tubing. The trocar and canula were thrust into the vein in opposition to the blood-current, and pushed home to the projecting tube. The trocar

was then withdrawn, and the canula left in the vein, its lower end being closed by a small plug. The blood-current was thus made to flow through the elastic tube, and could be directed as I chose to guide it. This trocar



might be of use in paracentesis, as the stream could be guided away from the patient into any convenient vessel.*]

V. INFLUENCE OF MOTION ON FRESHLY DRAWN BLOOD.

We have already seen that Spallanzani and some other writers, arguing mainly from pathological data, were inclined to the opinion that motion only was necessary to keep the blood in a fluid state. We have seen, on the other hand, that Hewson and many other authorities as vigorously opposed this view, and adduced very sound arguments why it should not be considered as

* The trocar was made for me by Mr. Weedon, surgical instrument maker, Hart Street, Bloomsbury, whose courteous attention in carrying out different designs I have great pleasure in acknowledging.

correct. The simple explanation of these differences lies, as is often the case, in the fact that the extremes of both lines of argument are wrong, while there is a nucleus of truth in each.

In speaking of the effects of confining blood in segments of veins, in the cellular tissue, in glass tubes, in the piece of intestinal tube, and under mercury, many of the questions relating to the effects of motion were answered indirectly. In so far as these experiments have gone, they have supported fully the statement of Hewson, that rest alone will not account for coagulation. For it will be remembered that, when portions of vein were included in the ligatures, the blood they contained remained fluid for a long time (in one case, two hours and a quarter), although in a state of absolute rest. The same occurred in blood drawn into the cellular tissue. I also remarked in chapter III, p. 124 (Exp. xxxiv), that placental blood would often remain fluid in the vessels for twenty minutes or more, although not in motion; and that the rapidity of coagulation depends more on the extent to which the placental surface is exposed to the open air, than on any other cause. These remarks, as well as the more forcible considerations which spring from the experiments last described, all bear on the subject of motion, and negative the theory of a statical cause of coagulation. To follow them to the end more certainly, I performed the subjoined experiments.

EXPERIMENT CLXV. *Blood agitated in a Closed Bottle.* A bottle capable of holding two fluid ounces was filled with blood. The stopper of the bottle was placed in securely, and the blood was agitated briskly by shaking the bottle. It did not coagulate for seven minutes and

thirty seconds. Other blood, drawn at the same time from the same subject, and placed in a similar bottle, but left at rest, coagulated firmly in three minutes and forty-five seconds, in the form of the simple red clot. The shaken blood, when it coagulated, did so by a distinct separation of the fibrin, which floated on the top of the fluid portion.

EXPERIMENT CLXVI. *Agitation of Blood exposed to Cold, in an Open Vessel.* Another fluid ounce of blood, placed in an open mouthed vessel, was exposed to a temperature of 10° Fahr. by surrounding the vessel containing it with ice and salt. It was now agitated by shaking, and did not coagulate for six minutes and forty-five seconds. It then separated, without the admixture of the fibrin with the blood-corpuscles; the fibrin, being left free, floated at the top of the fluid.

[EXPERIMENT CLXVII. *Blood agitated in a Closed Bottle.* I performed another experiment of the same nature as Experiment CLXV, but using calf's blood. A two-ounce bottle was filled and securely stoppered, and the blood was steadily kept in an oscillating motion. The blood coagulated in seven minutes, leaving, as in the former case, a pale fibrinous coating at the top of the fluid. Blood drawn from the animal used in this experiment coagulated in two minutes on exposure to the air.

EXPERIMENT CLXVIII. *Agitation of Blood in a Closed Vessel.* I received from the throat of a calf two ounces of blood. One ounce was placed in a bottle capable of holding one and a half fluid ounce. The remainder was poured into a similar bottle, and was left at rest, with the mouth of the bottle open. The first bottle was then stopped, and the blood it contained was kept

in gentle motion up and down. At the end of two minutes, the blood left at rest and exposed to the air was firmly coagulated; that in motion in the closed bottle was still perfectly fluid, and remained so for three minutes longer. At this time the fibrin began to separate, and the form of coagulum which ensued consisted of a fibrinous layer floating in the uncoagulable fluid of serum and corpuscles.]

Whipping out Fibrin from Blood. The fact is as old as the hills, that the mere whipping of blood by the hand or the bunch of twigs is sufficient to separate the fibrin. The experiment, however, is well worthy of observation; for, if watched carefully a great many times, it yields useful facts. In the slaughter-house the men are practically aware of many interesting points relating to this mode of separating fibrin. They know, for example, that if the day is intensely cold, the blood requires more whipping than on warm days; conversely they know that, if the day is very hot, there is little time for securing a good separation, because the blood sets so quickly. They know, too, that the substance they whip out, and which from its stringy appearance they call the "veins", is the cause of the setting. They are aware that blood from an animal exhausted from long and hard driving yields little of the plastic matter. They consider it a readier process to receive the blood into a narrow pail previously to whipping it, than into a wider and more shallow vessel. And lastly, if they are anxious to obtain a full amount of fibrin, they take the precaution to catch the blood immediately from the wound, and to get it flowing in as brisk a stream as possible, so that they may commence to agitate it while it is still perfectly fluid.

The effects of this simple agitation upon blood vary considerably; the variations depending on the way in which the operation is performed. If the hand and wrist, or a piece of stick, be dipped into blood, and be then carried round in a circle with moderate briskness, but quietly, so that no splashing occurs, and the same surface of blood remains at the top, the whole mass, in fact, turning at once,—under such circumstances, the fibrin, undergoing as it is a transition from the soluble to the insoluble form, finds a suitable *point d'appui* on the surface of the foreign body, and, clinging to it, permits the blood-corpuscles to go their own way to the bottom of the serum. In this case, the coagulating process, though much modified in manner, is not much so in regard to time; the fibrin being left on the foreign body in about the same period as it would take to form a solid or semi-solid mass with the blood-corpuscles. But if, in the act of agitation, the blood be so stirred as to expose it largely to the atmosphere, then the coagulating process is much quickened, and only part of the fibrin adheres to the stick, the remainder becoming separated so as to blend with the red corpuscles before they have time to sink, and to form a red clot with them. Hence the men who are accustomed to extract fibrin, make it a point to stir the blood with moderate slowness, to insure a good product of fibrin. It is when buffy blood is stirred rudely, that the effect noticed by Sydenham takes place; that is to say, the buffy coat does not form, the fibrin coagulating so quickly as to entrap the blood-corpuscles prior to their descent.

There is nothing in these physical facts different from what we would expect from *à priori* reasoning. The principle involved in the quickened coagulation of

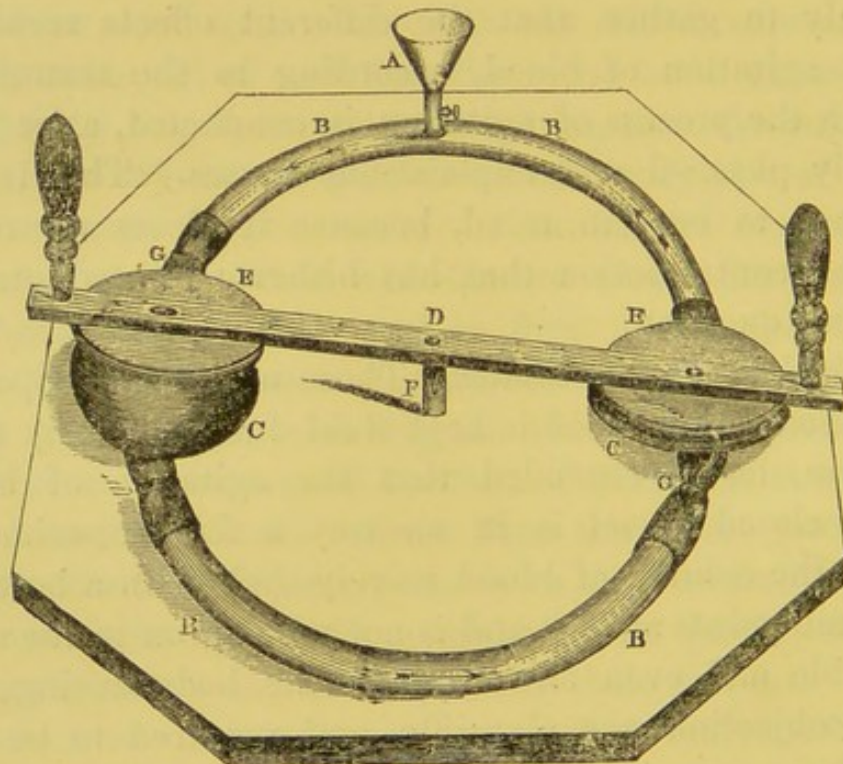
blood during violent agitation *in the open air*, may be conceived as in the abstract the same as that being at work in the vacuum experiment. Under both circumstances, a free surface is exposed, and the result is the same. This point is well illustrated in the experiment already related of blowing common air through blood.

Again, there is nothing remarkable or contradictory in the experiments already related, where the blood, being confined in stoppered vessels, and being agitated, did not coagulate for seven minutes. For, in this case, although the blood was kept constantly in agitation, it was moving in a closed canal, in some degree as in its own vessels. In a bottle firmly closed, indeed, coagulation goes on more slowly under agitation than it would if the blood remained at rest.

From what has been here observed, I wish the reader mainly to gather, that the different effects resulting from agitation of blood, according to the manner in which the process of agitation is conducted, arise from purely physical and explainable causes. This is important to bear in mind, because it clears up much of the contradiction that has hitherto existed on the present question.

Blood in Circular Motion. Those who have supported the theory that blood is kept fluid during life by mere motion, have contended that the agitation of blood in a closed vessel is in no way a fair experiment; since the column of blood merely shaken in a bottle is in some points at rest, and is not moving on in the same equable and even circuit as in the body during life. This objection was plausible, and required to be met by direct experiment. It occurred to me, therefore, to devise an artificial circulation, and, by mechanical

means, to keep a column of blood in steady circular play. I should waste time by describing the many mechanical difficulties which I met with in this simple experiment. The difficulties arose mainly from the impossibility of making valves that should exactly imitate those in the body, and should play as well. In one apparatus, which was worked by a double piston, I used metallic valves, and succeeded in sustaining a water current through it. With blood, however, it would not answer at all; for the fibrin adhered to the valves at once, and blocked up the tubes. At last I thought of the single heart of fishes, and took this in some measure for a pattern, with the difference of inventing a mode by which valves within the tubes might be dispensed with. In the end, the apparatus represented



here was devised, and answered well. It was made

up of two bags (cc) of thin vulcanised India rubber. The bags were each capable of holding an ounce and a half of fluid. From each bag ran out two tubes of the same material. These tubes were three inches in length, and were slipped on to two curved glass tubes (B B B B), so as to complete a circuit with the bags, which were opposite to each other in the semi-circumference on each side. The circuit thus made was fixed on a strong wooden stand. A light beam (D) extended across the table from one bag to the other; each end of the beam being provided with a kind of cushion (E E) adapted to the bag. The beam turned vertically on a pivot (P) in the centre, and was provided with a handle at each end for assisting the movements.

By simple spring valves (G G) placed at opposite positions at the termination of each of the arms of the beam, the passage of the fluid was kept in one direction; and, by the movement of the beam first on to one bag and then on to the other, the onward motion was secured.

[When the apparatus was to be used, blood freshly drawn was poured into the circuit. In my first instrument, which was sent in to Guy's Hospital, and which was hastily made, the blood was introduced by slipping off one of the India rubber tubes from the glass tube, and then rejoining them. In this way Experiment CLXIX was performed. Afterwards, I improved the apparatus by fitting to it at the upper part a funnel (A) with a stop-cock, which stood upwards at a right angle with the tube. When the apparatus was filled, the stop-cock was turned, and the motion of the beam was commenced. By a little care and dexterity, the process of filling was performed in half a minute.]

When freshly drawn blood was introduced so as to fill

the apparatus in the way described above, and was set in motion in the circuit by the action of the levers, it never coagulated so as to stop the current; but this ultimate result was due chiefly to the gradual separation of the fibrin, which deposited on the inner surfaces of the India rubber bags. At the same time, steady circular motion of this kind, in a closed circuit having the least possible tendency at any point to retard the current, shewed a marked effect in delaying coagulation: for I found that the separation of fibrin in the apparatus was not immediate, since blood, drawn in a fluid state from the apparatus after it had been kept in motion ten minutes, and in one instance a quarter of an hour, coagulated on removal. But it has an interesting bearing on some points in pathology, to know that, after a longer lapse of time, the fibrin commenced to be deposited in the interior of the bags, whence it could be washed in fine filamentous threads. After this separation, the blood of course remained permanently fluid. The blood-corpuscles were uninjured.

EXPERIMENT CLXIX. *Blood in Circular Motion.* The apparatus already named was filled with blood immediately after it had been drawn from a free wound in the neck of a heifer. The artificial circulation was at once set up, and was steadily continued without interruption for forty minutes. As the blood was being propelled from one sac to the other, a distinct pulsation could be felt in the elastic tubes. By gently compressing these, the fluid character of the blood could be ascertained. After the motion had been kept up for ten minutes, a little blood (about half a drachm) was allowed to escape, by slightly raising one of the India rubber tubes from over the glass tube. This blood,

flowing out in a fluid state, and of a bright red colour, coagulated in three minutes. Ten minutes later, a little more blood, drawn in the same way, shewed scarcely any tendency to coagulate; and, at the end of the experiment, the whole of the blood, on being received from the apparatus into a vessel, was found defibrinated and permanently fluid. I afterwards washed out, from the bags of the apparatus, the fibrinous filaments, which seemed to have been separated exclusively in the bags, and were perfectly free from any red colouring matter.

[EXPERIMENT CLXX. *Blood in Circular Motion.* The apparatus already named, as modified in the description, was filled with blood freshly drawn from an ox, and was immediately set in motion. After the motion had been continued fifteen minutes, a little blood was withdrawn, and coagulated on exposure to the air at rest. Some more blood, drawn after a continuance of the motion for fifteen minutes longer, shewed no coagulating power, being defibrinated. The fibrin, as in the previous case, was deposited in filamentous layers in the India rubber bags. This experiment was repeated many times with the same result.

The series of experiments narrated in this chapter supply, in brief, the following facts.

1. *Temperature.* The power of coagulation of blood is reduced in proportion as the blood is absolutely brought down in temperature. Such reduction of temperature may be carried to freezing point: the frozen blood remains uncoagulated until the application of heat; but, on the blood being thawed and exposed to a higher temperature, the process of coagulation manifests itself. Conversely, coagulation is quickened in proportion as

the blood is raised in temperature above its natural standard, near to the degree at which the albumen coagulates. If two specimens of blood, taken at the same time from the same animal, be placed in such positions as to insure an absolute difference in temperature, there is an absolute difference in the periods of coagulation.

2. *Addition of Water to Blood.* The addition of distilled water to blood, in the proportion of equal parts of each liquid, does not materially influence the period of coagulation, unless the temperature of the water added be raised to that of the blood; under which circumstance, the coagulation is quickened. The addition of distilled water in excess to blood retards coagulation; and, when carried to an extreme, causes a simple separation of fibrin in a pale flocculent or gelatinous form.

3. *Addition of Dense Fluids to Blood.* The admixture of blood with fluids at or above its own density materially retards coagulation, and in some instances gives rise to the separation of fibrin in an upper layer or coat.

4. *Exposure to or Exclusion from Air.* Free exposure of blood to air quickens coagulation. The vacuum also quickens coagulation. Exclusion from air, whether in a vessel of an animal, or in an inorganic structure, retards coagulation; and when to perfect occlusion pressure is added, the retardation is sustained.

5. *Motion.* Agitation of blood in the open air quickens coagulation. Motion in a closed vessel retards coagulation. Blood received into a closed circuit made up of inorganic materials, and constructed so as to imitate closely in physical respects *the* circulatory system, may be kept in motion in such circuit for a brief period without coagulating; but ultimately the fibrin is deposited on the expanded parts of the circuit.]

CHAPTER V.

EXPERIMENTAL INQUIRY INTO THE CHEMICAL AGENCIES INFLUENCING THE COAGULATION OF THE BLOOD.

"Biassed neither by preconceived opinions, nor attached to particular views, I have desired to look at all things through the laws of induction, and have endeavoured to avoid what is illusory, and to fix my vision on what is real, substantial, and abiding." PROF. EASTON.

A REFERENCE to the first chapter of this essay will recall to the mind of the reader how large a number of experimental inquiries have been made, to discover whether the coagulation of the blood is due to chemical causes.

Of these experiments, but few offer any direct or satisfactory solution of the question; while many have not the slightest bearing upon it. In conducting experiments, there has been too much proneness to consider the blood as if it were a fluid either disconnected from the body, or charged in the body with a variety of chemical substances, which chemical science has in no way shewn to be connected with it. Two classes of inquiries have thus been instituted; one, whether drawn blood can be retained in a fluid state by chemical agents; the other, whether coagulation can be expedited by chemical agents. In this way, blood has been subjected to the action of the mineral acids, of nitrate of potash, nitrate of soda, nitrate of ammonia, nitrate of lime,

nitrate of baryta, bichloride of mercury, chloride of strontium, and a host of other substances which it is not necessary to repeat. In the application of these chemicals, they have sometimes been injected into the circulatory system by the veins, and at other times added to drawn blood. But the results obtained have necessarily been unsatisfactory, and have failed to solve the question of coagulation. It may be true that a strong solution of nitrate of soda prevents coagulation. But to what does this lead? Nitrate of soda should first be proved to exist in the living blood. If it does not exist there, how can it keep the blood in a fluid state? Conversely, does the fact that coagulation follows the injection of bichloride of mercury into the veins, aid us in determining the cause of this phenomenon, as it occurs spontaneously? The question requires no answer.

In the forthcoming researches, I have studied to avoid the empirical line of inquiry, under the conviction that a few decisive experiments, conducted on a systematic and natural basis, would be most effectual in throwing light on the chemical theory of coagulation. In laying out my plans, therefore, I assumed, as a rational basis, the institution of such experiments mainly as might be suggested by a consideration of the component parts of the blood itself, or of the body.

The inquiry, thus arranged, admits of division into two questions.

1. Does the blood naturally contain any agents which have the power of holding the fibrin in a state of solution?

2. If there is an agent in blood possessing this power, why does it lose its influence when blood is drawn and

subjected to those physical influences which we have already proved from experiment to promote coagulation?

Let us primarily consider the first of these questions.

As the blood floats along in its natural circuit, it has been chemically as well as physically considered as made up of, 1. Organic substances, as fibrin, albumen, red and colourless corpuscles, and oil; 2. Water; 3. Certain free gases, viz. nitrogen, oxygen, and carbonic acid; 4. Soluble salts, viz. lactate of soda, chloride of sodium, chloride of ammonium, carbonate of soda, phosphate of soda, chloride of potassium, and sulphate of potassa; 5. Insoluble salts, viz. phosphate of lime, phosphate of magnesia, phosphate of iron, and the carbonates of lime and magnesia; 6. An exceedingly minute portion of a free alkali, supposed to be potassa or soda.

Regarding these constituent parts, it is to be observed that they cannot all be supposed to exist in the blood at the same time. Thus it would seem impossible for chloride of ammonium to exist in the presence of free potassa or soda; and similar chemical objections might perhaps be urged against the presence of other of the agents named; but, inasmuch as all these have been found in the *analysis* of the blood, it is to be inferred that their elementary parts at least there existed; and, as we cannot be expected to know intimately what the exact chemical combinations of circulating blood are, those detailed above come fairly under the range of experimental research. If it be surmised that one or other of the individual constituents named above has the power of preventing coagulation, the questions would be, What is this agent? What is the power it exerts? Does it simply hold the fibrin in solution? Or does it give rise to some form of indirect or catalytic chemical action?

In taking up this inquiry, we may first reject such of the blood-constituents as cannot from their nature be supposed to effect any chemical change leading to the constant solution of fibrin. With this view, we may safely set aside the insoluble saline substances; viz. the phosphates of lime, magnesia, and iron, and the carbonates of lime and magnesia, and may base our inquiries mainly on the effects of the soluble salts, the alkalies, the acids, and the gases.

I. SOLUBILITY OF FIBRIN.

In conducting the following experiments, certain precautions were taken bearing on the points mentioned above. First, the fibrin was always obtained from the mixed blood (venous and arterial) of a bullock. Secondly, it was rendered as pure as possible, by being submitted for forty-eight hours to a brisk current of water. Thirdly, in all cases the fibrin, after being dried, was separated into portions of two and a half grains each, which were then minutely divided so as to expose a wide surface, and submitted to the action of a thousand grains of such solution as was employed. Thus, as regarded quantity, the fibrin approached the same proportion to the solution as it does to the blood flowing through the body under ordinary circumstances. Fourthly, the strengths of the solutions were varied; the natural proportion in the blood of each constituent used being, however, always considered as a standard. Fifthly, the chemicals were all carefully tested, and their purity satisfactorily proved. Sixthly, each experiment was repeated several times before any conclusion was drawn from its results.

a. Fixed Alkalies. EXPERIMENT CLXXI. *Fibrin in a*

Solution of Potassa. A solution of potassa was made, containing four grains to 1000 of water. In this solution were placed two and a half grains of fibrin. The fibrin commenced to dissolve immediately, and at the end of four hours formed a gelatinous mass, which hung together and floated in the solution, and was coloured slightly brown. In five days it was entirely dissolved.

EXPERIMENT CLXXII. *Fibrin in a Solution of Potassa.* A solution of potassa was made, containing two grains to 1000 of water. Two and a half grains of fibrin were now added. The solution of the fibrin speedily commenced, and was completed in eight days.

EXPERIMENT CLXXIII. *Fibrin in a Solution of Potassa.* A solution of potassa containing one grain in 1000 of water, received two and a half grains of fibrin. The effects were almost identical with those in the last experiment; but it required eleven days to effect complete solution.

EXPERIMENT CLXXIV. *Fibrin in a Solution of Potassa.* A solution of potassa, containing half a grain to 1000 of water, was made to receive two and a half grains of fibrin. In four hours the fibrin had assumed a gelatinous translucent appearance. It required eighteen days to effect complete solution.

EXPERIMENT CLXXV. *Fibrin in a Solution of Soda.* A solution of soda, containing two grains in 1000 grains of water, received two and a half grains of fibrin. The fibrin was dissolved in seven days.

EXPERIMENT CLXXVI. *Fibrin in a Solution of Soda.* A solution of soda, containing one grain in 1000 grains of water received two and a half grains of fibrin. Thirteen days were required for complete solution of the fibrin.

b. Salts. EXPERIMENT CLXXVII. *Fibrin in a Solution of Chloride of Sodium.* Into a solution of eight grains of chloride of sodium in 1000 grains of distilled water, two and a half grains of fibrin were introduced. At the end of five days no change whatever had occurred.

EXPERIMENT CLXXVIII. *Fibrin in a Solution of Chloride of Sodium.* To a solution of four grains of chloride of sodium in 1000 grains of water, two and a half grains of fibrin were added. At the end of ten days no solution had occurred.

EXPERIMENT CLXXIX. *Fibrin in a Solution of Chloride of Potassium.* Two and a half grains of pure fibrin were placed in a solution of two grains of chloride of potassium to 1000 grains of water. There was no effect after a lapse of five days; but decomposition commenced on the sixth.

EXPERIMENT CLXXX. *Fibrin in a Solution of Chloride of Potassium.* Ten grains of pure fibrin were placed in 1000 grains of a saturated solution of chloride of potassium in water. The fibrin was rendered slightly gelatinous, and rather translucent; but no further change took place.

EXPERIMENT CLXXXI. *Fibrin in a Solution of Chloride of Ammonium.* Two and a half grains of pure fibrin were added to a solution of two grains of chloride of ammonium in 1000 grains of water. The solution failed to dissolve the fibrin during a lapse of five days; on the sixth day, putrefaction commenced.

EXPERIMENT CLXXXII. *Fibrin in a Solution of Chloride of Ammonium.* Ten grains of pure fibrin were placed in a saturated solution of chloride of ammonium. The solution weighed 1000 grains. The fibrin was rendered slightly gelatinous in appearance; but no further effect was apparent during ten days digestion.

EXPERIMENT CLXXXIII. *Fibrin in a Solution of Sulphate of Potassa.* Into a solution composed of two grains of sulphate of potassa and a thousand grains of distilled water, two and a half grains of fibrin were introduced. In twelve hours no change whatever had taken place. At the end of five days the results were unaltered.

EXPERIMENT CLXXXIV. *Fibrin in a Solution of Carbonate of Soda.* Two and a half grains of fibrin were added to a solution of two grains of carbonate of soda, in 1000 grains of water. In five days there was no material change.

EXPERIMENT CLXXXV. *Fibrin in a Solution of Carbonate of Soda.* Two and a half grains of fibrin were added to a solution of one grain of carbonate of soda, in 1000 grains of water. The results were the same as in the last experiment.

EXPERIMENT CLXXXVI. *Fibrin in a Solution of Phosphate of Soda.* Two and a half grains of fibrin were added to a solution of two grains of phosphate of soda, in 1000 grains of water. No change had taken place in ten days.

EXPERIMENT CLXXXVII. *Fibrin in a Solution of Phosphate of Soda.* Ten grains of fibrin were added to a solution of forty grains of phosphate of soda, in 1000 of water. There was no visible action after a lapse of twenty-four hours.

EXPERIMENT CLXXXVIII. *Fibrin in a Solution of Lactate of Soda.* Two and a half grains of pure fibrin were placed in 1000 grains of water, to which had been added two grains of lactate of soda. There was no action until the fibrin became putrid, several days later.

EXPERIMENT CLXXXIX. *Fibrin in a Solution of Lactate of Soda.* Ten grains of fibrin were added to 1000 grains

of a nearly saturated solution of lactate of soda. The fibrin became very slightly gelatinous, but exhibited no further tendency to dissolve.

EXPERIMENT CXC. *Fibrin in a Solution of Lactate of Ammonia.* Into a very weak solution of lactate of ammonia, two grains of the salt to 1000 of water, two and a half grains of fibrin were introduced. No solvent action ensued.

EXPERIMENT CXCI. *Fibrin in a Solution of Lactate of Ammonia.* In a strong solution of lactate of ammonia ten grains of fibrin were placed. It was rendered slightly gelatinous, but with no other effect previously to putrefaction.

As these experiments on the effects of the alkalies, and of various blood-salts, in relation to the solution of fibrin, were made with great care, and were often repeated with the same results, they may, I believe, be relied on as absolute. The inference to which they inevitably lead is, that fibrin is soluble in simple alkaline solutions of various strengths. The rapidity of solution is much increased by agitation. At first, the fibrin expands in the solution, and assumes a gelatinous appearance; by and by it divides into small portions, and gradually disappears. It would seem that soda is a rather more powerful solvent of fibrin than is potassa. The insolubility of fibrin in solutions of salts, when these are perfectly pure and contain no free alkali, was well marked in all the experiments.

c. *Various Organic Substances.* While the above named chemical substances have been assumed as the most common and active agents existing in the blood, and as having an influence on the solubility of fibrin, there are certain others connected with the body, which call

for passing notice ; viz. formate of soda, urate of ammonia, uric acid, urea, kreatine, lactine, sugar, lactic acid, formic acid, inosinic acid, and butyric acid.

It was considered worth the labour to inquire how far these agents act on fibrin.

EXPERIMENT CXCH. *Fibrin in a Solution of Formate of Soda.* Two and a half grains of fibrin were placed in a solution of two grains of the formate of soda in 1000 of water. No effect whatever resulted.

EXPERIMENT CXCHH. *Fibrin in a Solution of Formate of Soda.* Ten grains of fibrin were added to 1000 grains of a saturated solution of formate of soda. No solvent action was perceptible.

EXPERIMENT CXCHV. *Fibrin in a Solution of Urate of Ammonia.* Two and a half grains of fibrin were added to 1000 grains of a solution containing as much urate of ammonia as could be taken up. No effect was produced until decomposition commenced.

EXPERIMENT CXCHV. *Fibrin in a Solution of Urea.* Two and a half grains of fibrin were added to 1000 grains of water, containing in solution two of urea. No solvent action was perceptible.

EXPERIMENT CXCHVI. *Fibrin in a Solution of Kreatine.* Two and a half grains of fibrin were placed in 1000 grains of water, containing two grains of kreatine. No solvent action took place.

EXPERIMENT CXCHVII. *Fibrin in a Solution of Lactine.* Two and a half grains of fibrin were placed in 1000 grains of a solution containing thirty grains of lactine. No result was apparent.

EXPERIMENT CXCHVIII. *Fibrin in a Solution of Lactine.* Into 1000 grains of a solution of lactine, containing fifteen grains, two and a half grains of fibrin were introduced without effect.

EXPERIMENT CXCIX. *Fibrin in a Solution of Grape-sugar.* Into 1000 grains of a solution containing sixty grains of grape-sugar, two and a half grains of fibrin were introduced. No effect was produced.

EXPERIMENT CC. *Fibrin in a Solution of Grape-sugar.* Two and a half grains of fibrin were introduced into 1000 grains of a solution containing thirty grains of grape-sugar. No result was produced.*

EXPERIMENT CCI. *Fibrin in a Solution of Uric Acid.* Two and a half grains of fibrin were placed in a mixture of two grains of uric acid with 1000 of water. No solvent action took place.

EXPERIMENT CCII. *Fibrin in a Solution of Lactic Acid.* Two and a half grains of fibrin were added to a mixture of thirty grains of ordinary solution of lactic acid (10 per cent.) and 970 grains of water. No solvent action was evidenced.

EXPERIMENT CCIII. *Fibrin in a Solution of Lactic Acid.* Ten grains of fibrin were placed in 1000 grains of the same dilute lactic acid. The fibrin was rendered gelatinous, but did not dissolve.

EXPERIMENT CCIV. *Fibrin in a Solution of Formic Acid.* Two and a half grains of fibrin were placed in a mixture of thirty grains of ordinary formic acid and 970 grains of water. There was no noticeable result.

EXPERIMENT CCV. *Fibrin in a Solution of Formic Acid.* Ten grains of fibrin were placed in 1000 grains of the solution of formic acid. The fibrin was rendered rather gelatinous, but was not dissolved.

EXPERIMENT CCVI. *Fibrin in a Solution of Inosinic Acid.* Two and a half grains of fibrin were placed in a

* Solutions of cane-sugar of various strengths were tried with the same negative results.

solution of two grains of inosinic acid in 1000 of water. No solvent action was shewn. In five days decomposition had commenced.

EXPERIMENT CCVII. *Fibrin in a Solution of Butyric Acid.* Two and a half grains of fibrin were added to a mixture of thirty grains of dilute butyric acid and 970 grains of water. The fibrin was made gelatinous in five minutes, and in twelve hours was partly dissolved.

EXPERIMENT CCVIII. *Fibrin in a Solution of Butyric of Acid.* Ten grains of fibrin were placed in 1000 grains of dilute butyric acid. The fibrin became gelatinous almost instantly, but did not dissolve as in the alkaline solution.

From the last named experiments, it appears that, with the exception of butyric acid, all the substances used proved inert as regards a soluble influence on fibrin. Butyric acid would seem, according to Lehmann, to be rather a normal constituent of blood than abnormal. The acid is volatile.

II. EFFECTS OF CHEMICAL AGENTS ON FRESHLY DRAWN BLOOD.

The preceding details contain a sketch of the effects of various substances on fibrin. I now proceed to record the effects of the same and of other agents on freshly drawn blood.

The experiments about to be related will convey a correct idea of the effects of those chemical substances, some of which certainly, others possibly, exist in circulating blood, or, at all events, in the body.

It may be well to premise these experiments by stating that, in performing them, an ounce of blood was always used. It was received, as it flowed from the animal,

into a graduated vial. The chemical agent about to be used was dissolved in the smallest possible portion of distilled water, and this solution was put into the bottle, which had previously been well washed with distilled water and dried. In trying the effect of the agent upon the blood, nothing more required to be done than to receive the blood from the neck of the animal into the bottle containing the solution, and gently to shake it once or twice, to secure perfect admixture.

In order to make accurate comparisons, I took special care, in performing each experiment, to receive another ounce of blood in an empty vial, perfectly clean, and of the same shape and size as that containing the solution. I was thus enabled to note the period of *natural* coagulation in every specimen of blood employed.

a. Fixed Alkalies. EXPERIMENT CCIX. *Effect of Potassa on Blood.* One fluid ounce of blood was received into a bottle containing 1.19 grain of hydrate of potassa dissolved in thirty minims of water. The colour was slightly darkened; the blood did not coagulate, but remained fluid until decomposition commenced. The blood-corpuscles, examined immediately after the experiment, had a contracted appearance, and some were disintegrated—a result which was also observed in the experiments with soda, about to be related.

EXPERIMENT CCX. *Effect of Potassa on Blood.* One fluid ounce of ox's blood was received into a bottle containing seven minims of liquor potassæ (about half a grain of potassa) and twenty-three minims of water. Feeble coagulation took place in fifteen minutes.

EXPERIMENT CCXI. *Effect of Potassa on Blood.* A fluid ounce of blood from the neck of an ox was mixed with a quarter of a grain of anhydrous potassa dissolved

in thirty minims of water. Firm coagulation had set in in four minutes; the blood of the animal coagulated naturally in two minutes.

[EXPERIMENT CCXII. *Effect of Potassa on Blood.* One ounce of blood from the same animal was received in a vessel containing one-sixth of a grain of hydrate of potassa with half a drachm of water. The blood coagulated in two minutes and a half; the clot was soft and dark, and eventually a considerable amount of serum exuded from it.

EXPERIMENT CCXIII. *Effect of Potassa on Blood.* One ounce of blood from the neck of an ox was received into a vessel containing one-eighth of a grain of hydrate of potassa in solution with thirty minims of water. The blood coagulated in two minutes. The clot was moderately firm. The blood of the animal coagulated also in two minutes on simple exposure to the air.

EXPERIMENT CCXIV. *Effect of Potassa on Blood.* One ounce of blood from the same animal was received a moment afterwards into a vessel containing one-tenth of a grain of hydrate of potassa in solution with half a drachm of water. Coagulation occurred in two minutes, the clot being dark and moderately firm.

EXPERIMENT CCXV. *Effect of Potassa on Blood.* One ounce of freshly drawn mixed blood from the neck of an ox was received into a bottle containing one grain of hydrate of potassa with thirty minims of water. The blood commenced to thicken in ten minutes, but did not coagulate fully for two hours; it then set into a firm but dark clot, from which no serum exuded. The blood of the animal used in this case coagulated naturally in two minutes and a half.]

EXPERIMENT CCXVI. *Effect of Soda on Blood.* One

ounce of fluid blood was received into a bottle containing 1·27 grain of hydrate of soda with thirty minims of water. The blood shewed no tendency to coagulate ; it remained fluid until decomposition ensued. The blood-corpuscles were found, when examined microscopically, to be contracted, broken up, and irregular.

[EXPERIMENT CCXVII. *Effect of Soda on Blood.* One ounce of blood from the neck of an ox was received into a vessel containing the fourth of a grain of hydrate of soda in solution with half a drachm of water. Coagulation took place in four minutes, the clot being dark but firm.

EXPERIMENT CCXVIII. *Effect of Soda on Blood.* One ounce of blood from the same animal was received into a bottle containing one-sixth of a grain of hydrate of soda in solution with thirty minims of water. The blood coagulated in a firm but dark clot in three minutes. The blood of the animal used in these experiments coagulated in two minutes on exposure to the air.

EXPERIMENT CCXIX. *Effect of Soda on Blood.* One ounce of blood from the same animal was received in a vessel containing one-tenth of a grain of hydrate of soda in solution with half a drachm of water. The blood coagulated in two minutes and thirty seconds, the clot being of a bright red in its upper, and almost of a jet black in its lower half.

b. Salts. EXPERIMENT CCXX. *Effect of Chloride of Sodium on Blood.* I received one ounce of blood from the neck of a sheep, and placed it in a bottle containing one half drachm of chloride of sodium. The blood remained fluid. Stopping the bottle firmly, I retained this blood for thirteen months. At the end of this period I reopened the bottle, and found the blood as fluid as before.

I repeated Mr. Gulliver's experiment of adding water to the blood, but could not induce coagulation by this means. The blood had undergone some decomposition.

EXPERIMENT CCXXI. *Effect of Chloride of Sodium on Blood.* One ounce of freshly drawn sheep's blood was received in a vessel containing twenty grains of chloride of sodium with thirty minims of water. After standing twenty hours at rest, this blood remained in great part fluid, but contained one or two loose clots; it retained its red colour. The blood of the animal used in this experiment coagulated firmly in two minutes.

EXPERIMENT CCXXII. *Effect of Chloride of Sodium on Blood.* One ounce of blood freshly drawn from the neck of the same animal as in the last experiment was received into a vessel containing fifteen grains of chloride of sodium in thirty minims of water. It commenced to coagulate in one hour, and formed a firm red clot from which no serum exuded.]

EXPERIMENT CCXXIII. *Effect of Chloride of Sodium on Blood.* One fluid ounce of freshly drawn ox's blood was received into a bottle containing ten grains of chloride of sodium in thirty minims of water. Coagulation commenced in four minutes and fifteen seconds. Another ounce of blood, from the same animal, coagulated naturally in three minutes and forty-five seconds on exposure to air. The colour was slightly darkened in the blood to which the salt was added. Under the microscope, the blood-discs were found contracted.

[EXPERIMENT CCXXIV. *Effect of Chloride of Potassium on Blood.* One ounce of blood from the neck of an ox was received into a vessel containing twenty grains of chloride of potassium in solution with half a drachm of water. In three minutes this blood commenced to

thicken, and underwent a dark jelly-like coagulation without any extrication of serum.

EXPERIMENT CCXXV. *Effect of Chloride of Potassium on Blood.* One ounce of blood from the same animal was received into a vessel containing ten grains of chloride of potassium in solution with thirty minims of water. Coagulation occurred in three minutes, the clot being very dark and loose, and yielding abundance of serum, which was almost of a black colour. The blood of the animal used in these two experiments coagulated firmly in two minutes.]

EXPERIMENT CCXXVI. *Effect of Chloride of Potassium on Blood.* One fluid ounce of blood was received into a vessel containing ten grains of chloride of potassium in thirty minims of water. The colour of the blood was slightly darkened; but firm coagulation took place in four minutes. The blood naturally coagulated in three minutes and a half.

EXPERIMENT CCXXVII. *Effect of Chloride of Ammonium on Blood.* One fluid ounce of freshly drawn blood was received into a vessel containing ten grains of chloride of ammonium dissolved in thirty minims of water. No coagulation ensued for six hours; the bottle during that time being firmly corked. On removing a little (about a drachm) of blood from the bottle, and placing it in a wine-glass, left uncovered, firm coagulation took place in an hour and a half, the blood in the closed bottle still remaining fluid. On microscopical examination of this blood, no breaking up nor peculiar modification of the blood-corpuscles was observed. The blood of the animal used in this experiment coagulated in seven minutes and fifteen seconds on exposure to the air, the temperature of the day being 43° Fahr.

[EXPERIMENT CCXXVIII. *Effect of Chloride of Ammonium on Blood.* One ounce of freshly drawn blood from the neck of a sheep was received into an open vessel containing five grains of chloride of ammonium in thirty minims of water. Coagulation occurred in five minutes, the clot being dark and firm; but little serum exuded from it. The blood of this animal, exposed to the air, coagulated firmly in one minute and a half.

EXPERIMENT CCXXIX. *Effect of Chloride of Ammonium on Blood.* One ounce of blood from the animal named in the last experiment was received into a vessel containing two and a half grains of chloride of ammonium with thirty minims of water. Coagulation occurred in two minutes and a half, the clot being dark but firm; but little serum exuded.]

It will be remembered that chloride of ammonium did not cause the solution of pure fibrin when added to it.

[EXPERIMENT CCXXX. *Effect of Sulphate of Potassa on Blood.* One ounce of freshly drawn mixed blood from the neck of a sheep was received into a vessel containing ten grains of sulphate of potassa with thirty minims of water. Coagulation occurred in seven minutes, the clot being firm and red; a large quantity of serum exuded from the clot. The natural period of coagulation was one minute and a half.

EXPERIMENT CCXXXI. *Effect of Carbonate of Potassa on Blood.* One ounce of mixed blood from the throat of a sheep was received into a vessel containing ten grains of carbonate of potassa in one ounce of water. Twenty hours after this blood had been at rest, it retained its red colour, and formed a very feeble coagulum. The blood of the animal used in this experiment coagulated naturally, on exposure to the air, in one minute and a half.

EXPERIMENT CCXXXII. *Effect of Carbonate of Potassa on Blood.* One ounce of mixed blood from the same animal as in last experiment was received a moment or two later into a vessel containing five grains of carbonate of potassa in thirty minims of water. After twenty hours rest, this blood was a little thickened, and contained a feeble coagulum. The blood was of a bright red colour.

EXPERIMENT CCXXXIII. *Effect of Acetate of Potassa on Blood.* One ounce of blood from the neck of a sheep was received in a vessel containing ten grains of acetate of potassa in thirty minims of water. Coagulation occurred in three minutes and a half, the clot being firm and a bright red; a considerable quantity of serum exuded from this clot.

EXPERIMENT CCXXXIV. *Effect of Acetate of Potassa on Blood.* One ounce of freshly drawn blood from the same animal was received into a bottle containing five grains of acetate of potassa with thirty minims of water. Firm coagulation occurred in two minutes and a half; a large quantity of serum exuding from the clot. The natural period of coagulation of this blood, on exposure to the air, was one minute and a half.

EXPERIMENT CCXXXV. *Effect of Sulphocyanide of Potassium on Blood.* One ounce of freshly drawn blood from the neck of an ox was received into a bottle containing five grains of the sulphocyanide of potassium in solution with thirty minims of water. At the end of two hours the greater part was still fluid, but one or two small clots had formed; the process of coagulation went on very slowly, and twelve hours elapsed before the mass of blood had become an uniform clot.

EXPERIMENT CCXXXVI. *Effect of Sulphocyanide of Po-*

tassium on Blood. One ounce of blood from the neck of the same animal was received into a bottle containing two grains and a half of sulphocyanide of potassium in solution with thirty minims of water. The blood remained fluid for nearly two hours, when it gradually set into a firm clot, from which there was no exudation of serum. The blood of the animal used in these two experiments coagulated, on simple exposure to the air, in two minutes.]

EXPERIMENT CCXXXVII. *Effect of Carbonate of Soda on Blood.* A fluid ounce of fresh blood was mixed with ten grains of carbonate of soda in thirty minims of water. Coagulation commenced in four minutes, but the coagulum did not become firm. The natural period of coagulation in this blood was three minutes and a half.

[EXPERIMENT CCXXXVIII. *Effect of Carbonate of Soda on Blood.* One ounce of mixed blood from an ox was received into a vessel containing five grains of carbonate of soda in thirty minims of water. The blood remained fluid. Six hours after it had been at rest it was a little thicker than before, and contained one or two soft clots. The colour remained of a bright red. After the blood to which the salt had been added had remained twenty hours at rest, it had separated into two portions—a serous portion above, and a dark column beneath; when the serum was poured off, the dark mass was found so feebly coagulated that it poured like thick treacle into a cup. The blood of the animal used in this experiment coagulated naturally, on exposure to the air, temperature 60°, in two minutes and a half.]

EXPERIMENT CCXXXIX. *Effect of Lactate of Soda on Blood.* One fluid ounce of freshly drawn blood was received into a bottle containing two grains and a half

of lactate of soda. Coagulation commenced in three minutes and forty-five seconds. The blood in this case coagulated naturally in the same period.

EXPERIMENT CCXL. *Effect of Formate of Soda on Blood.* One fluid ounce of blood was mixed in a bottle with thirty minims of water and five grains of formate of soda. Coagulation took place in three minutes and forty-five seconds; the natural period of coagulation of the same blood being three minutes and a half. The temperature of the air was 51° Fahr.

EXPERIMENT CCXLI. *Effect of Phosphate of Soda on Blood.* One fluid ounce of blood was received into a bottle containing a solution of ten grains of phosphate of soda ($2 \text{ NaO}, \text{HO}, \text{PO}_5$) in thirty minims of distilled water. The blood coagulated in four minutes and fifteen seconds; the natural period of coagulation being three minutes and forty seconds.

[EXPERIMENT CCXLII. *Effect of Phosphate of Ammonia on Blood.* One ounce of mixed blood from the neck of a sheep was received into a vessel containing ten grains of phosphate of ammonia. Twenty hours afterwards, this blood retained its red colour and the most perfect fluidity. The blood of the animal used in this experiment coagulated naturally, on exposure to the air, in one minute and a half.

EXPERIMENT CCXLIII. *Effect of Phosphate of Ammonia on Blood.* One ounce of mixed blood from the same animal was received into a bottle containing five grains of phosphate of ammonia in thirty minims of water. Twenty hours after being at rest, this blood remained in great part fluid. There were in it one or two very soft small clots. The blood was of a bright red colour.

EXPERIMENT CCXLIV. *Effect of Phosphate of Ammonia*

on Blood. One ounce of freshly drawn mixed blood from the neck of an ox was received into a bottle containing two and a half grains of phosphate of ammonia with thirty minims of water. At the end of an hour the blood remained perfectly fluid; but on gentle agitation, exposed to the air, it began to thicken, and in another hour it formed a thick dark clot, from which there was a considerable exudation of serum. The blood of this animal, exposed to the air, coagulated naturally in two minutes and a half.]

EXPERIMENT CCXLV. *Effect of Urate of Ammonia on Blood.* One ounce of blood was mixed with half a drachm of a saturated solution of urate of ammonia. Coagulation took place in four minutes and fifty seconds; which was also the time required for the coagulation of the blood in the natural state.

EXPERIMENT CCXLVI. *Effect of Lactate of Ammonia on Blood.* One fluid ounce of blood was received into a bottle containing five grains of lactate of ammonia. Coagulation was produced in four minutes. The blood coagulated naturally in three minutes and forty-five seconds.

EXPERIMENT CCXLVII. *Effect of Butyrate of Ammonia on Blood.* One ounce of blood was received into a bottle containing thirty minims of dilute but neutral solution of butyrate of ammonia. Coagulation took place in six minutes. The natural period of coagulation of the blood used in this experiment was six minutes and a half.

c. Acids. EXPERIMENT CCXLVIII. *Effect of Hydrochloric Acid on Blood.* Hydrochloric acid can never be presumed to be present in the free state in blood. It enters, however, into the composition of several blood-

salts; and, as some chemists have hinted at their decomposition, it was thought fair to try its effects.

One ounce of fresh blood was drawn into a bottle containing ten drops of the concentrated pure acid in thirty minims of water. Coagulation was firmly set up in forty-five seconds, the fluid being darkened. The natural period of coagulation of this blood was four minutes and thirty seconds. The quantity of acid here employed was obviously too small to precipitate the albumen in the form of hydrochlorate. Some other explanation of the effects of this acid on blood must be sought for eventually.

[EXPERIMENT CCXLIX. *Effect of Hydrochloric Acid on Blood.* One ounce of blood from the neck of an ox was received into a vessel containing five minims of hydrochloric acid with thirty minims of water. It changed at once into a thick dark clotted mass.

EXPERIMENT CCL. *Effect of Hydrochloric Acid on Blood.* One ounce of blood was received from the throat of the same animal into a vessel containing two minims of hydrochloric acid with thirty minims of water. It coagulated within a minute in a dark viscid clot. The blood of this animal, on simple exposure to the air, coagulated in two minutes.

EXPERIMENT CCLI. *Effect of Phosphoric Acid on Blood.* One ounce of blood from the neck of a sheep was received into a bottle containing fifteen minims of phosphoric acid with thirty minims of water. The blood coagulated in three minutes and three quarters, the clot being dark and moderately firm. The corpuscles were rendered very much shrunken and irregular. The blood of this animal, exposed to the air, coagulated in two minutes.

EXPERIMENT CCLII. *Effect of Phosphoric Acid on Blood.*

One ounce of blood from the neck of the same animal was received the next moment in a vessel containing five minims of phosphoric acid with thirty minims of water. The blood coagulated in three minutes; the clot being dark, but moderately firm.

EXPERIMENT CCLIII. *Effect of Acetic Acid on Blood.*

One ounce of sheep's blood was received into a bottle containing fifteen minims of acetic acid. The liquid became of a dark colour, and assumed a treacly appearance; and, at the end of twenty-four hours, had undergone no further change. There was no trace of coagulum. The blood of the animal coagulated naturally in two minutes.

EXPERIMENT CCLIV. *Effect of Acetic Acid on Blood.*

One ounce of mixed blood from the throat of an ox was received into a vessel containing ten minims of acetic acid. The effect on the blood was at once marked; the fluid became thick, treacly, and of a dirty hue; it underwent no coagulation for forty-eight hours. The natural time of coagulation was two minutes.

EXPERIMENT CCLV. *Effect of Acetic Acid on Blood.*

One ounce of blood from the neck of the same animal was received the next moment in a vessel containing five minims of acetic acid. The blood remained fluid for rather more than an hour, and then set in a firm dark clot, from which no serum exuded. The corpuscles in all the specimens of blood to which the acetic acid had been added were shrunken, and in some measure dissolved; their appearance differed, however, entirely from that of the corpuscles acted on by the alkalies.]

EXPERIMENT CCLVI. *Effect of Uric Acid on Blood.*

One fluid ounce of blood was received into a bottle

containing two and a half grains of uric acid and thirty minims of water. It coagulated in three minutes and thirty seconds; while the blood in its natural state coagulated in three minutes and forty-five seconds. The temperature of the air was 51° Fahr.

[EXPERIMENT CCLVII. *Effect of Hippuric Acid on Blood.* One ounce of blood from the neck of an ox was received into a vessel containing two grains of hippuric acid with thirty minims of water. No difference was observed in the coagulation of this blood and of that which was exposed to the air naturally. The blood of the animal, on simple exposure to the air, coagulated in two minutes.]

EXPERIMENT CCLVIII. *Effect of Lactic Acid on Blood.* One fluid ounce of blood was made to flow into a bottle containing thirty minims of dilute lactic acid (ten per cent.). In the course of half a minute, the blood became black and thick; in forty-five seconds it was solidified to the consistence of new cheese. Rubbed between the fingers, the blood had a greasy feel, and appeared to be perfectly homogeneous, no filaments of fibrin being discernible. The natural period of coagulation of the blood used was four minutes and a half.

EXPERIMENT CCLIX. *Effect of Lactic Acid on Blood.* One ounce of freshly drawn blood from the neck of an ox was received into a vessel containing five minims of solution of lactic acid with thirty minims of water. The blood coagulated simultaneously with an ounce of other blood drawn at the same time into a vessel of similar shape and size, the period in each case being two minutes and a half.

[EXPERIMENT CCLX. *Effect of Lactic Acid on Blood.* I laid bare the jugular vein of a cat, inserted a small tube in the direction of the current, and endeavoured

to throw in a solution of lactic acid. As the acid came into contact with the blood, a similar change occurred to that noted in the last experiment. The blood became dark, treacly, and homogeneous, communicating a slimy and gritty feel to the fingers. I was unable to throw in the acid, the pipe becoming clogged up. When the tube was withdrawn, a few drops of the thick disintegrated blood oozed into the wound. I caught this in a watch-glass; it thickened and dried up, but underwent no definite coagulation.

EXPERIMENT CCLXI. *Effect of Lactic Acid on Blood.*

I drew three ounces of venous blood from an ox into a bottle surrounded by freezing mixture; and, stopping the bottle firmly, kept the blood for half an hour in a frozen state. I then gently thawed it until it became quite fluid, and divided it into three equal parts. One part was set aside, exposed to the air at 60°; it coagulated in four minutes. To the second part, I added ten drops of dilute lactic acid. The acid had the same effect as noticed in the last experiment. To a third part I added five drops of the acid. The special effect was less marked; and in four minutes there was a semi-coagulation, but the clot was soft, dark, and slimy.

These experiments with lactic acid were repeated on several occasions with the same results.]

EXPERIMENT CCLXII. *Effect of Formic Acid on Blood.*

One fluid ounce of blood from an ox was received into a bottle containing thirty minims of dilute formic acid. It had not coagulated when examined at the end of an hour and a half. The colour was nearly changed to black, and the fluid appeared decomposed. Under the microscope, no blood-corpuscles were apparent.

[EXPERIMENT CLXIII. *Effect of Formic Acid on Blood.*

One ounce of blood from the neck of an ox was received into a bottle containing thirty minims of dilute formic acid with thirty minims of water. As the acid and blood commingled, the blood assumed a dark character and a treacly consistence, remaining thick, but entirely fluid, for forty-eight hours. The blood had a peculiar broken up character, and when spread on a glass looked almost black, but left after a time a white deposit, which soon dried, and had a greasy character. The blood of the animal used in this experiment coagulated firmly in two minutes.

EXPERIMENT CCLXIV. *Effect of Formic Acid on Blood.* One ounce of blood from the animal named in the last experiment was received into a vessel containing twenty minims of formic acid with thirty minims of water. The blood coagulated in five minutes in a dark soft clot, which had a peculiar broken up character. The corpuscles had a contracted appearance.

EXPERIMENT CCLXV. *Effect of Formic Acid on Blood.* One ounce of blood freshly drawn from the neck of a sheep was received into a bottle containing ten minims of formic acid with thirty minims of water. The blood coagulated in two minutes in a tolerably firm clot, from which but little serum exuded; the clot was rather dark in colour, and the blood-corpuscles were shrunken. The blood of the animal coagulated naturally in two minutes.]

EXPERIMENT CCLXVI. *Effect of Inosinic Acid on Blood.* One fluid ounce of ox's blood was received into a bottle containing two and a half grains of inosinic acid, obtained from the juice of meat by Liebig's method. This blood coagulated in three minutes and forty-five seconds; the natural period of coagulation being the same.

EXPERIMENT CCLXVII. *Effect of Butyric Acid on Blood.* One ounce of ox's blood, received into a bottle containing five minims of butyric acid and thirty minims of water, coagulated in four minutes.

EXPERIMENT CCLXVIII. *Effect of Butyric Acid on Blood.* One ounce of blood was received into a bottle containing four minims of butyric acid and thirty minims of water. Coagulation took place in four minutes and twenty seconds.

EXPERIMENT CCLXIX. *Effect of Butyric Acid on Blood.* One ounce of blood was received into a bottle containing three minims of butyric acid and thirty minims of water. It coagulated in five minutes.

EXPERIMENT CCLXX. *Effect of Butyric Acid on Blood.* One ounce of blood was received into a bottle containing two minims of butyric acid and thirty minims of water. Coagulation took place in five minutes.

EXPERIMENT CCLXXI. *Effect of Butyric Acid on Blood.* One ounce of blood was received into a bottle containing one minim of butyric acid in thirty minims of water. It coagulated in five minutes and thirty seconds. The blood used in these five experiments coagulated naturally in six minutes and a half, the temperature of the air being 43° Fahr.

d. Organic Substances. EXPERIMENT CCLXXII. *Effect of Urea on Blood.* One fluid ounce of ox's blood was received into a bottle containing one grain of pure urea dissolved in thirty minims of water. Coagulation took place in eight minutes; and in the natural blood in seven and a half minutes; the temperature of the day being 40° Fahr.

EXPERIMENT CCLXXIII. *Effect of Kreatine on Blood.* One fluid ounce of ox's blood was subjected in the same

manner to thirty minims of saturated solution of pure kreatine, containing two and a half grains of the principle itself, obtained from the juice of meat by Liebig's process. The blood coagulated perfectly in three minutes and forty seconds, without change of colour; the time of natural coagulation being three minutes and forty-five seconds. The temperature of the air was 51° Fahr.

EXPERIMENT CCLXXIV. *Effect of Lactine or Milk Sugar on Blood.* One fluid ounce of blood was allowed to flow into a bottle containing five grains of lactine dissolved in thirty minims of water. Coagulation took place in four minutes and fifty seconds. The natural period of coagulation was four minutes and a half: the temperature of the day was 48° Fahr.

EXPERIMENT CCLXXV. *Effect of Saccharine or Cane Sugar on Blood.* One fluid ounce of blood was received into a bottle containing a solution of five grains of saccharine in thirty minims of water. The period of coagulation was seven minutes and forty-five seconds, both in the blood experimented on and in natural blood. The temperature of the day was very low.

EXPERIMENT CCLXXVI. *Effect of Glucose or Grape Sugar on Blood.* One fluid ounce of blood was received into a bottle containing five grains of glucose in thirty minims of water. The period of coagulation was the same as in the last experiment, but the clot was firmer.

[*e. Galvanism.* Although apart from the strict subject of this chapter, I may record a few experiments in which the effect of galvanism on newly drawn blood was tried.

EXPERIMENT CCLXXVII. *Effect of the Galvanic Current on Blood.* I took two pieces of quarter-inch glass tubing,

each three inches long, and bent them into the form of horse-shoes. I now received a little blood from the jugular vein of a young dog; and, setting the two tubes upright, filled them with the blood. Into the open ends of one of the tubes I inserted the wires leading from a simple battery of two plates, allowing the wire on each side to dip for the space of a few lines into the blood. The blood in the other tube was left merely exposed to the air, the temperature of which was 65° . The blood through which the galvanic current passed coagulated a few seconds later than the other blood. Both had firmly coagulated in four minutes: there was no difference in the appearance of the clots.

EXPERIMENT CCLXXVIII. *Effect of the Galvanic Current on Blood.* Blood from the jugular vein of another dog was experimented on in a similar way. The blood under the galvanic current began to coagulate in two minutes, and formed a firm clot; that simply exposed to the air had coagulated slightly in a minute and a half, and in two minutes was a firm and uniform clot.

EXPERIMENT CCLXXIX. *Effect of the Galvanic Current on Blood.* I received into each of two watch-glasses three drops of my own capillary blood, derived from a small wound. An assistant arranged the galvanic apparatus. The poles of the battery were immersed at a slight distance from each other in one specimen of the blood; the other portion was left simply exposed to the air. The blood under the galvanic current coagulated in seven minutes. That simply left in the air coagulated a few seconds sooner; probably from being accidentally spread over a rather wider surface.

EXPERIMENT CCLXXX. *Effect of the Galvanic Current on Blood.* I received into each of two watch-glasses four

drops of capillary blood, derived from a puncture in the finger of a friend. The poles of the battery were immersed in one specimen of the blood; the other portion was left simply exposed to the air. The blood under the galvanic current coagulated in two minutes; that simply exposed to the air in the same time.

In none of these experiments did the blood darken under the galvanic current; nor was the coagulum in any way modified in quality.]

SUMMARY.

In reviewing these experiments, the results obtained are few and simple, so far as healthy blood is concerned. They are:—

1. That the fluidity of the blood seems essentially to depend on the fibrin being held in solution by some chemical agent.

2. That the free fixed alkalies, soda and potassa, possess the power, in certain definite degrees, both of dissolving fibrin and of holding blood fluid. That for holding blood permanently fluid, the proportion of either alkali must not be less than one grain to the fluid ounce, or one part in 505 by weight.

3. That no normal blood-salt has the power of effecting the solution of fibrin, nor yet of holding blood fluid, except when added in proportions which would be incompatible with life if introduced into the circulation.

A great deal has been said about the effects of chloride of sodium on blood; and experiments have been over and over again made, to prove that this salt possesses the property of keeping blood in a state of fluidity. This fact is undeniable; but, inasmuch as twenty grains of the salt are required to keep an ounce of blood fluid, it is impossible to presume for an instant that chloride

of sodium is the natural blood-solvent. To produce any solvent effect on fibrin itself, a saturated solution of the salt is required; and even then the result is imperfect.

In reference to the various abnormal constituents of the blood, and their influence on coagulation, it is to be observed that the results obtained from the experiments related, although important, are rather to be considered as bearing on pathological than on physiological questions. I leave, therefore, the facts recorded with regard to these constituents as mere historical details, interesting to be remembered, but diverging somewhat from the point immediately before us.

Although it is clearly proved that the free alkalies—soda and potassa—exert the property of dissolving fibrin and keeping blood fluid, it is in no way proved that they are the cause of fluidity. Before we could arrive at such a conclusion, we must ascertain which of them, if either, is really present in the blood in the free state. As bases, both exist in the blood; and as the serum of blood is feebly alkaline, it has been presumed that the alkalinity of necessity depends upon the presence of one or the other of these alkalies, or their alkaline salts. It may be so; but even this is difficult to suppose; for if it is true, as has been asserted by various chemists, that chloride of ammonium exists in normal blood, it is difficult to understand how either potassa or soda can exist free in the presence of this salt.

But, in the absence of any chemical objections of the above nature, there is one simple truth which once and for all negatives the hypothesis that the fluidity of living blood depends on the presence of soda or potassa, or of any fixed alkaline salt, in the blood. The circulating blood is fluid; the drawn blood, left at rest under fa-

vouring conditions, coagulates. And it is granted that living blood contains one or other of the free alkalies or their alkaline salts. Yet the last admission in no way affects the two previous facts, because drawn blood must contain the same fixed agents as blood circulating in the vessels of the body. Indeed, the arguments that have been used to prove that the free alkalies do exist in the circulating blood, have of necessity been deduced from the observation of that fluid after its abstraction. To prove that blood flowing through the healthy system is alkaline is impossible; but, as it is found alkaline after it is drawn, the inference is that it was so before. At the same time, it is evident that, if such fixed alkaline agents were capable of sustaining the fluidity of the blood during life, they ought to do so afterwards; which we know quite well not to be the fact.

[*Effect of Serum on newly drawn Blood.* In experiments on the serum of blood, I have found the serum sometimes neutral, but in the majority of cases feebly alkaline. But that it is never sufficiently alkaline to hold freshly drawn blood fluid, is proved by the very fact of being able to obtain the serum by spontaneous separation.

However, to determine the solvent effect of naturally alkaline serum, I performed the following experiments.

I received from the neck of an ox two quarts of blood, and set it aside that the serum might separate. When this had taken place, I carefully decanted off the serum. It had a specific gravity of 1.030, at a temperature of 60° Fahr. The fluid had a very feeble alkaline reaction. I next made use of it as follows.

EXPERIMENT CCLXXXI. *Admixture of Serum with Blood.* I caught half an ounce of blood from the neck of an ox, and received it into a cup containing one drachm of the

serum. Coagulation was perfect in two minutes and a half, the clot being firm and uniform.

EXPERIMENT CCLXXXII. *Admixture of Serum with Blood.* Half an ounce of blood from the same animal was received into a cup containing two drachms of serum. Coagulation took place at the same time as in the last experiment, the clot being equally firm and uniform.

EXPERIMENT CCLXXXIII. *Admixture of Serum with Blood.* I received half an ounce of blood from the neck of the same animal into a cup containing half an ounce of the serum. Coagulation commenced in two minutes and a half; and at the end of three minutes the clot was as firm as in the previous two instances. The blood of the animal used in these experiments coagulated naturally in two minutes and twenty seconds, on exposure to the air at a temperature of 58° Fahr.

EXPERIMENT CCLXXXIV. *Admixture of Serum with Blood.* One half ounce of freshly drawn mixed blood from the neck of an ox was received into a cup containing half an ounce of the serum. It coagulated in three minutes; the clot was dark, but firm and uniform.

EXPERIMENT CCLXXXV. *Admixture of Serum with Blood.* Two drachms of blood from the neck of the same animal were received into a cup containing half an ounce of the serum. The blood began to gelatinise in three minutes; and in four minutes it formed a loose but uniform clot, from which ultimately a considerable amount of serum exuded.

EXPERIMENT CCLXXXVI. *Admixture of Serum with Blood.* One drachm of blood was received into a cup containing half an ounce of serum. The blood began to gelatinise in four minutes: in five minutes it formed an uniform but soft clot, from which a considerable amount of serum was pressed out. The blood of the

animal used in these three experiments coagulated naturally in three minutes on exposure to the air.

EXPERIMENT CCLXXXVII. *Admixture of Serum with Blood.* Half a drachm of ox's blood was received into a cup containing half an ounce of serum. It commenced to gelatinise in five minutes, and then formed a very loose clot, which floated in an abundance of serum.

EXPERIMENT CCLXXXVIII. *Admixture of Serum with Blood.* Half a drachm of blood from the neck of the same animal was received into a cup containing one ounce of serum. The blood remained fluid for fifteen minutes; then began to gelatinise; and in half an hour had formed a soft clot, floating in much fluid.

EXPERIMENT CCLXXXIX. *Admixture of Serum with Blood.* Half a drachm of blood from the neck of the same animal was received into a vessel containing two ounces of serum. In this case the fluid generally became slightly gelatinous, but there was no distinct separation of clot. The blood of the animal used in these three experiments coagulated naturally in three minutes on exposure to the air.

These experiments were repeated with other serum, and on the blood of other animals, sheep especially, so often and with such unerring results, that they may be received as absolute representatives of the influence of serum. By comparing these experiments with those related in chapter iv, pp. 155-172, it will be seen that the influence of serum is analogous to that which arises from other fluids of a high specific gravity. How little the bare fact of the alkalinity of the serum has to do with the suspension of coagulation, is shewn by the simple truth illustrated in Experiment CCLXXXVIII, that when one part of blood, itself containing its presumed normal amount of fixed alkali, is mixed with sixteen

times its measure of normal serum, coagulation occurs, with no other difference than that which arises from the physical admixture.

Thus the theory of the fixed alkaline salts, or of normal alkalinity of serum, as the solvent agent of the fibrin of circulating blood, is definitely excluded.]

But, while this chemical hypothesis thus breaks down, its place is no better supplied by the chemical arguments that fibrin, as fibrin, does not exist in circulating blood at all. In chapter II, page 53, this argument has been fully disposed of. Fibrin coagulates in aneurisms, on threads introduced into arteries, in vessels obstructed by ligature, in the occluded vessels of the dead body, and in the serous cavities when effused into them. It exudes as plastic lymph on the free surface of membranes; it coagulates there. How could any of these things occur if fibrin, as fibrin, did not exist in the circulating blood?

[Again, the other argument advanced by some physiologists, as Virchow, that the coagulation of fibrin is the result of contact with oxygen, is equally fallacious: inasmuch as coagulation takes place in the presence of nitrogen or other simple gas, from which oxygen is excluded, as readily as in oxygen itself; and even more readily *in vacuo* than under most other physical conditions.

As regards the effects of acids, we have seen that butyric acid dissolves fibrin; but as, when added to blood, it quickens coagulation, its influence as a solvent is excluded: while the formic and lactic acids, which modify the coagulating process, do not dissolve fibrin. These, therefore, may be rejected; not only for the reasons here given, but because the blood is alkaline.]

CHAPTER VI.

EXPERIMENTAL INQUIRY INTO THE CHEMICAL AGENCIES INFLUENCING THE COAGULATION OF THE BLOOD (CONTINUED).

"No more causes of things ought to be admitted, but such as are both true and sufficient to explain the phenomena." SIR ISAAC NEWTON.

EVOLUTION OF GASEOUS MATTERS FROM BLOOD.

[In our preceding inquiries, physical and chemical, we have been led irresistibly to the conclusion, that motion is not sufficient to account for fluidity, nor rest for coagulation; we have seen that exposure to the air is not alone sufficient to account for coagulation, though it is a favouring circumstance; and that mere confinement from air will not of itself sustain fluidity. We have seen that contact with living tissues is not alone competent to account for fluidity; for, while coagulation occurs in the presence of a living tissue, we have also seen fluidity sustained under certain conditions in contact with inorganic materials. We have seen that temperature is not sufficient of itself to account either for fluidity on the one hand, or coagulation on the other; inasmuch as the normal temperature of the body favours the coagulation of drawn blood, and is yet combined in the body with the circulating fluid blood. We

have seen, in regard to the effects of chemical agents, that while fibrin is evidently held fluid by some chemical principle, it is most clear that this cannot be one of the *fixed* substances; or it would continue to sustain the fluidity of blood, whether within or without the body.

We are thus driven, by the purest steps of exclusive reasoning, to the investigation of a new point;—namely, Is the coagulation of blood dependent on the evolution of some volatile substance, under circumstances favourable to its extrication ?]

The idea that the evolution of a gaseous product from the blood is the cause of coagulation, was indeed put forward, as has already been stated, by Sir Charles Scudamore and Polli, who supposed, also, that it was to the escape of carbonic acid gas that the process of coagulation is mainly due. Scudamore did not, however, prove this position, but the contrary; for he found that carbonic acid, passed through blood, had no marked effect in retarding coagulation. This important fact, however, both of them did prove: that coagulation proceeds in proportion as carbonic acid and other gases are given off—the most important observation that had been made on the subject since Hewson's remark regarding the effects of exposure to the atmosphere.

On looking back to all that had been done, and to my own investigations, the conviction became more and more powerful that, in principle, Scudamore and Polli were right respecting the escape of some volatile substance, however wrong they might be in detail. In this direction, indeed, all evidence points, as a reference to chapter iv will prove.

[In this chapter, as the details of physical experiments advanced step by step, this view of the evolution

of gaseous matter advanced also so steadily and convincingly, as to become, by mere accumulation of circumstantial evidence, as near to demonstration as such evidence could bring it. Let us follow this chapter step by step, and examine to what it leads.

Temperature, above the standard of the body, quickens coagulation ; *cold* retards it, and, carried to an extreme, altogether prevents it. *Water* at ordinary temperature added to blood, in proportion above the amount of blood used, retards coagulation, as though by retaining the volatile principle in solution for a longer time. *Fluids of greater densities* added to blood have the same effect. The *vacuum* quickens coagulation ; the more intensely as the vacuum is more perfect. The same quantity of blood *exposed to air* over a wide surface, whether in thin stream or in extensive layer, coagulates more quickly than if retained in mass in a small space. Blood *occluded from air* in the vessel of an animal, or in organic tubes under cold and pressure, is prevented from coagulating. Blood *in motion in a closed* circuit, or in a vessel, has its coagulation retarded, while by agitation in the open air its coagulation is quickened.

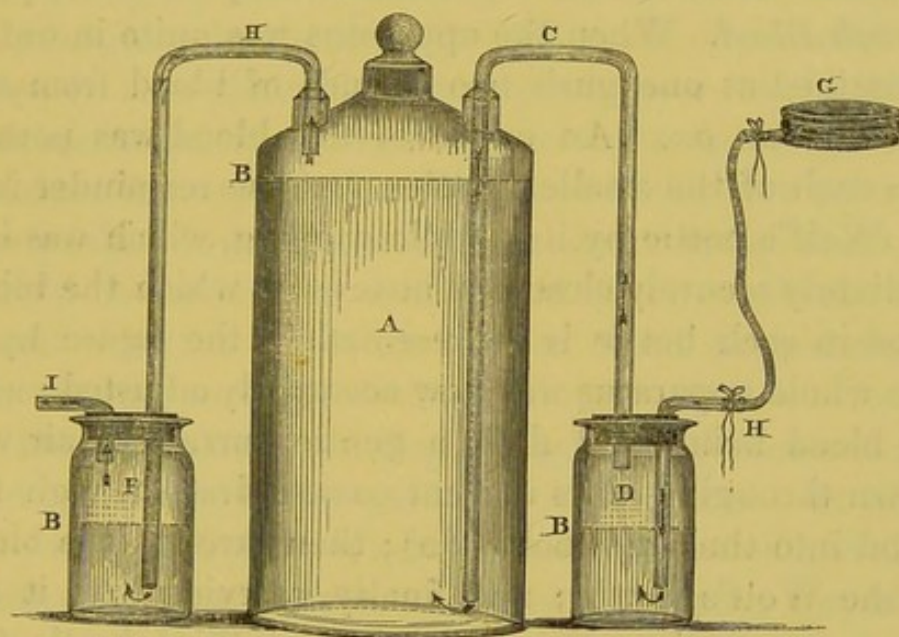
These facts lend irresistible evidence to the truth of the theory now before us for consideration.]

But, even with these strong arguments in its favour, the theory is far from being proved. Every effect which has been noticed might, after all, be only a coincidence. To test the truth of the theory, therefore, became a plain and necessary duty.

In commencing an inquiry in this direction, I felt that it would be most rational and business-like, not at once to examine the nature of the substances thrown off in vapour by coagulating blood, but to ascertain

primarily whether that vapour itself had any influence. The result is given in the succeeding narrative.

Transmission of Blood-Vapour through Blood. I fitted up a simple apparatus as follows. A Wolf's bottle (A) capable of holding three pounds of fluid blood, was fitted with three good corks, so as to make it quite air-tight. A bent tube (c) was fitted into one of the corks, so as to descend nearly to the bottom of the bottle by one end, and to be inserted by the other in a smaller bottle (D) placed near the Wolf's bottle. From the other side-opening passed also a glass tube, which



merely dipped into the neck of the Wolf's bottle, and bent over so as to pass to the bottom of another small bottle (F), of the same size and shape as that already mentioned. The two small bottles were also securely corked; but, in addition to the tubes already named as passing to them from the Wolf's bottle, two other tubes (H and I) emerged from them. When the apparatus was fitted up, it was easy, by means of a small pair of

bellows (G) attached to the long tube (H) proceeding from one of the small bottles, to throw a current of air through the whole of the bottles. The current, commencing in the attached tube (H), passed to the bottom of the small bottle (D), ascended through one of the bent tubes (C) into the Wolf's bottle, descended to its bottom through the long arm of the tube, then ascended out of the Wolf's bottle, passed to the bottom of the other smaller bottle (F), and finally, ascending to the upper part of the smaller bottle, escaped through the open tube (I) into the air.

EXPERIMENT CCXC. *Transmission of Blood-Vapour through Blood.* When the apparatus was quite in order, I obtained at one gush two pounds of blood from the throat of an ox. An ounce of this blood was poured into each of the smaller bottles, and the remainder into the Wolf's bottle by its middle opening, which was immediately securely closed. The level at which the blood stood in each bottle is represented in the figure by B. The whole apparatus was now accurately adjusted; and, the blood being still fluid, a gentle current of air was blown through. This current passed first through the blood into the small bottle (D); then through the blood in the Wolf's bottle; and finally, carrying with it the blood-vapour, into the blood in the third bottle (F). The result was in the highest degree striking. The blood through which air was first passed coagulated in two minutes; that in the Wolf's bottle coagulated in three minutes; while the blood in the third bottle, which for a time received the full charge of the vapour, retained its red colour and its full fluidity for eight minutes and a half; as long, in fact, as any vapour could be sent through it. When the vapour failed, and air

only began to circulate, this blood coagulated feebly, the fibrin separating and floating at the top.

I repeated this experiment frequently, with the same general result. On one occasion, it was modified by an accident; but the accident proved an advantage.

EXPERIMENT CCXCI. *Transmission of Blood-Vapour through Blood.* Having, as I thought, perfectly fitted up the apparatus described, I proceeded to perform an experiment as before. To my surprise, as the current passed over, the lower part of the blood in the bottle (F), which was presumed to be charged with vapour, began to coagulate rapidly and to darken, while all above remained of a bright colour and fluid. When the experiment was over, I found that this phenomenon arose from a simple mechanical accident. In fitting in the tube which was to conduct the vapour from the large bottle, the tube was not pushed down far enough, so that it stood about one inch from the bottom of the blood in the small one. The result was that this lower inch of blood did not receive the vapour, and therefore coagulated.

This experiment, trifling though it would seem at first sight, has important pathological bearings. It shows why a current of blood, checked in any vessel, and there held stationary, does of necessity coagulate; for, in the living body, the solvent principle, although not driven along by a pair of bellows, as in my experiment, is borne by the blood-stream, by which the same end is effected.

In considering the experiments thus related, and in pointing out their practical meaning, it is important to observe that the action of the blood-vapour, as thus used, is necessarily limited as to effect. The necessity for driving the vapour over by air unavoidably caused it to be largely diluted; and the volatile products

evolved by two or three pounds of blood are thus speedily disposed of. The result of the experiments, however, was, notwithstanding this drawback, all important; and, it being now obvious that in the blood-vapour lay the solvent of the fibrin, it became a task to ascertain what this solvent itself could be.

Before entering on this investigation, I repeated my experiment of shaking one ounce of blood in a two-ounce closed bottle, with the same effect as when I tried it before; viz., a marked retardation of the process of coagulation. This result materially strengthened the case.

In chemistry, few operations are more difficult than the detection of highly volatile substances evolved during evaporation. In looking over the works of chemical writers, I found that the majority of those who spoke at all about the vapour of blood, named as its component parts water, carbonic acid, nitrogen, and oxygen.

Carbonic Acid. I tested for carbonic acid by receiving blood into a large Wolf's bottle, and driving the vapour which arose through solutions either of lime or of baryta. In six experiments, I found traces of carbonic acid in only two instances. In other experiments, I drove the vapour of the same blood through two solutions of litmus, one pure, the other slightly acidified with acetic acid; so that the merest trace of acid or of alkaline vapour would change the colour in one of the solutions. Blood-vapour passed through these solutions made no difference in four cases; in two, it produced the slightest turn to red in the blue solution towards the close of the experiments. In these last named cases, I found that carbonic acid was passing over; since, on

changing the test-tube containing the litmus solution for one containing a solution of lime, carbonate of lime was formed. I also received blood into a carboy, and inserted litmus paper, slightly reddened, into the neck, corking the vessel tightly afterwards. No result followed.

Having failed, after several attempts, to obtain decisive evidence of the evolution of free oxygen or nitrogen from the blood, I allowed for the moment the probability of such an evolution, and then endeavoured to ascertain what would be the effect of exposing blood to the influence of carbonic acid, oxygen, and nitrogen. If, under either of such influences, the blood exhibited no modification in its coagulating property, the inference I felt would be, that to the escape of none of these agents could the process be attributed.

EXPERIMENT CCXCII. *Carbonic Acid driven through Blood.* Through two ounces of fresh ox's blood a stream of carbonic acid gas was gently passed. After four minutes, coagulation rapidly commenced; and, by plugging the tube through which the gas entered, prevented its further access to the blood.

EXPERIMENT CCXCIII. *Oxygen driven through Blood.* One fluid ounce of blood from the same animal was received into a bottle filled with oxygen gas. Its colour became much brightened; and it coagulated firmly in two minutes and a half.

EXPERIMENT CCXCIV. *Nitrogen driven through Blood.* Through two ounces of blood from the same animal nitrogen gas was gently driven from a bladder during half a minute. Coagulation commenced in four minutes and fifteen seconds. The colour of the blood was slightly darkened. The natural period of coagulation of the

blood used in these three experiments was three minutes and a half.

It thus appears that oxygen rather quickens than retards coagulation; an effect which I once before observed, in an experiment of another kind: while carbonic acid and nitrogen rather impede the process. The difference, however, is too slight to give either of them an importance as causes of fluidity.

[I have repeated these experiments by receiving blood into bottles filled with the three gases, the result being to prove that there is no special influence exerted over coagulation by any one of them, under the same physical conditions.]

At this point, I was brought to the same position as Sir Charles Scudamore; with the advantage of feeling morally sure that something still remained in the rear, which should be sought after.

EVOLUTION OF AMMONIA FROM BLOOD.

In seeking for this volatile principle, instead of undertaking at once an analysis of blood-vapour, I recurred once more to the constituent parts of blood, as they have been given by various experimentalists, dividing these into their component parts, and selecting from the latter for experiment such as were volatile. From the peculiar influence of the fixed alkalies in dissolving fibrin, the idea sprang up to ascertain whether it were possible that the volatile alkali, ammonia, which, being given as the base of a blood-salt by some experimentalists, came fairly within the range of experiment, was evolved with the other blood-gases in the process of coagulation.

In none of the writings on the blood to which I had access, was there any reference to the possibility of

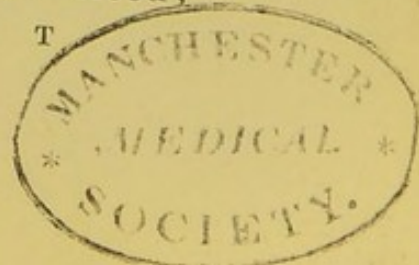
the spontaneous evolution of ammonia from newly drawn healthy blood. Yet there was nothing very objectionable in such a view, for ammonia can be produced in the body; and it is one of the most common agents in the chemistry of organic nature. Any way it was present for examination, and could not be reasonably or fairly excluded without experiment. To learn whether ammonia had any part in the process of coagulation, two things were required; 1. To discover if it were given off from freshly drawn blood; and if so, 2. To ascertain what influence it had on blood drawn from the body.

In entering on the first of these inquiries, I endeavoured primarily to ascertain whether, by passing the vapour of blood over a rod dipped in diluted hydrochloric acid, the well known white vapour of chloride of ammonium, formed by the union of the acid with the alkali, could be obtained.

EXPERIMENT CCXCV. *Testing Blood-Vapour with Hydrochloric Acid.* I had several pounds of ox's blood received into a large carboy with a long neck. I then quickly inserted the cork, with a piece of wire projecting downwards from it, to which was attached a small sponge made of asbestos and wetted with hydrochloric acid. The result was *nil*, although the experiment was several times repeated.

I had already exhausted the reddened litmus test; it was therefore unnecessary to repeat it.

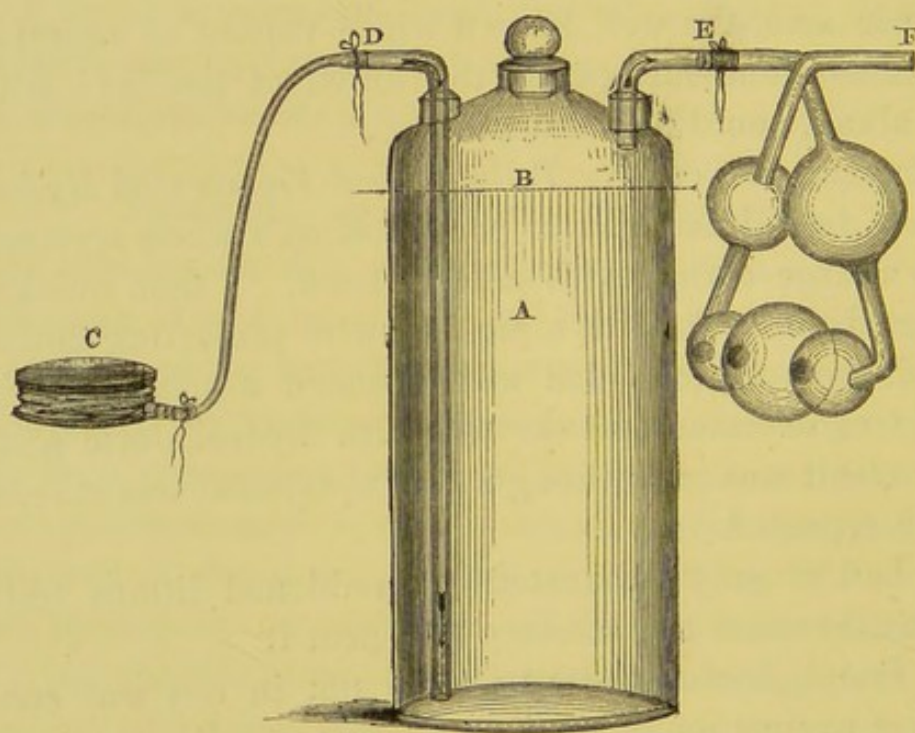
I found, however, that it was not in any way conclusive against ammonia that these tests did not indicate its presence in blood-vapour; for I ascertained by a trial experiment that, if one grain of ammonia were added to 450 grains of blood, it could not be detected by the rod test, as being evolved from the blood;



although it kept the blood fluid so long as the bottle in which it was contained was well corked, and possibly escaped when the bottle was uncorked, as the blood then coagulated. Moreover, the escape of water vapour from newly drawn blood is so copious, that the white fumes of chloride of ammonium, even if present, would be obscured by it. Some other more delicate tests were therefore required, and were instituted.

Formation of Ammonio-Chloride of Platinum. The first test used was the ordinary one for obtaining crystals of ammonio-chloride of platinum.

EXPERIMENT CCXCVI. *Formation of Ammonio-Chloride of Platinum from Blood-Vapour.* An apparatus was fitted up with a Wolf's bottle (A), as in the experiment



of transmitting blood-vapour through blood. To the free end of the long descending tube (D) the bellows (C) were attached. The free end of the short or exit tube

(E) was connected with one of Liebig's potash-bulbs (F) charged with perfectly pure hydrochloric acid. The Wolf's bottle being two-thirds filled with freshly drawn blood, and quickly closed, the vapour arising from the blood was blown briskly through hydrochloric acid, until the blood was fully coagulated. The acid was poured into a clean evaporating dish, solution of perchloride of platinum was added to it, and the mixture was carefully evaporated in the water-bath. The result was a deposit of the crystalline salt of ammonio-chloride of platinum, which was afterwards well washed in a mixture of alcohol and ether.

EXPERIMENT CCXCVII. *Formation of Ammonio-Chloride of Platinum from Blood-Vapour.* On the day after making the above experiment, I repeated it. The blood was drawn from a bullock. The apparatus worked well, and a free amount of blood-vapour was driven through the acid. The result was more decisive than in the former experiment.

EXPERIMENT CCXCVIII. *Formation of Ammonio-Chloride of Platinum from Blood-Vapour.* This experiment was conducted in the same way as the preceding, the subject being a heifer. The result was well marked, in a copious formation of the yellow salt.

EXPERIMENT CCXCIX. *Formation of Ammonio-Chloride of Platinum from Blood-Vapour.* The blood of an ox was experimented on in the same manner, with a similar result: there was a copious deposit of the salt.

In all these experiments, the same quantity of blood was used; viz., one imperial quart. The current of air was gently kept up for five minutes after the blood had coagulated. The air made for itself channels in the clotted blood, and thus passed freely through it. The

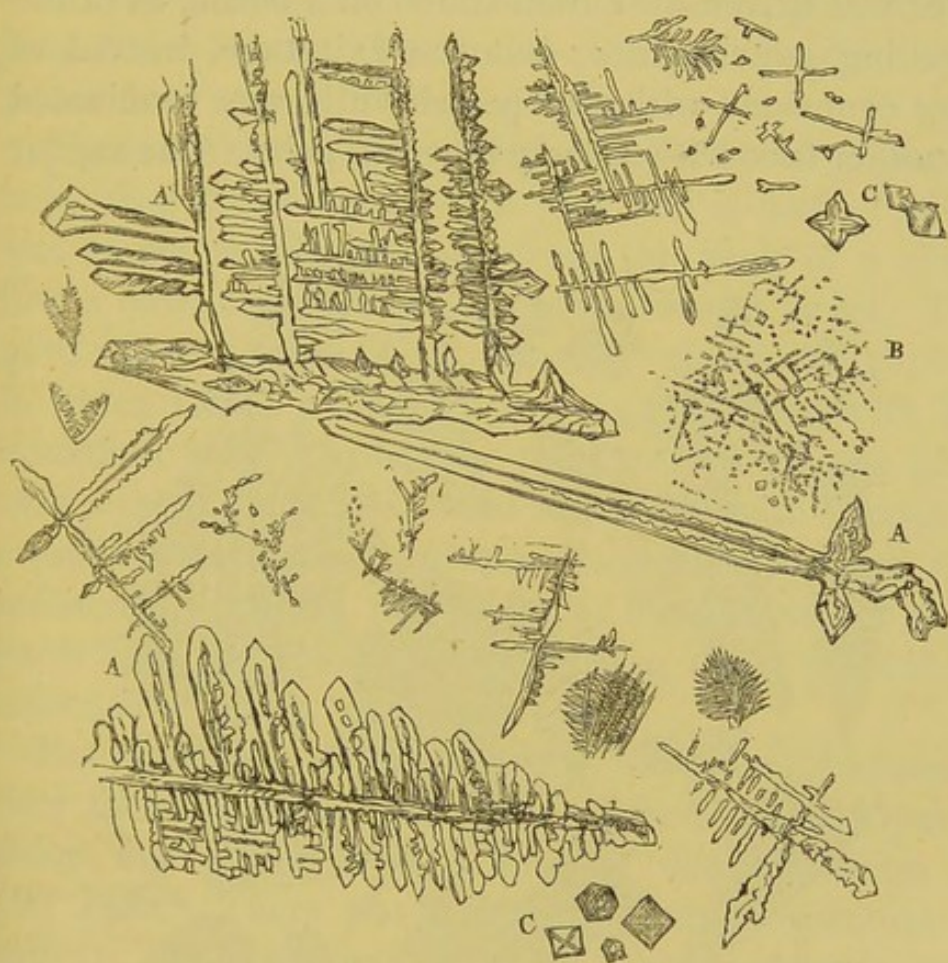
amount of precipitate obtained varied. The first experiment yielded a little more than 3 grains; the second, 2.14 grains; the fourth as much as 4.7 grains. But as the amount of gaseous exhalation is greatest when the blood is first drawn, and as the blood used was caught in an open vessel, and transferred to another vessel, it is obvious that much of the vapour was lost.

EXPERIMENT CCC. *Formation of Ammonio-Chloride of Platinum from Blood - Vapour.* The experiment was repeated with the blood of a sheep; but, owing to the rapidity with which coagulation took place, not above half a pint could be introduced into the bottle. The current of air was at once set up, and continued for ten minutes. Notwithstanding the small quantity of blood, the amount of ammonio-chloride of platinum obtained was little inferior to that in the first experiment.

EXPERIMENT CCCI. *Formation of Ammonio-Chloride of Platinum from Blood-Vapour.* The experiment was repeated on the blood of another sheep with a similar result.

Formation of Microscopic Crystals of Chloride of Ammonium. While the preceding experiments were in progress, another test suggested itself; namely, the production of microscopic crystals of chloride of ammonium from blood-vapour, by means of hydrochloric acid. If a little pure dilute hydrochloric acid be placed in a microscope glass and held over solution of ammonia for a moment, and the glass be then gently warmed, a field of the microscopic crystals will be formed. The crystals take various appearances; and in the opposite sketch, taken from a group examined by a quarter-inch lens, the artist, Mr. Aldous, has very skilfully depicted them in all their varieties, some (A) being larger, and others (B) more minute.

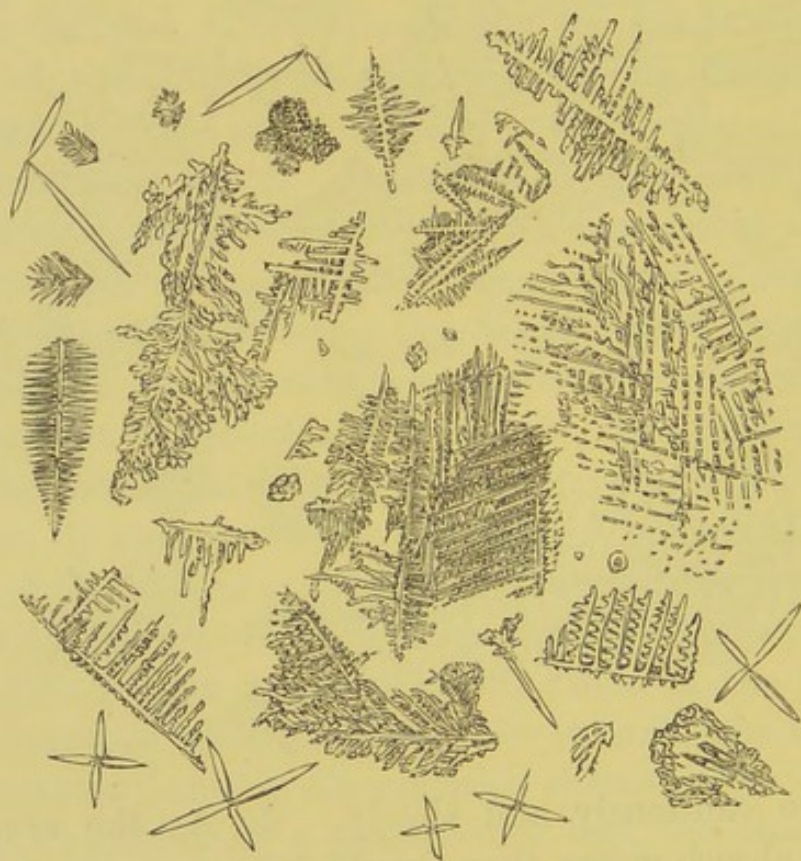
[In order to apply this process safely to the detection of ammonia in blood-vapour, certain conditions are required. 1. The acid used must be distilled over twice, or even oftener, to secure its perfect purity. 2. Before being used, a little of it is to be placed on the microscope glass, evaporated to dryness, and examined by the microscope, to see that it contains no crystallisable substance. 3. In evaporating, the process must



be done cautiously and slowly. 4. As the crystals rapidly absorb water, they should be examined directly after experiment. 5. To prevent fallacy, another microscope glass, moistened with the same acid, should be held at a short distance from the blood experimented.

on, dried, and examined for comparison. With these precautions, the microscope test is at once as delicate as it is easy and satisfactory. I have tried various tests for ammonia since this first suggested itself; but return to it as comprising the advantages of every qualitative test with least trouble and disadvantage.]

EXPERIMENT CCCII. *Formation of Chloride of Ammonium from Blood-Vapour.* The vapour from the blood of a heifer was driven over from the Wolf's bottle, as in the preceding experiments; but the exit tube, instead of being connected with the potash-bulb, was terminated in another tube with a finely tapering point. The vapour



being driven briskly over from some freshly drawn blood, was directed by the fine end of the tube upon a thin layer of hydrochloric acid, placed in the cell of a

common microscope glass. When the vapour had been thus directed for three minutes, the glass was gently dried. As the drying proceeded, a fine white cloud became visible on the part of the glass forming the cell. The microscope revealed the presence of a field of the crystals of chloride of ammonium, which are here shewn. They are a fair representation of those formed from blood-vapour.

EXPERIMENT CCCIII. *Formation of Chloride of Ammonium from Blood-Vapour.* The process was performed on blood taken from an ox. The result was the same.

[EXPERIMENT CCCIV. *Formation of Chloride of Ammonium from Blood-Vapour.* A pint and a half of blood was drawn, in the open air, from the neck of a sheep into a bowl, and was briskly whipped with twigs. This gave rise to a more than ordinary evolution of vapour, in which I held a microscope glass moistened with hydrochloric acid. After four minutes, I dried the glass over a spirit lamp, and found it studded with groups of crystals as before. For comparison, another glass, also moistened with acid, was placed at the distance of eight yards from the blood; this, on being dried, yielded no evidence whatever of crystals.

EXPERIMENT CCCV. *Formation of Chloride of Ammonium from Blood-Vapour.* One pint of fresh blood from a sheep was mixed with a pint of distilled water at 100° Fahr. There was a free and rapid evolution of vapour. The microscope glass, moistened with acid and held in this vapour, was dotted over its entire surface with the crystals.

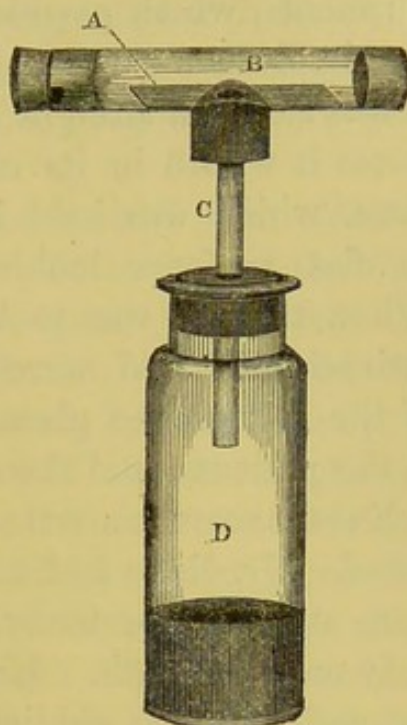
When a microscope glass is simply held over blood-vapour in the air, the objection may be made that the ammonia comes from the air itself; and, although this

objection is met by the precautions given above, it may be removed still better by excluding the air altogether, as in the succeeding plans.]

One very simple plan consists in the use of a glass vase, of the kind used for "potichomania". This holds a large quantity of blood, and offers a wide surface for evaporation. Into the hollow cover of the vase is inserted a movable wooden shelf, to the under surface of which a microscope glass is attached by India rubber bands. The vase having been filled with freshly drawn blood, and the under surface of the microscope glass having been moistened with hydrochloric acid, the cover, made air-tight by a few bands of India rubber, is immediately put on. The ammonia arising from the blood combines with the hydrochloric acid, and leaves chloride of ammonium distributed over the glass. In my first experiments, I chiefly used the apparatus above described, and obtained crystals of chloride of ammonium from the blood of various animals—heifers, bullocks, and sheep especially, not once failing in twenty-five consecutive experiments.

[EXPERIMENT CCCVI. *Copious Deposition of Chloride of Ammonium from Sheep's Blood.* A sheep was one day killed, which was evidently in an enfeebled state, either from disease or from over fatigue. I should presume from fatigue; for there was no manifest organic disease on inspection. A pint of blood was drawn from this animal into the potichomania jar, and the lid with the acidified microscope glass was put on. On gentle evaporation, the most copious deposit of the chloride I have ever seen, formed on the glass, which was, indeed, frosted over its entire surface. The blood in this instance was fully five minutes coagulating, a period extraordinarily long in regard to sheep's blood.

I afterwards made an instrument of another kind, as depicted in the drawing. A pint bottle (D), with a well fitting cork, has a tube (C) inserted through the cork. The upper part of the tube is blocked for supporting a small glass cylinder (B) lying horizontally across it. The glass cylinder is perforated in its centre with a hole through which the upright glass tube passes. The cylinder is closed at one end; and the other is fitted with a stopper. When it is to be used, a microscope glass (A), moistened with hydrochloric acid, is placed, as indicated, in the cylinder, the acidified surface downwards over the tube.



EXPERIMENT CCCVII. *Formation of Chloride of Ammonium from Blood-Vapour.* I received half a pint of blood from the neck of a sheep into the bottle (D); then inserted the cork with the tube (C), and the cylinder containing the microscope glass and acid. The blood coagulated in two minutes; but the bottle was allowed to stand for half an hour. Then the cylinder (B) was removed, and placed under a bell-jar over sulphuric acid in a sand-bath at 100° Fahr. When the microscope glass, thus dried, was removed, it was found, as before, dotted over with crystals of chloride of ammonium.

In these days of no blood-letting, it is a difficult thing to obtain human blood in quantity for the purpose of experiment. However, through the kindness of Mr.

Betts, cupper, of Wimpole Street, I have been enabled to perform, with the blood of the human subject, three experiments, which possess peculiar interest. I arranged for Mr. Betts a cupping-glass for experimental purposes. It was simply a straight cupping-glass, having stretched across it within in its middle part a short microscope glass, which was held in place by two slips of cork, its flat surfaces looking upwards and downwards. When the cup was to be used, two or three drops of hydrochloric acid were placed on the upper surface of the microscope glass: the scarifications were made in the patients, and the cup was applied.

EXPERIMENT CCCVIII. *Ammonia evolved from Human Blood.* Mr. Betts had a patient to cup, who was an old man, and who for many years had been cupped regularly once a month. He was thin, and sickly looking; but suffered from giddiness and affection of the head if the cupping were not performed. Mr. Betts arranged the glass as I had directed him, and, after scarifying, placed it on the back of the patient, and drew off about four ounces of blood. He then removed, emptied, and gently dried the cupping-glass, and at once brought it to me for examination. On the glass slide, there were a few crystals of chloride of ammonium: but, on looking at the upper and clean part of the cup, I observed there several groups of small white specks, on which, with a little trouble, I brought the microscope to bear. They resolved themselves into fine groups of chloride of ammonium crystals.

EXPERIMENT CCCIX. *Ammonia evolved from Human Blood.* A short time afterwards, Mr. Betts repeated the experiment on another patient, who was in the prime of life, and was bled to meet a plethora; for he who

takes in too much must have too much let out. The glass was applied, removed, and dried, as before. In this case, the microscope again revealed groups of the crystals, which, as in the previous instance, were not deposited on the slip which bore the acid, but on the upper part of the cupping-glass.

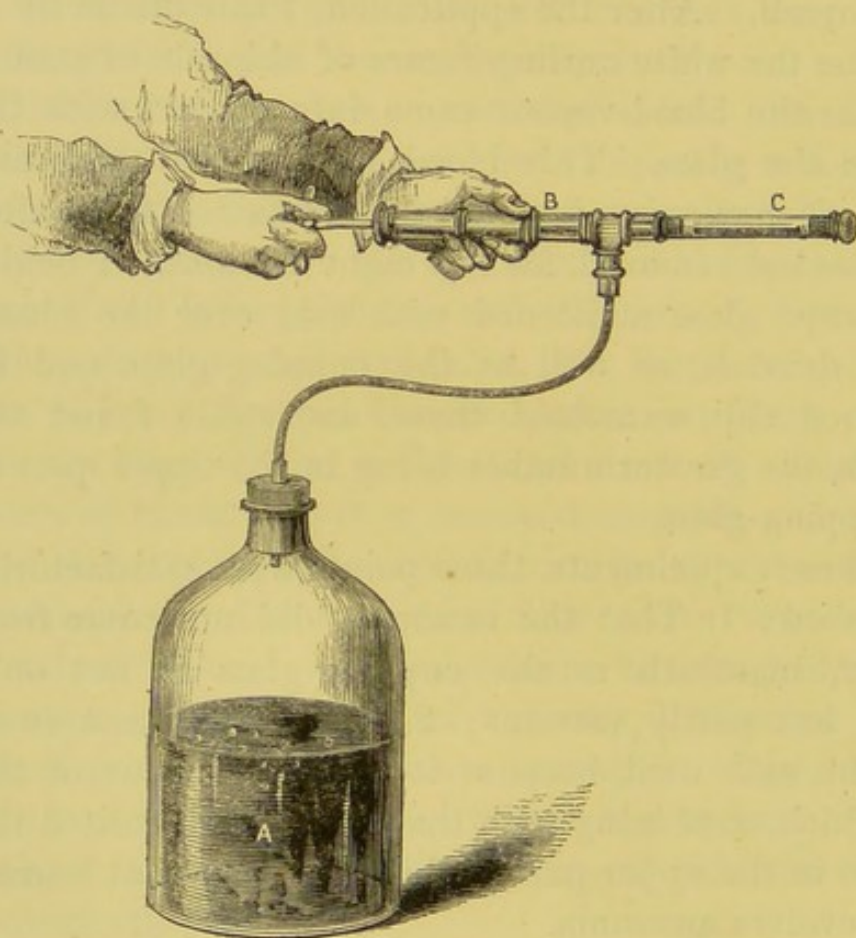
EXPERIMENT CCCX. *Ammonia evolved from Human Blood.* On another occasion, Mr. Betts cupped the first mentioned patient; and was so good as to send for me to take part in the experiment. I arranged the glass myself. After the application, I saw distinctly in the glass the white curling fumes of chloride of ammonium, as the blood-vapour came into contact with the acid on the glass. This blood, unlike what generally occurs when cupping is performed, remained fluid, after the glass was removed, for full eight minutes. I held a microscope glass moistened with acid over the blood, gently dried it, as well as the cupping-glass and its contained slip, examined these, and again found the crystals, the greater number being in the upper part of the cupping-glass.

In these experiments, three points were satisfactorily established: 1. That the ammonia did not come from the air, inasmuch as the cupping-glass is not only closed, but partly vacuum; 2. That it did not come from the acid used, because it was the vapour of the acid which, combining with the ammonia, deposited the crystals in the upper part of the glass; 3. That human blood evolves ammonia.

Against the experiment, there is one disadvantage, which, indeed, applies to the preceding experiments; namely, that, as the fumes of chloride of ammonium are formed, they descend and are absorbed by the blood, so

that the product is in a great measure lost. I suspect that the prolonged fluidity of the blood in Experiment cccviii might have been due to such absorption, inasmuch as the blood drawn from another scarification into a simple glass partly coagulated in the glass before its removal.

To remove still further all objections as to the source of the ammonia, and to prevent the reabsorption of ammonia by the surface of the blood, I made another apparatus, of which a drawing is supplied.



This consists of a large bottle (A) for holding the blood. From the neck of the bottle a tube emerges, which is connected by its opposite end to the suction

opening of an air-pump syringe (b). To the escape opening of the air-pump a glass cylinder (c) containing a microscope glass moistened with hydrochloric acid is attached, the further end of the glass cylinder being closed by a silk valve opening outwards. The blood being introduced into the bottle and the stopper inserted, the gases from it are pumped over the microscope glass in the cylinder, pushing open the silk valve in their escape.

EXPERIMENT CCCXI. *Formation of Chloride of Ammonium from Blood-Vapour.* I received into the bottle a quart of blood from the neck of an ox, inserted the stopper, and pumped the vapour into the glass cylinder over the microscope glass moistened with acid. I continued this process as long as I could draw over vapour; but I could not succeed in removing all the vapour that was present. The tube enclosing the microscope glass was now removed closed, and the whole was gently dried. When dried throughout, the microscope glass, being removed, yielded magnificent groups of crystals. In two patches on this glass the crystalline character of the deposit could be seen by the naked eye. The blood coagulated naturally in four minutes.

EXPERIMENT CCCXII. *Formation of Chloride of Ammonium from Blood-Vapour.* I repeated the experiment on the blood of a sheep. The result was the same; but in this case the crystals were mainly distributed on the inner wall of the cylinder surrounding the microscope glass.

EXPERIMENT CCCXIII. *Formation of Chloride of Ammonium from Blood-Vapour.* The experiment was repeated on the blood of another sheep, with the same result. In this case, also, the formation of crystals occurred in the glass cylinder around the microscope

glass. Pouring a few minims of distilled water into the cylinder, I dissolved out its contents, and receiving the solution on a flat surface of glass, evaporated it down. The deposit yielded beautiful fields of chloride of ammonium crystals.

EXPERIMENT CCCXIV. *Formation of Chloride of Ammonium from Blood-Vapour.* I repeated the experiment on the blood of a sheep with results precisely the same. The evolution of vapour from the blood in this, as in the preceding instances, was copious, and the coagulation of the blood exceedingly rapid.

EXPERIMENT CCCXV. *Evolution of Ammonia from Human Blood.* At page 127, I have recorded the case of a child, which died from cyanosis, with tuberculous deposit in the lungs. I removed from this child a few drachms of blood from the right side of the heart, and placed it, within two hours after its removal from the body, in the bottle described at page 281. The microscope was moistened with hydrochloric acid, and the lower part of the bottle was immersed in water at 100°. In half an hour, on removing the microscope glass and cautiously drying, I found it finely frosted with crystals of the chloride of ammonium.

It is worthy of observation that, after blood has coagulated, the evolution of ammonia and of watery vapour does not instantly cease, unless the clot be placed at a temperature at or below 32° Fahr., when all gaseous evolution stops, and also the further act of separation into clot and serum. If, on the other hand, a recently formed clot be divided into small pieces, and be placed in a vessel surrounded by water at 100° Fahr., there is a rapid separation of serum, and a continued evolution of vapour; the contraction of the clot being, in a word, but an extension of the first act of coagulation.

EXPERIMENT CCCXVI. *Evolution of Ammonia from recent Blood-Clot.* I caught a pint of blood from the neck of a sheep, and allowed coagulation to take place. I then divided the clot with a sharp knife into several sections, without removing it from the bottle in which it was contained, but immersing the bottle in water at 100° Fahr. The result was a free evolution of vapour, and a rapid separation of serum. A microscope glass moistened with hydrochloric acid, and suspended over the blood in the bottle for ten minutes, yielded on being dried fine groups of crystals of chloride of ammonium. Another microscope glass, moistened in the same way with acid, was simply exposed to the air of the room in which the experiment was performed. On being dried and examined, it shewed no trace whatever of crystals.]

EFFECT OF AMMONIA ON FIBRIN AND BLOOD.

Thus far, then, by a few simple experiments, the mere fact of the evolution of ammonia from blood freshly drawn became clearly demonstrated; although the amount evolved was unquestionably minute. But this fact, however interesting, and however contrary to the idea that ammonia would exist in the blood and make the round of the circulation without specific purpose, might after all be a mere coincidence, like the evolution of carbonic acid. The volatile alkali might have other use than that of holding blood fluid. It might be a mere excrete.

To dig deeper, therefore, into this question, it was necessary to change the line of inquiry, to adopt an approach to the synthetical method, and to ascertain what effect ammonia produces when added to fibrin, or when added to blood.

Effect of Ammonia on Fibrin. I commenced by adding fibrin to weak solutions of ammonia in the same manner as I had already exposed this substance to potassa and soda, and taking the same precautions. A variety of experiments were performed, of which I shall give three or four illustrations.

EXPERIMENT CCCXVII. *Effect of Ammonia on Fibrin.* Ten grains of moist fibrin were placed in a solution containing five grains of ammonia (NH_4O) in one thousand grains of water, in a closed bottle. As in the preceding experiments with the alkalies, the fibrin first became gelatinous, and then slowly dissolved. Fifteen days were required for complete solution.

EXPERIMENT CCCXVIII. *Effect of Ammonia on Fibrin.* Ten grains of moist fibrin were placed in a solution of two and a half grains of ammonia in 1000 grains of water. Solution took place after the same manner. Seventeen days were required for the completion of the process.

EXPERIMENT CCCXIX. *Effect of Ammonia on Fibrin.* Ten grains of fibrin were placed in a solution of two grains of ammonia in 1000 grains of water. Solution took place in twenty-one days.

[This solvent effect of ammonia on fibrin I had observed many years before these experiments were made. In 1850 (as I have since found by reference to my report-book), being then occupied with the subject of fibrinous concretions in the heart, I removed from the right auricle of a child, at a *post mortem* examination, a large pure fibrinous clot. I divided this clot into portions of ten grains each, and subjected them to various solutions, with the view of ascertaining whether any ordinary medicinal substance could be administered in cases where these depositions were

diagnosed, so as to produce their solution within the body. The inference drawn from these inquiries was, that ammonia promised the best results; and, in a paper afterwards read before the Medical Society of London, in speaking of the sinking symptoms, which, as I believe, sometimes result from concretion in the heart, I explained that it was possibly in such cases that ammonia had been found useful as a *dernier ressort*; and, in reference to this remedy, drew a distinction between this class of cases, where its administration was reasonable, and another class of cases, where the sinking was due to an opposite condition of blood—that is to say, where the blood is deficient in fibrin, and where the remedy would possibly only add to the disease.

The experiment here referred to was briefly noted at the time, as follows.

EXPERIMENT CCCXX. *Effect of Ammonia on Fibrinous Concretion.* Ten grains of fibrin from a concretion formed in the heart of Maria P. (death from broncho-pneumonia), were placed in a mixture of twenty minims of liquor ammoniæ (specific gravity .880) with two ounces of water. The fibrin was divided into small pieces before being introduced. It soon commenced to gelatinise; and in five days had entirely disappeared, forming a sticky solution, which evolved ammonia freely. I kept this solution nearly four years, closed up in its bottle; during which time it seemed to undergo no change.

It is clear from the above experiments (and, indeed, the fact had been pointed out before by other observers), that ammonia, like its fellow alkalies, dissolves fibrin. The process is slow, as I take it, for the mere physical reason that the surface of fibrin exposed to the solvent is limited, the fibrin not being added particle by particle,

and spread over a great extent of solution, as in the circulation, but *en masse*, to a small amount of fluid. This, however, does not interfere with the leading fact—the solubility of fibrin in the alkali.]

Effect of Ammonia on Blood. The next point consisted in ascertaining the influence of ammonia in holding blood fluid.

EXPERIMENT CCCXXI. *Effect of Ammonia on Blood.* An ounce of freshly drawn mixed blood from an ox was received into a bottle containing eight grains of ammonia with thirty minims of water. No coagulation took place; the colour of the blood was slightly darkened. The blood-corpuscles were destroyed; but small granules were present in abundance. The natural period of coagulation was four minutes and a half.

EXPERIMENT CCCXXII. *Effect of Ammonia on Blood.* One ounce of freshly drawn blood from the jugular vein of a large dog was received into a bottle containing two grains of ammonia in fifteen minims of water. No coagulation took place for several hours, so long as the bottle was kept stoppered; but, when the stopper was removed, coagulation slowly commenced, and was completed in four hours. The blood-corpuscles were modified, some of them being disintegrated.

EXPERIMENT CCCXXIII. *Effect of Ammonia on Blood.* One fluid ounce of blood from the same dog was received into a bottle containing one grain of ammonia in ten minims of water. No coagulation took place for several hours in a stoppered bottle; but a little of the blood, on being exposed in a wine-glass, coagulated in forty-five minutes. It evolved no such amount of ammonia as could be detected by a glass rod dipped in hydrochloric acid. The blood-corpuscles in this case

were unaltered. The natural period of coagulation of the blood used in this and the preceding experiment was one minute and thirty seconds.

[EXPERIMENT CCCXXIV. *Effect of Ammonia on Blood.* Five hundred grains of blood from the neck of an ox were received into a bottle containing one grain of ammonia with twenty minims of water. Ten hours afterwards, the blood remained perfectly fluid, was very dark, and evolved ammonia freely. Twenty-four hours afterwards, it was still perfectly fluid.

EXPERIMENT CCCXXV. *Effect of Ammonia on Blood.* Five hundred grains of blood from the neck of the same animal were received into a bottle containing three-fourths of a grain of ammonia with twenty minims of water. The colour of the blood darkened more than in the preceding cases; at the end of ten hours the blood remained quite fluid. Twenty-four hours afterwards, it was still perfectly fluid.

EXPERIMENT CCCXXVI. *Effect of Ammonia on Blood.* Five hundred grains of blood from the neck of the same animal were received at the same time into a bottle containing one half grain of ammonia with twenty minims of water. The blood was left exposed in the same atmosphere as in last experiment. At the end of six hours it remained completely fluid; at the end of ten hours it was rather thicker than before, but was still uncoagulated. Twenty-four hours afterwards, it was rather thicker than before, but still fluid.

EXPERIMENT CCCXXVII. *Effect of Ammonia on Blood.* Five hundred grains of blood freshly drawn from the same animal were received into a bottle containing one-fourth of a grain of ammonia with twenty minims of water. The blood remained fluid for twenty-three

minutes as it stood exposed to the air, the temperature of which was 58° Fahr. It evolved ammonia freely for several minutes. After the twenty-three minutes, coagulation commenced; and, at the half hour, the whole blood was in a firm but rather dark clot. The blood of the animal used in these four experiments coagulated naturally in two minutes on exposure to the air.

EXPERIMENT CCCXXVIII. *Effect of Ammonia on Blood.* One thousand grains of mixed blood from the neck of a sheep were received into a bottle containing one grain of ammonia with sixty minims of water. Three hours afterwards, this blood was a little thicker than before, but still fluid; it evolved ammonia freely at this time.

EXPERIMENT CCCXXIX. *Effect of Ammonia on Blood.* One thousand grains of blood from the same animal were received into a bottle of the same size, containing one half grain of ammonia with sixty minims of water. Feeble coagulation occurred at the end of thirty-five minutes. The clot became firmer; but was looser than in the two following instances.

EXPERIMENT CCCXXX. *Effect of Ammonia on Blood.* One thousand grains of blood from the same animal were received into a bottle of the same size, containing one-third of a grain of ammonia with sixty minims of water. The blood remained fluid for twelve minutes, and then coagulated in a firm red clot, from which serum exuded.

EXPERIMENT CCCXXXI. *Effect of Ammonia on Blood.* One thousand grains of blood from the same animal were received into a bottle containing one quarter of a grain of ammonia with sixty minims of water. The blood coagulated firmly in a bright red clot in three minutes. The blood of the animal used in

these experiments coagulated firmly in one minute on simple exposure to the air, at a temperature of 60° Fahr.

EXPERIMENT CCCXXXII. *Effect of Ammonia on Blood.*
I received from the neck of an ox five hundred grains of blood into a wide-mouthed vessel containing one-fifth of a grain of ammonia with a drachm of distilled water. The blood was exposed to a temperature of 60° Fahr. It coagulated in four minutes in a bright and moderately firm clot.

EXPERIMENT CCCXXXIII. *Effect of Ammonia on Blood.*
Five hundred grains of blood from the neck of the same animal were received into a vessel containing one-tenth of a grain of ammonia with one drachm of distilled water. Coagulation occurred in three minutes on exposure at 60° Fahr., as in last experiment. The clot was firm and bright. The blood of the animal coagulated in two minutes on simple exposure to the air at the same temperature.

EXPERIMENT CCCXXXIV. *Effect of Ammonia on Blood.*
One thousand grains of blood from the neck of another ox were received into a bottle containing one grain of ammonia with sixty minims of water. The blood remained fluid for three quarters of an hour, and then formed a firm coagulum on exposure to the air.

EXPERIMENT CCCXXXV. *Effect of Ammonia on Blood.*
One thousand grains of blood from the same animal were received into a wide-mouthed bottle containing three-quarters of a grain of ammonia with sixty minims of water. Coagulation took place in ten minutes; the clot being dark but firm. The blood of the animal coagulated in four minutes on simple exposure to the air.

EXPERIMENT CCCXXXVI. *Effect of Ammonia on Blood.*
One thousand grains of blood from the neck of a heifer were received into a vessel containing one grain of ammonia with sixty minims of water. This blood, exposed to the air at 60° Fahr. in a cup an inch wide, remained fluid for three hours, and then set into a very loose but red clot.

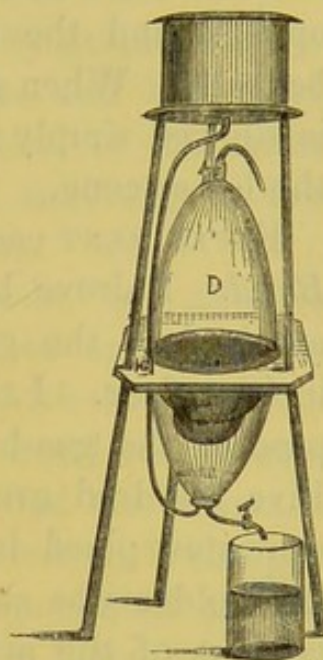
EXPERIMENT CCCXXXVII. *Effect of Ammonia on Blood.*
One thousand grains of blood from the neck of the same animal were received next moment into a bottle containing three-quarters of a grain of ammonia with sixty minims of water. Coagulation took place in seven minutes, the clot being dark but firm; serum exuded from it freely.

EXPERIMENT CCCXXXVIII. *Effect of Ammonia on Blood.*
One thousand grains of blood from the neck of the same animal were received into a vessel containing half a grain of ammonia with sixty minims of water. Coagulation took place in four minutes and a half, the clot being dark but firm. A considerable amount of serum exuded from it.

EXPERIMENT CCCXXXIX. *Effect of Ammonia on Blood.*
I received from the neck of the same animal one thousand grains of blood into a bottle containing one-fourth of a grain of ammonia in sixty minims of water. Coagulation took place in three minutes. The clot was firm, but rather dark in colour. Serum exuded from it freely. The blood of the animal used in these experiments coagulated in two minutes and a half on exposure to the air at a temperature of 60° Fahr.

Transmission of Ammonia in Vapour through Blood.
I had made the gas-holder sketched opposite. Its construction is simple. Two conical vessels of glass

(the upper one of which is represented by D) are placed with their bases together as indicated. Within the double cone thus made is an India-rubber conical bag. The base of this is grasped between the bases of the two conical vessels. The bag is thus loose in the double cone; and if air or water be driven into either cone at their apices, the bag is distended and is pushed into the opposite cone. When the bag is entirely filled, it adapts itself accurately to the side of the cone in which it may lie. At the upper part of the gas-holder is a reservoir for water; but the reservoir empties itself into the lower part of the double cone, so as to push the bag before it in filling the holder, and so drive out any contained gas through the tube emerging from the apex of the upper cone (D). The point in this gas-holder is, that there is always a layer of India-rubber interposed between the gas used, and the air or water by which it is displaced. The capacity of the gas-holder being known, any measure of gas introduced into it can be retained in it for a time without being absorbed by the water, while either air or water can be used as the displacing medium. If the gas-holder is filled with water from beneath, the gas is introduced by the upper escape tube; the stop-cock in the lower escape tube is turned open, and as the gas flows in at the top, the water flows out at the bottom. When the gas has to be displaced, the bottom stop-



cock is closed ; and the water, poured into the reservoir and let flow through the tube connecting it with the apex of the lower cone, rises in the lower cone and displaces the gas by the upper escape tube. If air is made the displacing medium, a bellows is attached to the end of the lower escape tube ; the stop-cock is opened, and the double cone is filled with air from beneath. When gas is introduced from above, the air is allowed simply to escape by the tube at the apex of the lower cone.

EXPERIMENT CCCXL. *Ammonia Vapour driven through Blood.* I drove by evaporation one half grain of ammonia into the gas holder, together with 350 cubic inches of air. I then connected a tube with the escape pipe of the gas-holder in the apex of the upper cone. Five hundred grains of blood from the neck of an ox were now placed in a long test-glass, and the tube from the holder was carried to the bottom of the blood. A current of the air charged with the ammonia vapour was gently driven through the blood by air pressure. The blood became bright red in colour, and, after five minutes, commenced to coagulate by separation of fibrin, which floated at the top in loose filaments. Not more than a fourth of the ammoniated air passed through the blood. The blood of this animal, exposed to air simply in a test-tube, coagulated in four minutes.

EXPERIMENT CCCXLI. *Transmission of Ammonia Vapour through Blood.* One and a half grain of ammonia in solution, with six minims of water, were driven by evaporation into the gas-holder, which already had received 350 cubic inches of air. Five hundred grains of blood were received into a test-tube as before ; and the ammoniated air was driven through it much more

gently than on the previous occasion. The blood remained fluid for twelve minutes, while this process was going on; a fourth part of the ammoniated air having been driven through. The current was then stopped, and simple air was driven through two hundred and fifty grains of the blood; coagulation took place in three minutes. The remaining two hundred and fifty grains were set aside in an evaporating dish at rest; and had firmly coagulated in half-an-hour. The blood of the animal used in this experiment coagulated naturally in four minutes, at a temperature of 50° Fahr.

EXPERIMENT CCCXLII. *Transmission of Ammonia Vapour through Blood.* One grain of ammonia was diffused as before into the gas-holder, with three hundred and fifty cubic inches of air. Five hundred grains of fresh blood from an ox were now poured into a potash-bulb. The potash-bulb was connected with the gas-holder, and a fourth part of the ammoniated air was driven very gently through it. The blood remained fluid for twelve minutes. The potash-bulb was next detached, and common air was driven through it. In five minutes, the current of air was stopped by the blood coagulating in the last bulb, nearest the escape tube. The blood in the other bulbs was allowed, therefore, to be at rest; and in half an hour coagulation had taken place throughout. The blood of the animal coagulated naturally in five minutes on exposure to the air at a temperature of 48° Fahr.]

EXPERIMENT CCCXLIII. *Effect of Sesquicarbonate of Ammonia on Blood.* One ounce of blood from an ox was received into a bottle containing thirty minims of water and four and a half grains of sesquicarbonate of ammonia. It did not coagulate in the bottle; but,

exposed to the air in a wine-glass, it coagulated in two hours and three-quarters. The blood-corpuscles remained perfect.

EXPERIMENT CCCXLIV. *Effect of Sesquicarbonate of Ammonia on Blood.* One ounce of the same blood, with half a drachm of water and two and a quarter grains of sesquicarbonate of ammonia, in a corked bottle, coagulated feebly in twenty-two minutes.

EXPERIMENT CCCXLV. *Effect of Sesquicarbonate of Ammonia on Blood.* One ounce of blood from the same animal, mixed with thirty minims of water and one and one-eighth grain of sesquicarbonate of ammonia, coagulated in a corked bottle in ten minutes.

EXPERIMENT CCCXLVI. *Effect of Sesquicarbonate of Ammonia on Blood.* One ounce of the same blood, mixed with thirty minims of water and 0.56 grain of sesquicarbonate of ammonia, coagulated in nine minutes.

EXPERIMENT CCCXLVII. *Effect of Sesquicarbonate of Ammonia on Blood.* One ounce of blood, received into a bottle containing thirty minims of water and 0.28 grain of sesquicarbonate of ammonia, coagulated in eight minutes and fifteen seconds. The natural period of coagulation of the blood used in the preceding five experiments was seven minutes and a half.

[*Relative Effects of the Alkalies.* I received from the neck of an ox fifteen hundred grains of mixed blood, and treated it as follows.

EXPERIMENT CCCXLVIII. *Effect of Potassa on Blood.* Five hundred grains of the blood were poured into a glass cup containing one grain of hydrate of potassa with thirty minims of water. The cup was set on the water bath at 96° Fahr. The blood remained permanently fluid, becoming of a very dark colour.

EXPERIMENT CCCXLIX. *Effect of Soda on Blood.* Other five hundred grains of the same blood were placed in another cup of the same size and shape, containing one grain of hydrate of soda with thirty minims of water. The cup was placed on the water bath at 96° Fahr. The blood remained permanently fluid, becoming dark.

EXPERIMENT CCCL. *Effect of Ammonia on Blood.* The remaining five hundred grains of blood were placed in another glass cup of the same size and shape, with one grain of ammonia and thirty minims of water. This cup also was placed in the same water bath with the previous two. This blood became dark like the others; and for a time it evolved ammonia freely. In four hours it had set into a firm clot. The blood of the animal used in these three experiments coagulated naturally in three minutes and a half on exposure to the air.

I repeated the experiments with the three alkalies on the blood of a sheep, with the same results; namely, *permanent* fluidity of the blood to which the fixed alkalies were added, and *temporary* fluidity of that to which the volatile alkali was added.*

Effect of Physical Agencies on Ammoniated Blood. Turning back to the experiments narrated above, we learn definitely the fact that ammonia not only possesses remarkable powers, even in very small proportions, of holding blood fluid, but further, that blood to which ammonia has been added remains but temporarily fluid; that, under favouring influences, the ammonia exerts its volatile force, leaves the blood, and allows coagula-

* When, in the preceding experiments, and also in those which are to come, reference is made to hundreds or a thousand grains of blood as having been used, it is to be understood that the blood was received into vessels which had been ascertained to contain the respective quantities mentioned.

tion. We have seen, moreover, incidentally, that in excess the solvent effect of ammonia extends from the fibrin to the corpuscles; but we have also seen (and this is an all-important practical fact) that ammonia, added in more minute quantities, possesses the power of holding the fibrin in solution without affecting the blood-corpuscles. Lastly, we have indicated incidentally, in one or two experiments, that the same physical conditions which favour or retard natural coagulation of blood, also and in like manner favour or retard the coagulation of blood to which ammonia has been added. This latter point is better illustrated in the succeeding experiments.

Temperature. EXPERIMENT CCCLI. *Effect of Temperature on Ammoniated Blood.* I received from the neck of a sheep sixteen ounces of mixed blood, and added to it four grains of ammonia dissolved in sixteen minims of water. I now stoppered the bottle carefully, and kept it thirty-six hours. At the end of this time it was quite fluid and dark. I next drove through it a current of oxygen for fifteen minutes; it at once became of a bright red colour, but shewed no further sign of coagulation. I then divided it into two portions, and placed them in evaporating dishes. One dish was placed in a water-bath at 96° , and kept there for two hours. The other dish was left simply exposed to the air at a temperature of 64° . At the end of two hours, the blood in the water-bath retained its red colour, was a little thicker in consistency, but still uncoagulated; while the blood exposed merely to the air had again become dark, and was as fluid as ever. The blood in the water-bath was left in that position, the fire being turned off, so that the water cooled. This was late at night; in

the morning the blood was found a firm well made clot, a little darker than when I left it. The blood exposed to the air at 64° was still quite fluid, and remained so for two days, when it gradually coagulated into a firm dark clot, with copious exudation of serum.

EXPERIMENT CCCLII. *Effect of Increased Temperature on Ammoniated Blood.* One thousand grains of mixed blood from the neck of a sheep were received into a bottle containing one grain of ammonia with sixty grains of water. The bottle, with the stopper removed, was now placed in water at 120° Fahr., a thermometer, the bulb of which was immersed in the blood standing at 94° Fahr. This blood commenced to coagulate in four minutes and a half, and in five minutes was a firm and uniform clot.

EXPERIMENT CCCLIII. *Effect of Simple Exposure to Air on Ammoniated Blood.* One thousand grains of mixed blood from the neck of the same animal were received at the same time into an empty bottle, of the same size as the one named in last experiment, together with the same quantity of ammonia. The blood was left simply exposed to the air at 60° Fahr., and coagulated firmly in six minutes.

EXPERIMENT CCCLIV. *Effect of Reduced Temperature on Ammoniated Blood.* One thousand grains of mixed blood from the neck of the same animal were received into a bottle containing one grain of ammonia with sixty of water. The bottle was then immersed in a freezing mixture, so that a thermometer, the bulb of which was placed in the blood, stood at 35° Fahr. In ten minutes this blood began to gelatinise; and in fifteen minutes it had formed a firm clot. The blood of the animal used in these experiments coagulated

firmly on simple exposure to the air within a minute after its abstraction from the body.

EXPERIMENT CCCLV. *Effects of Increased Temperature on Ammoniated Blood.* Five hundred grains of blood from the neck of an ox were received into an open vessel containing one-fifth of a grain of ammonia. The vessel containing this blood was immersed (and had been so that it might be warmed through) in water at 110° Fahr. This blood had formed a firm clot in three minutes.

EXPERIMENT CCCLVI. *Effect of Simple Exposure to Air on Ammoniated Blood.* Five hundred grains of blood from the same animal were received into a similar vessel containing one-fifth of a grain of ammonia in six grains of water. The blood coagulated at a temperature of 60° Fahr. in four minutes, the clot being bright but of loose consistence.

EXPERIMENT CCCLVII. *Effects of Reduced Temperature on Ammoniated Blood.* Five hundred grains of blood from the neck of the same animal were received into an open vessel containing the same amount of ammonia, viz., one-fifth of a grain. The vessel was then immersed in a freezing mixture, in which the thermometer stood at 10° Fahr. After keeping the blood in this position twenty-five minutes, I withdrew it from the freezing mixture, and breaking it up gently with my finger, as it was feebly frozen, I exposed it to a temperature of 50°. In three minutes it was quite fluid, but instead of coagulating at once, as in previous experiments where cold simply was used, it remained fluid fifteen minutes longer, and then solidified slowly into a bright but rather soft coagulum, from which serum exuded freely. The blood of the animal used in these experiments

coagulated in two minutes on simple exposure to the air at 60°.

I received from the neck of a heifer one thousand grains of mixed blood into a cup containing one grain of ammonia with sixty minims of water. The blood was thus held perfectly fluid, so long as it was enclosed in a stoppered bottle.

EXPERIMENT CCCLVIII. *Effect of Increased Temperature on Ammoniated Blood.* Two hundred and fifty grains of this blood were placed in a test-glass, which was then immersed in water at 98° Fahr. In three quarters of an hour the blood had thickened; and in one hour it was a firm uniform clot, from which serum eventually exuded freely.

EXPERIMENT CCCLIX. *Effect of Simple Exposure to Air on Ammoniated Blood.* Two hundred and fifty grains of the same blood were placed in a similar test-glass, and were left exposed to the air at a temperature of 60°. After five hours the blood commenced slowly to thicken; and at the end of seven hours it formed a feeble gelatinous clot. The red colour was retained. It was now placed in a water bath at 96°; and in an hour it had set into a firm, uniform clot, moulded to the vessel.

EXPERIMENT CCCLX. *Effect of Reduced Temperature on Ammoniated Blood.* Two hundred and fifty grains of the same blood were placed in a test-glass and surrounded by an ice mixture, in which the thermometer stood at 34°; at which mean temperature the cold fluid was kept. The blood became of a bright red colour; and, after standing seven hours, was still entirely fluid. The hydrochloric acid rod test detected no evolution of ammonia. I now removed the test-glass from the

cold solution to a vessel containing water at 96°. Ammonia was soon distinctly evolved, and in twenty minutes the fluid had thickened, and a small clot had appeared. In one hour this blood had firmly coagulated.

Addition of Water. Two hundred and fifty grains of mixed blood from the neck of a heifer were charged with one-fourth of a grain of ammonia in fifteen minims of water. The blood was thus held fluid in a closed bottle. Two hours afterwards, I divided this blood into four portions, and experimented on them as follows.

EXPERIMENT CCCLXI. *Admixture of Ammoniated Blood with Water at 96° Fahr.* Forty grains of the blood were placed in a cup with forty minims of water at 96°. In thirteen minutes the blood commenced to gelatinise, and soon set into a gelatinous coagulum, from which a large quantity of serum was poured out.

EXPERIMENT CCCLXII. *Admixture of Ammoniated Blood with Water at 96° Fahr.* Another forty grains of the same ammoniated blood were placed in a cup with one hundred and twenty minims of water at 96° Fahr. This blood gelatinised in ten minutes into a loose brilliant clot; from which a large quantity of water was squeezed out.

EXPERIMENT CCCLXIII. *Admixture of Ammoniated Blood with Water at 96° Fahr.* Other forty grains of the ammoniated blood were received in another cup containing half an ounce of water at 96° Fahr. This blood gelatinised in eight minutes into a soft and brilliant clot, from which a large amount of water exuded.

Exposure to, or Exclusion from, Air. EXPERIMENT CCCLXIV. *Effect of Exposure to Air on Ammoniated Blood.* One thousand grains of mixed blood from the neck of

a sheep were received into a bottle containing one half grain of ammonia with sixty grains of water. The bottle was left with the stopper out, so that the blood was exposed to the air. Coagulation commenced in thirty-five minutes; the clot becoming uniform but loose. The temperature of the air was 60° Fahr.

EXPERIMENT CCCLXV. *Effect of Exclusion of Air on Ammoniated Blood.* One thousand grains of mixed blood from the neck of the same animal were received into a bottle of the same size as last, containing one half grain of ammonia with sixty of water. The blood exactly filled the bottle. The stopper was inserted firmly, and, with this exception, the blood was left the same as in last experiment. Three hours later, the blood remained completely fluid. The blood of the animal used in these experiments coagulated naturally on exposure to the air, temperature 60°, in one minute.

EXPERIMENT CCCLXVI. *Effect of Exposure to Air on Ammoniated Blood.* One thousand grains of mixed blood from the neck of a sheep were received into a wide saucer containing half a grain of ammonia with sixty minims of water. Firm coagulation occurred in fifteen minutes, the clot being of a bright red colour.

EXPERIMENT CCCLXVII. *Effect of Partial Exclusion of Air on Ammoniated Blood.* One thousand grains of mixed blood from the neck of the same animal were received next moment into a bent tube, thirty-two inches long, similar to the one described at p. 203. In the lower bend of the tube was half a grain of ammonia with sixty minims of water. The blood commenced to gelatinise at the end of an hour, and formed a feeble but uniform clot, with free exudation of serum.

EXPERIMENT CCCLXVIII. *Effect of Exclusion of Air*

on Ammoniated Blood. One thousand grains of blood from the same animal were received into a bottle which it exactly filled, and which contained half a grain of ammonia with sixty minims of water. The bottle was securely stoppered and left at a temperature of 60° Fahr. Three hours and a half afterwards, this blood was found as fluid as at the moment when it was first drawn. The blood of the animal used in this experiment coagulated naturally on exposure to the air in two minutes.]

To one ounce of freshly drawn blood, one grain of ammonia, in solution, was added. The blood remained fluid so long as it was confined in the bottle. Two equal portions of this blood were now placed in two wine glasses.

EXPERIMENT CCCLXIX. *Effect of the Vacuum on Ammoniated Blood.* One half of this blood was placed under the bell of an air-pump, and the air was exhausted. The blood coagulated in four hours. The other portion, simply exposed to air, was firmly coagulated in eight hours.

[One thousand grains of blood from the neck of a heifer were received into a bottle containing one grain of ammonia with sixty minims of water. The blood thus suspended in a state of fluidity was subjected to the following experiments.

EXPERIMENT CCCLXX. *Effect of the Vacuum on Ammoniated Blood.* Half an ounce of the blood thus obtained was placed, ten minutes after its removal, in a wide evaporating dish; it was then put under the air-pump and the air was extracted. After being under the pump twenty minutes, bubbles of gas commenced to be slowly evolved, and in half an hour the blood had set in an uniform but soft clot.

EXPERIMENT CCCLXXI. *Effect of Exposure to Air on Ammoniated Blood.* Another half ounce of the same ammoniated blood was placed, at the time when the vacuum experiment commenced, in an evaporating dish of the same shape and size as that under the pump. This blood commenced to thicken in thirty-five minutes, but two hours later, though gelatinous, it admitted of being poured from one vessel to another in a continued stream: it ultimately formed a firm clot. The temperature of the air was 58° Fahr.

EXPERIMENT CCCLXXII. *Effect of Simple Exclusion from Air on Ammoniated Blood.* Another half ounce of the same ammoniated blood was placed in a bottle firmly stoppered. At the end of three hours this blood was as fluid as at first, but, on exposure to the air at 58° Fahr., in an open cup, it thickened, and in two hours had become a feeble coagulum.

Five hundred grains of blood from the neck of a sheep were received into a bottle containing one half grain of ammonia in thirty minims of water. This blood was divided into two parts and treated as follows.

EXPERIMENT CCCLXXIII. *Effect of the Vacuum on Ammoniated Blood.* Two hundred and fifty grains of this blood were placed in an evaporating dish under the bell of an air-pump, and the air was extracted. After working at the pump for a few minutes, I observed small bubbles of gas commence slowly to arise. The blood coagulated in twenty-five minutes.

EXPERIMENT CCCLXXIV. *Effect of Exposure to Air over a Wide Surface on Ammoniated Blood.* The other two hundred and fifty grains were placed in a saucer, so as to form a thin layer. The blood was then exposed to the air at 60° Fahr. At the end of twenty-five minutes

the blood was a little thicker than at first; and in thirty-five minutes it had formed a feeble clot. The blood of the animal used in these experiments coagulated naturally in two minutes on simple exposure to the air.

Five hundred grains of blood from the neck of another sheep were received into a bottle containing half a grain of ammonia with thirty minims of water. This blood was then divided into two portions.

EXPERIMENT CCCLXXV. *Effect of the Vacuum on Ammoniated Blood.* Two hundred and fifty grains of this blood were placed in an evaporating dish, and exposed to the vacuum. Small bubbles of gas slowly escaped as before; and coagulation was firm in twenty minutes.

EXPERIMENT CCCLXXVI. *Effect of Exposure to Air over a Wide Surface on Ammoniated Blood.* The remaining two hundred and fifty grains of blood were placed in a saucer, and exposed to the air at 60° Fahr. Coagulation commenced at the end of twenty-three minutes; and in twenty-nine minutes there was an uniform clot, but less firm than that in the vacuum. The blood of the animal coagulated naturally in forty seconds on exposure to the air.

EXPERIMENT CCCLXXVII. *Transmission of Ammoniated Blood through Tubes of different Diameters.* I drew six thousand grains of blood from the neck of an ox, and added to it six grains of ammonia with an ounce of water. I then repeated with this blood the experiments related at page 184, *i. e.*, I poured it into the vessel with emptying tubes of different diameters as there depicted, and caught the blood in beakers as before. The blood continued to stream through the tubes without intermission for twenty-five minutes; and, as the centre vessel emptied itself into the beakers,

their contents were steadily and orderly re-poured into the centre vessel. At the end of the twenty-five minutes, the current stopped from coagulation in the small tube, the point of which was the thirty-second of an inch in diameter, and such blood as last flowed through it coagulated in the beaker. At the end of half an hour, the current in the sixteenth of an inch tube stopped from the same cause, and the blood it had poured into the beaker also coagulated, and at the end of thirty-seven minutes, the blood passing through the eighth of an inch tube, underwent the same change. At this moment, the larger mass of blood flowing through the quarter inch tube was fluid, and continued in current until forty-five minutes had elapsed; then a long gelatinous coagulum filled and hung from the tube, and the current stopped. A few minutes later still, the mass of blood remaining in the centre vessel had formed a loose clot, which eventually became very firm. The blood of the animal used in this experiment coagulated naturally in four minutes. The temperature of the day was 56° Fahr.

Rest and Motion. EXPERIMENT CCCLXXVIII. *Effect of Agitation in a Closed Vessel on Ammoniated Blood.* One thousand five hundred grains of mixed blood from the neck of a sheep were received into a bottle with a narrow neck, containing one half grain of ammonia with sixty minims of water. I placed my thumb firmly over the neck of the bottle, and kept the fluid in gentle oscillation. The blood remained fluid for seven minutes, and I poured it into a beaker. On returning it to the bottle, it commenced to coagulate, evolving ammonia feebly. It formed a firm red clot.

EXPERIMENT CCCLXXIX. *Effect of Rest on Ammoniated*

Blood. Other fifteen hundred grains of blood from the neck of the same animal were received next moment by an assistant into a wide open cup containing half a grain of ammonia with sixty minims of water. It was thus left at rest exposed to the air at 60° Fahr., and coagulated firmly in four minutes, the clot being of a bright red colour. The blood of the animal used in these two experiments coagulated, on simple exposure to the air, in one minute.]

EXPERIMENT CCCLXXX. *Whipping out Fibrin from Ammoniated Blood.* I received two pints of blood from the neck of a bullock. Each pint was placed in a basin of the same size and shape. The temperature was 50° Fahr. Immediately before the blood was received in the basins, I moistened the inner surface of each with thirty minims of liquid ammonia (sp. gr., .882). When filled with blood, the basins were placed side by side on the same table, together with another portion of blood which had not been ammoniated. The blood in one of the basins containing ammonia was now briskly whipped. In three minutes and sixteen seconds, the natural blood coagulated; the ammoniated blood that was whipped evolved a very decisive odour of ammonia, which soon passed away, and, as it disappeared, the fibrin began to coagulate on the rods. The ammoniated blood left at rest evolved ammonia for half an hour, and then coagulated, separating into serum and clot, and evolving no more ammonia.

[EXPERIMENT CCCLXXXI. *Effect of Simple Whipping of Blood.* I caught five ounces of blood in a basin from the neck of an ox, and handed it to an assistant, who whipped it briskly with a bunch of twigs. The fibrin adhered to the twigs, and the blood was completely defibrinated in five minutes.

EXPERIMENT CCCLXXXII. *Effect of Whipping Ammoniated Blood.* From the neck of the same animal I received other five ounces of blood into a basin containing five grains of ammonia in solution with sixty grains of water, and handed it to another assistant, who commenced at once to whip it with a bunch of twigs, and continued this process for half an hour. The blood became of a bright red colour, but no fibrin adhered to the twigs. I now set this blood aside for eight hours, at a temperature of 60° Fahr. It retained its red colour, and evolved ammonia during the whole of this time, continuing also fluid. At the end of nine hours it commenced to thicken, and the ammoniacal odour was lost. At the end of ten hours it had coagulated, and formed an uniform firm and bright red clot.

EXPERIMENT CCCLXXXIII. *Effect of Rest on Ammoniated Blood.* From the neck of the same animal I received other five ounces of blood into a basin, containing five grains of ammonia with sixty minims of water. This blood was once gently stirred round, and was then set aside at the temperature of 60° Fahr. It became of a very dark colour. At the end of ten hours, this blood continued to evolve ammonia, and remained perfectly fluid. It was now poured a few times from one basin into another, and was left with a wide surface exposed to the air. At the end of twenty-four hours, it had coagulated in a moderately firm but diffuse clot. The blood of the animal used in this experiment coagulated on simple exposure to the air, and at rest, in three minutes.

I received three thousand grains of blood from the neck of a sheep, and added to it one grain and a half of ammonia with three drachms of water. I then

divided it into two portions, which were treated as follows.

EXPERIMENT CCCLXXXIV. *Effect of Whipping Ammoniated Blood.* One half of the blood was poured into a basin, and was whipped briskly with a bunch of twigs. In three minutes the twigs were loaded with fibrin, and the defibrination was perfect; since, on using another bunch of twigs, no further fibrin could be extracted, and the fluid remained uncoagulable.

EXPERIMENT CCCLXXXV. *Effect of Simple Exposure to Air and Rest on Ammoniated Blood.* The other half of the blood was placed in a similar basin, and simply exposed at rest to the air at 58° Fahr. Coagulation occurred in nine minutes.

EXPERIMENT CCCLXXXVI. *Simple Whipping of Blood.* A portion of blood, the same in quantity as in the preceding two experiments, was caught by an assistant from the neck of the animal, and was whipped with a bunch of twigs. This blood was entirely defibrinated in one minute. The blood of the animal used in these experiments coagulated naturally in one minute on exposure to the air.

Three thousand grains of blood from the neck of a sheep were caught in a vessel containing one grain and a half of ammonia with three drachms of water. This blood was divided into two portions.

EXPERIMENT CCCLXXXVII. *Ammoniated Blood in a Current.* One half of the blood was poured into a beaker, and was kept in constant current into another beaker, backwards and forwards. Coagulation occurred in four minutes, so that the whole mass could be turned out of one beaker into another in an uniform clot.

EXPERIMENT CCCLXXXVIII. *Ammoniated Blood at Rest.*

The other half of the blood was placed in a basin and allowed to remain at rest in the air at a temperature of 58° Fahr. It remained fluid for eight minutes; at the end of nine minutes, it had set into an uniform soft clot, which afterwards became firm. Serum freely exuded from it.

We thus see that the physical agencies exert, as a general rule, the same influences on artificially ammoniated blood as on natural blood, with one exception—namely, where water is added in excess. But here the exception proves the rule; for, as the ammonia was present in excess in the experiments named at p. 304, so it ought to obtain, that when this excess of the ammonia was distributed over a wider surface by the addition of water, the coagulation should be quickened as compared with the other ammoniated blood, though still slower than in natural blood. When Mr. Gulliver retained blood fluid for fifty-seven weeks with nitre, and then caused it to recoagulate by the free addition of water, as has been mentioned at p. 48, he performed virtually the same experiment with another chemical; that is to say, he largely diluted the added solvent.

When blood is naturally a long time coagulating, the same occurrence may sometimes take place, and may mislead the observer as to the effect of the addition of water to blood. The following experiment is in point.]

EXPERIMENT CCCLXXXIX. *Addition of Water to Blood.* Five drachms of water were put into a clean wide-mouthed bottle, and upon this four drachms of freshly drawn blood were poured and mixed with the water by gentle shaking. At the same time six drachms of water were placed in a similar bottle, and two drachms of the same blood were added to it. I thus obtained

two solutions, in one of which the blood preponderated, in the other, water. The results were as follows:—Blood drawn at the same time coagulated naturally in five minutes; the blood largely diluted with water coagulated more firmly in the same time; while the blood containing the small proportion of water was fluid for eight minutes, and at last formed only a feeble clot. A similar experiment has been recorded by Mr. Blake.

These results have a bearing on experiments xxxvi to xl, where water, thrown into the system in large quantities, produced fluidity of blood.

[*Production of Coagulation in Blood Surcharged with Ammonia.* I have shown in preceding experiments, that when excess of ammonia is added to blood, such blood remains permanently fluid at ordinary temperatures. It also acquires a dark colour on exposure to the air, and rapidly absorbs carbonic acid. But this blood, thus held fluid by the excess of its solvent, may be made to coagulate in ways very simple and striking. Addition of water at 96° is one mode by which this change can be established. Experiments ccclxi to ccclxiii illustrate this fact without further comment. The addition of very dilute solutions of acids leads to the same result. Exposure of such blood for some time in the water bath at 98° Fahr. is sufficient to ensure coagulation if the proportion of ammonia added be slight, and the blood be not excluded from the air.

EXPERIMENT CCCXC. *Coagulation of Blood held Fluid for Twenty Hours, by Exposure to a Temperature of 98° Fahr.* I placed in a bottle five hundred grains of white of egg, together with a quarter of a grain of ammonia in solution with two drachms of water. I then received into the same bottle five hundred grains of

mixed blood from the neck of an ox. Shaking these solutions together, I carefully stoppered the bottle containing them, and placed it in water at 32° Fahr. until such time as I could manage the following details.

I took a piece of glass tubing of half inch bore, closed it at one end like a test-tube, and then cut it to such a length that it would just hold the thousand grains of solution named above. This being done, I poured the solution into the glass tube, hermetically closed it, and set it aside in the perpendicular position at a temperature of 60° Fahr. In the course of one hour the blood-corpuscles began to sink, and in twenty hours they were all congregated in the lower three inches of the tube. I now filed a small hole in the tube at a line one inch above the corpuscles, and, re-opening the tube at the top, decanted off the upper and clear liquor. This was a viscid feebly pink solution, and may be considered as a kind of liquor sanguinis.

Returning to the blood-corpuscles and the remaining solution in the lower part of the tube, I turned the whole into an evaporating dish, and added a part of the supernatant solution. There was no trace whatever of clot; and, on gentle stirring, the corpuscles again commingled with the surrounding fluid. I then placed the evaporating dish with its contents in the water bath at 98° Fahr., gently stirring up the fluid occasionally. Ammonia was steadily evolved. In four hours feeble coagulation had occurred; and in six hours the whole was an uniform dark coagulum, from which no serum exuded.

But the most interesting fact in this matter is, that superammoniated blood may be made to coagulate by the very cautious addition of the fixed alkalies

or of the hydrate of lime. I subjoin experiments bearing on this demonstration.

EXPERIMENT CCCXCI. *Coagulation of Blood held Fluid by Ammonia on Addition of Potassa.* One hundred grains of blood from the neck of a sheep were received into a bottle containing one-twentieth of a grain of ammonia with two minims of water. The bottle was kept securely closed; and, twenty-four hours afterwards, the blood was found as fluid as at the moment when it was drawn. I now added to the blood one-twentieth of a grain of hydrate of potassa, and set the blood in a water-bath at 98° Fahr. It evolved ammonia feebly; and in two hours it had commenced to thicken, and soon set in a firm natural clot, modeled to the capsule containing it, and resembling in every way a recently formed natural coagulum. A little serum exuded. Another portion of the ammoniated blood, left simply exposed to the air, remained permanently fluid.

EXPERIMENT CCCXCII. *Coagulation of Blood held Fluid by Ammonia on Addition of Lime.* Sixty grains of mixed blood from the neck of a sheep were placed in a capsule containing one-twentieth of a grain of ammonia with three minims of water. This blood was thus rendered permanently fluid at ordinary temperatures, and soon acquired a dark colour. After twenty-four hours had elapsed, I added to it one half-drachm of water recently saturated with lime, and then placed it in its capsule in a water-bath at 98° Fahr. Ammonia was evolved; and in three hours the blood had set in a beautiful firm clot, which was modeled to the vessel: a considerable quantity of serum exuded from it, and it resembled in every way a recently and spontaneously formed coagulum.

EXPERIMENT CCCXCIII. *Coagulation of Blood held*

Fluid by Ammonia on Addition of Lime. One hundred grains of mixed blood from the neck of a sheep were received into a bottle containing one-tenth of a grain of ammonia with six minims of water. The blood remained fluid for twenty-four hours, exposed to the air at 60° Fahr. ; it also acquired a dark colour. At the end of this time, I took a grain of unslaked lime, slaked it, and made it into milk of lime with five minims of water. I then added the milk of lime to the blood in an open cup, setting the cup in a water-bath at 98°. Ammonia was now distinctly evolved ; and in four hours the blood had formed a dark feeble coagulum, from which serum exuded. Another hundred grains of blood from the same animal, which had been treated with ammonia in the same proportion, and which was simply left at rest at the same temperature (98°) did not coagulate.

In these experiments, especially if potassa or soda be employed as the displacing agent, the greatest delicacy is required. For, if too much of the alkali be added, it not only displaces the ammonia, but takes its place, and the fibrin is dissolved by the fixed alkali. This event, while it leads to apparent failure in many experiments, may be avoided with proper care. During the experiment, the blood should be kept at 98° Fahr.

Re-solution and Recoagulation of Blood-Clot. When once blood has coagulated, or when fibrin has been removed in the separate state, rapid re-solution either of red clot or simple fibrin is exceedingly difficult. This is due apparently to mere physical causes,—*i. e.*, the particles of fibrin come so closely and compactly together after their precipitation, that the solvent enters

into contact with a limited surface only of the substance to be dissolved. Thus time is required; and although in time solution is produced, the production of the solution is attended with changes in the fibrin which destroy in a great measure its ordinary and normal properties. The same modification is produced if the fibrin be evaporated to dryness, and be afterwards redissolved in an alkaline solvent. In the circulating blood, matters are arranged in a way which is inimitable out of the body. Bostock expresses with great force the conditions in the body, when he speaks of the fibrin being added, as it were, particle by particle; but he does not here express the whole fact, for it is probable, if not absolutely demonstrable, that the fibrin is never in other than in a fluid or semifluid condition during healthy life.

From these causes, the re-solution and recoagulation of blood-clot or of fibrin, *per se*, is an experiment not so easily done as might, *a priori*, be presumed from a perusal of the foregoing experiments. I have, however, seen this accomplished; first by accident or rather empirical experiment, and afterwards by a more accurate and systematic process. A few examples will convey the results of the researches which I have made on this subject.]

EXPERIMENT CCCXCIV. *Solution and Recoagulation of Coagulated Fibrin.* An assistant once brought to me from Mr. Mavor, the veterinary surgeon, eight ounces of blood which had been drawn from the jugular vein of a horse. The blood had coagulated slowly, giving a buffy coat an inch in thickness, which completely filled at its upper part the diameter of the long narrow vessel into which the blood had been received. The blood was thus spontaneously divided into two portions: the solid

fibrin lay at the top, and the serum and blood-corpuscles beneath. I made a hole with a glass rod through the centre of the fibrinous coagulum, and poured through it sixty minims of liquor ammoniæ, of specific gravity .882. The vessel was now closed and set aside at a temperature of 65° Fahr. In the course of half an hour, the coat of fibrin was much reduced in size, and, instead of lying close to the side of the vessel, it was floating easily on the fluid part. After the lapse of two hours, this dissolving process seemed to have ceased. The mouth of the vessel was now left open to allow evaporation. There was a free escape of ammonia. After two hours, on examination, I found that the lower and previously fluid part of the blood had become firmly coagulated into a red clot modeled to the bottle. The remainder of the original crust of fibrin adhered to it at the top.

In this first experiment in the present direction, the results, though arising in part through accident, were not less instructive. They proved the solvent effect of ammonia upon fibrin; and also that separated fibrin, thus held in solution and re-mixed with serum and blood-corpuscles, will, under favouring conditions for the escape of the solvent, be reprecipitated and give rise to the formation of red clot.

[EXPERIMENT CCCXCV. *Re-solution and Recoagulation of Blood Clot.* I had a few pounds of blood caught from the neck of an ox, and set it aside for twenty-four hours, that the serum might separate completely. When this had occurred, I removed from the clot two hundred and fifty grains, and placed this portion of clot in a mortar. I next drew off two hundred and fifty grains of the serum in which the clot floated. I then added a

minim and a half of liquor ammoniæ (specific gravity .882) to the serum; and, breaking up the clot in the mortar gently with my fingers, I gradually added to it the ammoniated serum, and gently triturated with the pestle, continuing this process until the whole of the clot had entered into solution. The process is very tedious, for small portions of clot slip from the pressure of the pestle; but with care and time the re-solution may be made perfect. When the clot was entirely dissolved, the solution formed had a slimy feel like newly drawn blood; and a drop of it, remaining on the warm hand, formed also a thin glutinous layer like fresh blood. I poured the solution thus made into an evaporating dish, and, adding to it a little milk of lime (made by slaking four grains of lime and adding water), placed the dish on water-bath at 100° Fahr. Ammonia was freely evolved, and in fifteen minutes the blood had reset into a dark clot, a little more treachy in character than the previous blood clot, but firm and uniform. A little serum exuded from this clot.

EXPERIMENT CCCXCVI. *Re-solution and Recoagulation of Blood-Clot.* I drew from the neck of a sheep a few ounces of blood, and set it aside that it might coagulate. I then weighed out two hundred and fifty grains of the clot before serum had exuded, placed it in a mortar, and triturated it, adding carefully ten minims of water containing one-sixth of a grain of ammonia. After one hour's constant trituration, during which five minims more of the ammonia solution were added, the clot was entirely dissolved; it formed a sticky solution, which smelt strongly of ammonia. This solution was now placed in an open vessel, and a little milk of lime, made from three grains of fresh lime, was added. The vessel

was next placed in the water bath at 98° Fahr. In three hours, the blood had coagulated.

EXPERIMENT CCCXCVII. *Re-solution and Recoagulation of Blood Clot.* In performing an experiment with my colleague, Dr. Halford, in which the jugular vein of a dog was laid bare, I punctured the vein, and drew off half an ounce of blood into an evaporating cup containing half a grain of ammonia dissolved in two minims of water. I next drew off another half ounce of the same blood into a clean evaporating dish, and allowed it to coagulate. The moment it coagulated, I transferred the clot to the dish containing the ammoniated blood, which was still fluid. I then gently broke up the clot with my fingers, and caused it to entirely redissolve in the ammoniated blood. The combined fluid was now set aside, and in half an hour it had formed an uniform coagulum.

This experiment, exceedingly simple to perform, is not always so successful as in the above example. On another occasion, where Dr. Halford and I were similarly engaged, I again performed the experiment; but, in mixing the blood-clot with the ammoniated blood, I stirred too quickly, and so separated the fibrin from both specimens. The result was a whipped blood, in which the fibrin floated in the defibrinated serum.

From the contraction of blood-clot there is a difficulty, as I have before shown, in perfectly redissolving the clot in alkaline solutions. To avoid the loss of time thus demanded, a simple plan is the following.

EXPERIMENT CCCXCVIII. *Re-solution and Recoagulation.* I received a thousand grains of blood from the neck of a sheep into a vessel containing a thousand grains of water. As soon as a clot had formed, and before there was any separation of water from it, I turned it into a mortar,

and, adding to it two-thirds of a grain of ammonia in solution with six minims of water, rubbed the clot up gently and steadily until complete solution had occurred. I then placed this solution in the water-bath at 98° , and added to it fresh milk of lime, made from eight grains of the alkaline earth. There was a free evolution of ammonia, detectable by the smell, for twenty minutes. The odour now became fainter, and in an hour the blood had again become a soft, dark, uniform clot, modeled to the containing cup.

In these experiments, potassa, as the displacing agent, is much better than lime, the clot being then firmer, of a brighter red, and better modeled. But more care is required in the addition of the potassa, an excess leading to continued solution, from the replacing of the volatile solvent by one which remains fixed in the fluid.

In so far, then, as experimental research can lead to practical results, we are brought by the simplest inductive evidence to the recognition of two facts,—the one obtained by the analytical, the other by the synthetical process of inquiry. The first is, that an ammonia is given off from blood freshly drawn; the second, that ammonia, added to blood thus drawn, suspends the process of coagulation, such suspension of the process being modified by precisely the same physical conditions, varying only in degree, as those which modify the process of ordinary coagulation.

I wish in this present work to push this proposition but little further. Various refinements of detail are open for argument and research; but for the full elaboration of these much time, thought, and work are demanded from the future. Meanwhile, as an index to what has to be done, one or two brief reflections come legitimately on the page.

The process of coagulation may be in part imitated by many simple plans. If a little isinglass be dissolved in hot water, and, when cooled, mixed up with defibrinated blood, it commingles with the blood and forms red coloured fluid. If this fluid be set aside so as to allow the isinglass to gelatinise, it forms with the blood a beautiful coagulum, wonderfully like the ordinary blood-clot. Even watery matter, like serum, will sometimes exude from this mass.

Now here the process of coagulation, if I may thus use the term, is the result of the evolution of heat simply; and in this respect the process differs in detail and in cause from normal coagulation of blood. But the general appearances as regards the changes which the fluid undergoes are the same—viz. the precipitation of a contractile substance in a mixture of serum and blood-corpuscles.

The deposition of the solid matter of collodion on the evaporation of the ether is a kindred process.

There are other substances than fibrin which, held in solution in ammonia, are precipitated on the withdrawal of that alkali. If twenty grains of shell lac be treated with half an ounce of boiling water, the shell lac rises to the top, adheres in a mass, but remains insoluble, and communicates no colour to the water. Let five minims of the stronger solution of ammonia be added, and the resin at once dissolves. Now treat the solution with hydrochloric acid, or cautiously with potassa or caustic lime, or expose it to heat over a wide surface of glass, and the resin is precipitated, with evolution of its solvent.*]

* In the manufacture of hats, the solvent property of the volatile alkali is thus taken advantage of. The wall of the hat is stiffened with shell lac, which is first

It is a question as yet undecided, in what form the volatile alkaline solvent of the fibrin exists in the blood. The extreme smallness of its amount in healthy blood, as well as the difficulty, of which mention must yet be made, of securing the capture of all that is given off in the halitus of a certain definite weight of blood, render the question now before us one of great practical difficulty. In my experiments, I have either liberated the ammonia, or, by passing it free or combined through hydrochloric acid, have fixed it in combination with that acid. As common ammonia (N H_3) it will possess, existing either in the free state, or in combination with carbonic acid in the form of volatile or neutral carbonate, all the properties necessary for sustaining fluidity under one set of physical conditions, and for allowing coagulation under conditions of an opposite nature. We might, therefore, assume its evidence in either of the states. We might, moreover, assume the possibility of its existence in each of these conditions in different parts of the blood-circuit, *i. e.* free in the arterial, in combination in the venous blood. In the ammonia which is evolved with the breath (of which an after-word will be supplied) there is a definite combination between the alkali and the carbonic acid, as will be proved hereafter. At the same time, it is clear that the combinations of ammonia with other blood-constituents are never in healthy blood so fixed as to prevent the elimination of the ammonia from blood itself, at a temperature of 98° Fahr., and exposed freely to the air.

dissolved in a weak solution of ammonia. The fabric is steeped in the solution; the ammonia is driven off by heat; and the resin, left stranded in the fabric, imparts the firmness which supports the body of the hat. The operation thus performed by the hatter, is possibly but a repetition of what occurs in nature, when the resin, after being brought fluid to the surface of the plant, is deposited in the solid state on exposure to the air.

[A question which also presents itself as of great interest is, whether the ammonia evolved in the blood halitus of *all* animals is ammonia as N H_3 , or an ammonia in which nitrogen is combined with a basic radical in lieu of the simple element. There are many ammonia bodies of this latter class, such as methyl-ammonia ($\text{C}_2 \text{H}_5 \text{N}$), ethyl-ammonia ($\text{C}_4 \text{H}_7 \text{N}$), biethyl-ammonia ($\text{C}_8 \text{H}_{11} \text{N}$), all having properties so closely allied to the simple ammonia (N H_3), that they may be considered practically (*i. e.* as regards effect) identical with the simpler form; and these ammonias seem so closely intimate with the organic changes, that a new and wide field of inquiry lies directly open in this direction. From analogy it may be supposed that these ammonias would exert, if present, the same influence on blood as the simpler and better known representative of this chemical series. But for the elucidation of this matter, which I shall not be slow to follow out and record at a future day, experiment is required. It must not only be determined whether an ammonia, having an identical formula, is present in each grand division of the animal kingdom, but whether the same rule obtains in the same animal under varying external conditions, and in conditions of disease. Meantime, I rest content in describing, by analytical and synthetical research, the influence of the simpler ammonia, and in leaving the fact of its influence already related as one of the major propositions of this work, and as the basis of all that may follow from it.]

It was at first a doubtful question with me, whether ammonia could be evolved from blood with sufficient rapidity to account for the rapidity of coagulation. This doubt was dispelled by the repeated observation that

the amount of ammonia, as obtained on the microscope glass in the form of chloride of ammonium, was not modified by the rapidity of coagulation if the experiment were expeditiously done. Thus in sheep's blood, which coagulates rapidly, the evidence of the crystals was as marked as in the case of ox's blood, where the process extended over three or four minutes. Thus the fact stood, that the rapidity of evolution held a direct relation to the rapidity of coagulation. The doubt was still further dispelled by the observation that ammonia added to blood is also driven off, and that coagulation proceeds in proportion to such evolution.

[But why such rapid evolution? The answer is simple, and is explained in those experiments, where blood surcharged with ammonia was treated with another alkaline substance. The chemist, in order to liberate ammonia, adds milk of lime or caustic baryta, and with gentle heat eliminates the volatile alkali from the substance containing it. What the chemist here performs in the laboratory, the nature chemist has anticipated. In the exquisite balance of the chemical forces in the blood, it is arranged that the blood is feebly alkaline from fixed alkali or alkaline salt; not sufficiently alkaline to hold fibrin in solution, but sufficiently so to leave the volatile alkali free for this purpose in the closed chambers of the circulation. When, however, the blood is exposed to the air or the vacuum, the volatile alkali, having no fixed combination, is evolved, each addition of temperature being now subservient to the more rapid evolution, and the fibrin is precipitated.]

The question, how or where the ammonia is formed in the body, I must leave open. The elements of the alkali, in whatever modification it may exist, are present.

In the organic world, the combination of these elements for the construction of the alkali is a common phenomenon. From the experiments of Milne-Edwards, it is known that a slight loss of nitrogen occurs in respiration. What is the destination of this? There is ammonia in the air. Is this a product from the animal world, or a gift to it? In the metamorphosis of the nitrogenous tissues in the living body, is an ammonia a normal and necessary product? These are mere suggestions, and as such are left with the reader.

The reason why the evolution of an ammonia from blood has not been previously shown is easily explained. It had not been looked for in blood-halitus. Notwithstanding Scudamore and Polli's laboured researches, it had not been absolutely proved that coagulation depends on the elimination of volatile matter at all. Lastly, the proportion of volatile alkali necessary for holding blood fluid, is so exceedingly minute, as compared with the mass of blood, that its presence might easily escape observation. Ammonia, indeed, could not be expected to be found in quantity in the serum or clot of healthy blood, its elimination occurring in the act of coagulation. According to the time at which the analysis of blood commenced after abstraction, and according to other accidental conditions, such as the healthy or modified condition of the blood operated on, a little of the alkali might or might not be fixed and retained. Hence some chemists have found, in their inquiries, evidence of chloride of ammonium; others have not. The explanation of the two facts is easily understood.

[In some extreme conditions of disease, however, where the alkali entered into combinations which fixed it for the chemist's hand, or where the proportion of

ammonia was raised, as in Dr. Blair's examples of the blood in yellow fever (to which reference will be made in the Appendix), the evidence of its presence was obvious enough.

To ascertain with precision the absolute quantity of ammonia required to hold fibrin in solution in the circulating blood, is a point surrounded with grave difficulties, not only on account of the smallness of the quantity itself, but from the fact that the physical conditions of the healthy circulation cannot be imitated to perfection out of the animal body, and that the proportion is obviously not the same in every kind of animal, nor yet in the same animal at all times. These facts are of immense moment. In sheep's blood, coagulation occurs in a period of time at least two-thirds less than in that of the ox, while ammonia must be added in larger quantities to sustain the fluidity of the blood of the ox than of the sheep. The inference from these facts is, that in ox's blood the amount of the volatile solvent is greater in proportion to the fibrin; while in the sheep, the amount is smaller in proportion to the fibrin. When, again, an animal is exhausted by fatigue, the coagulation of blood is slow, and the solvent evolved is better secured, as I have shown by experiment. In like manner, in exhausted states, the evolution of ammonia by the breath is more free and decided. These results are possibly due to a greater development of ammonia, as a result of metamorphosis of the tissues.

At first sight, the amount of ammonia required to hold blood fluid seems incredibly small when considered in relation to the mass of *blood*. But it is wrong to consider this relationship at all; for the point to be settled is, what proportion must the alkali bear to the

fibrin in any given quantity of blood? If, then, we take 2·2 grains of fibrin as the proportion normal to a thousand grains of blood, we have to discover how much of alkali would be required to hold this small quantity of fibrin in solution, in a serum already slightly alkaline, but not sufficiently so for such solution. Moreover, we have to consider this problem in connexion with the admirable physical arrangements of the circulation, by which it is insured, not only that the mass of fibrin thrown into the general circulatory channels is added particle by particle, but that, in the rapid circulation, the fibrin is held in solution for the brief space of time only, during which it remains in the blood before being given up to the tissues.

In health, there is unquestionably a definite relationship between the amounts of fibrin and of its solvent; which relationship is susceptible of but little variation without the development of general disorder. If the proportion of alkaline solvent is beneath the natural standard, the fibrin is imperfectly held in solution, and its deposition is imminent; while, if the proportion of alkali exceed the normal standard, not only is the fibrin held more decidedly fluid, but the blood-corpuscles also become subject to dissolution—an event which seems inevitable, if the quantity of alkali exceed one part in a thousand of blood.

Returning to the absolute question, what proportion of ammonia is required in the normal circulation to hold the fibrin in solution, there are two modes of investigation—the one directed to the detection of the exact amount of ammonia evolved from a given quantity of recently drawn blood—the other directed to the determination, as far as possible, of the smallest amount

of the alkali required to sustain the fluidity of drawn blood under conditions approaching, as nearly as possible, to the conditions of the circulation itself. Both these investigations are, however, attended with so many difficulties, that the results to which they lead can be considered as approximative only. The experiments given at pp. 274-6, while valuable in their way, must be accepted simply as qualitative; since a great loss of volatile matter occurred in transferring the blood from the animal operated on to the containing vessel. To render these more complete, I made several attempts to receive the blood at once in large quantities from the vessels of animals, and to wash over the gases evolved into an acid solution, driving the atmospheric air first through sulphuric acid, to remove all fallacies in reference to the traces of ammonia in the atmosphere. But, owing to the delicacy of the fact to be determined, and to the modifying influences detailed above, the results have been too varied to admit of close argument, though sufficiently valuable to lead to a longer series of similar observations.

By the synthetical process, some kind of approximation to the answer of the problem of quantity may be cautiously approached; for, although it does not show the *minimum* of alkali required for the solution of the fibrin in the normal circulation, it proves that a certain quantity there present is sufficient for all required purposes; and that an excess, over and above a certain proportion, would be detrimental. Thus Experiment cccxxvii shows that one-fourth of a grain of ammonia to five hundred grains of ox's blood, or, in other words, one grain of the alkali to two thousand of blood, are sufficient, even after exposure to the air, to hold the blood long fluid. Experiment cccxxx shows that one

grain of the alkali, in three thousand grains of sheep's blood, was sufficient to retain fluidity for twelve minutes; this blood being at rest and exposed to the air at 60° Fahr.

But the proportion of alkali is better shewn in Experiment CCCXLII, where a fourth of a grain of the alkali in vapour, diffused through 87·5 cubic inches of air, was sufficient, thus diluted, to retain the fluidity of five hundred grains of blood, so long as it gently passed through it. In this experiment, better than in any preceding, the relative positions of the ammonia and blood in the system were imitated. The blood, from the first fluid, was steadily supplied with the diluted portion of ammonia gas, which constantly passed in current with the air through the blood, at the rate of 0·12 cubic inch of the combined gas per second. With such thorough current of air through the blood, it is doubtful if any accumulation of ammonia would occur; and we must, therefore, leave the cause of the sustained fluidity to the equal and constant diffusion of the alkaline gas.

Another experiment further proves this point.

EXPERIMENT CCCXCIX. *Blood Retained Fluid by Ammonia and Motion.* I received two thousand grains of blood from an ox, added to it one fourth of a grain of ammonia in a drachm of water, and instantly transferred the whole to an apparatus similar to the one described at page 224. When the blood was fairly in its closed circuit, it was kept in steady circular motion for an hour. It was then withdrawn, entirely fluid; but, on exposure to the air, quickly underwent coagulation. There was no separation of fibrin within the bags.

To sum up, and as an approximation towards the fact, I opine, from all my experiments, that a propor-

tion of one part of alkali to sixteen of fibrin, or, in other words, nearly one part of alkali to eight thousand of blood containing 2·2 per thousand of fibrin, would be sufficient for retaining the perfect fluidity of normal circulating blood. The proportion may be less, but it need not be more.

Remak was, I believe, the first to observe that blood, which remains for a long time fluid, undergoes putrefaction very slowly. If ammonia be added in excess to blood, and the whole be then exposed to the air, there is a rapid absorption of carbonic acid, and putrefaction and coagulation are in like manner equally suspended. When, again, blood, which has coagulated, is set aside in a warm place and exposed to the air, so that putrefaction commences, there is a free development of ammonia and dissolution of the clot; and I have sometimes even been able to produce a soft coagulum in the fluid in which clot has been thus dissolved, on displacing the alkali by the addition of milk of lime at a temperature of 100° Fahr.

Irrespectively of the use of the volatile alkali as a blood-solvent, it is impossible to over-estimate its other properties in the animal economy. The learned Lehmann has anticipated me in pointing out that many of the processes of secretion and deposition of solid matters in the body may be connected with the removal of their volatile alkaline solvent. The coagulation of serous fluids, of chyle, and lymph, is possibly due to a similar evolution.

Lastly, the formation of ammonia in animal bodies, and its excretion from them, connects more intimately, as I shall afterwards show, the relationship which exists between the animal and vegetable worlds.]

CHAPTER VII.

PHENOMENON OF THE BUFFY COAT.

"The physiological consideration of the things which are according to nature, is to be first undertaken by medical men; since that which is in conformity with nature is right, and serves as a rule both to itself and to that which is wrong."
HARVEY.

THE peculiar form of coagulation denominated the "buffy coat," is essentially nothing more than a separation of fibrin in the isolated form from coagulating blood. The process, as thus conducted, does not differ much from what occurs when blood is briskly stirred and the fibrin is left floating at the top, except that in the latter case the fibrin is separated in irregular masses, not in one uniform mass as in buffy blood. Nasse has already shewn, and my own experiments corroborate his observations, that by merely arresting the process of coagulation by physical means, as by adding some thick substance, the molecules of fibrin are prevented from coming together, and the buffy coat sometimes results. My own experiments have further shown that, if coagulation is partially suspended for a time, (as by passing blood-vapour or diluted ammonia vapour through blood,) the fibrin rises to the top, and there forms a distinct layer. On the other hand, as Sydenham pointed out, the brisk agitation of even inflammatory

blood prevents the formation of the buffy coat—an observation, the truth of which I have had the opportunity of testing and confirming.

From these facts regarding the modified process of coagulation, we may lay it down as a general rule, that slowness in the process of coagulation is favourable to the formation of a buffy coat. There is, in truth, little difference between the formation of the fibrinous crust on the top of slowly coagulating blood, and the separation of fibrin in the heart and circulatory system in some forms of commencing death.

But if, under some circumstances, slow coagulation favours the formation of the fibrinous coat, there are cases where the effect is produced under the influence of other conditions. Among these stands first and foremost simple excess of fibrin. Dr. John Davy has accurately pointed out that inflammatory free fibrin often separates as quickly as natural blood coagulates, so that in such case the separation of the fibrin cannot depend on mere slowness of coagulation. In this blood there is an excess of fibrin; and in it two forms of coagulation are often set up. First, a portion of the fibrin becomes, as a general rule, entangled with the blood-corpuscles, and forms with them a red under clot. Secondly, the remaining portion of the fibrin rises to the top, and produces the peculiar crust known as the buffy coat. In the end, the serum is forced out, as in ordinary coagulation, by a continuance of the process by which the fibrin is separated and solidified.

In some instances, when an excess of fibrin exists, the process of coagulation is prolonged. In such cases, it is fair to presume, either that the volatile solvent of the fibrin is also present in increased quantity, or that

it is evolved with less freedom. The fibrin in these cases sometimes separates altogether and floats at the top, leaving the blood-corpuscles and serum alone at the lower part. But this is rare; for in thirty specimens of buffy blood which I carefully observed, I never failed to find evidence of fibrin in the lower part, mixed up with and enclosing the corpuscles. In some cases, it is true, the quantity was small, and imparted but little consistence; but in many others, it imparted as firm a consistence to the red lower clot, as it does to blood which has no fibrinous crust,—I mean blood ordinarily coagulated. Some authors have dwelt on the lighter specific gravity of fibrin, as compared with serum and blood-corpuscles. This is no doubt important in relation to the buffy coat; for, if fibrin were not lighter than both serum and blood-corpuscles, it would not float so easily in one and above the other. It becomes a fact, therefore, of the simplest physical kind, that fibrin, when coagulating separately, and not ballasted by blood corpuscles, will float to the top of the fluid like a cork in water.

Regarding the special effects of the volatile alkaline solvent of fibrin in the process of coagulation of buffy blood, it is to be remarked, that the buffy coat is not always identical with fibrin proper. I have not been able to conduct any careful inquiries as to the influence of the alkalies on the crust of inflammatory blood. But in one case, where I found a firm fibrinous clot in the right auricle of a child who had died from acute pneumonia, I tried the experiment of immersing portions of this clot in solutions of ammonia of various degrees of strength, and found that they were soluble.

The statements that have been made by authors

respecting the force of mutual attraction possessed by the red corpuscles of inflammatory blood are of greatest importance. But it remains yet to be seen, whether this attraction depends on the mere fact that the corpuscles are left free of entanglement from fibrin, or on a property inherent in themselves, and brought out more forcibly during the inflammatory diathesis.

For the production of a buffy coat, two conditions are alone sufficient, taken in conjunction with the lower specific gravity of fibrin as compared with the defibrinated fluid—viz: 1. Slow coagulation (*a*) from excess of the fibrin solvent, (*b*) from slow evolution of the solvent, as when dense fluids are added to healthy blood. 2. Absolute excess of fibrin.

But while these views are sufficient to explain the buffy coat, they in no way oppose or generally supersede the theory of Hunter and Schröder Van der Kolk, that, while inflammatory blood is still fluid, the red corpuscles, by virtue of an increased attraction in themselves, rush together, giving rise, first, to the red mottled appearance which Hunter so well described, and afterwards sinking in groups to the bottom, leaving the fibrin to rise in the serum. The objections, if they are objections, to this view are, that the corpuscles of inflammatory blood are not always found separate from fibrin; secondly, that the buffy coat will form in *non-inflammatory* blood, (where the attraction of the red corpuscles for each other certainly cannot be such as to modify definitely the whole process of coagulation,) if the process is impeded by the addition of fluids of a high specific gravity.

There is yet much, I had almost said all, to be learned in reference to the changes which occur in blood during inflammatory states; and the brevity of this chapter has arisen, I am sorry to say, from deficiency of experi-

mental matter, rather than from studied condensation.

[If I venture, in fine, to speak of inflammatory blood as blood in which the oxidation process is abnormally active, or let fall the suggestion that in this state the iron enclosed in the blood-cells may possibly have become the magnetic oxide, and that the rapid aggregation of these cells in inflammatory blood has thus some relation to the magnetic force, I do so open to the correction of more extended observation.]

CHAPTER VIII.

SUMMARY OF CONCLUSIONS AND PROPOSITIONS.

"Cum hæc per multa volumina, perque magnæ contentionis disputationes, a medicis sæpe tractata sint atque tractentur; subjiciendum est, quæ proxima vero videri possint."—CELSUS.

THE total of this essay is summed in two major and a few minor propositions.

1. *First Major Proposition.* The primary and essential part of the process of coagulation consists in the evolution of a volatile principle from blood.

[This is proved by the experiments which have gone before. These have shown that coagulation is *prevented* by exclusion from air or other gas, by cold, and by cold and pressure; and that it is *retarded* by motion in a closed circuit, and by addition of dense fluids. Conversely, other experiments have indicated that exposure to the vacuum, to the air, or other gases, motion during such exposure, and increase of temperature during such exposure, are each and all physical conditions which *quicken* coagulation.

With the escape of a volatile agent these conditions are all in perfect accord and harmony; in the presence of any other view, they become mere disjointed and even contradictory phenomena.

The proof is carried further still in the experiment of passing the vapour of blood through blood, and in the suspension of coagulation which succeeds.]

- II. *Second Major Proposition.* The volatile principle thus eliminated from blood is *ammonia*, differing perhaps in formula in different classes of animals, but serving essentially the same purpose in all.

[This proposition is proved by two series of experiments; first, by those which have shown that ammonia may be obtained from blood-vapour; and secondly, by the results which follow the addition of ammonia to newly drawn blood. Still further, but in the same direction, it is proved in the experiments of redissolving the blood-clot or the fibrin-clot in ammonia solutions, and reproducing coagulation by eliminating the ammonia.

Lastly, the proposition is exemplified by the experiments which show that, in blood held temporarily fluid by excess of ammonia, coagulation is favoured or retarded by the same physical agents as those which favour the normal coagulation of blood.] *or retard*

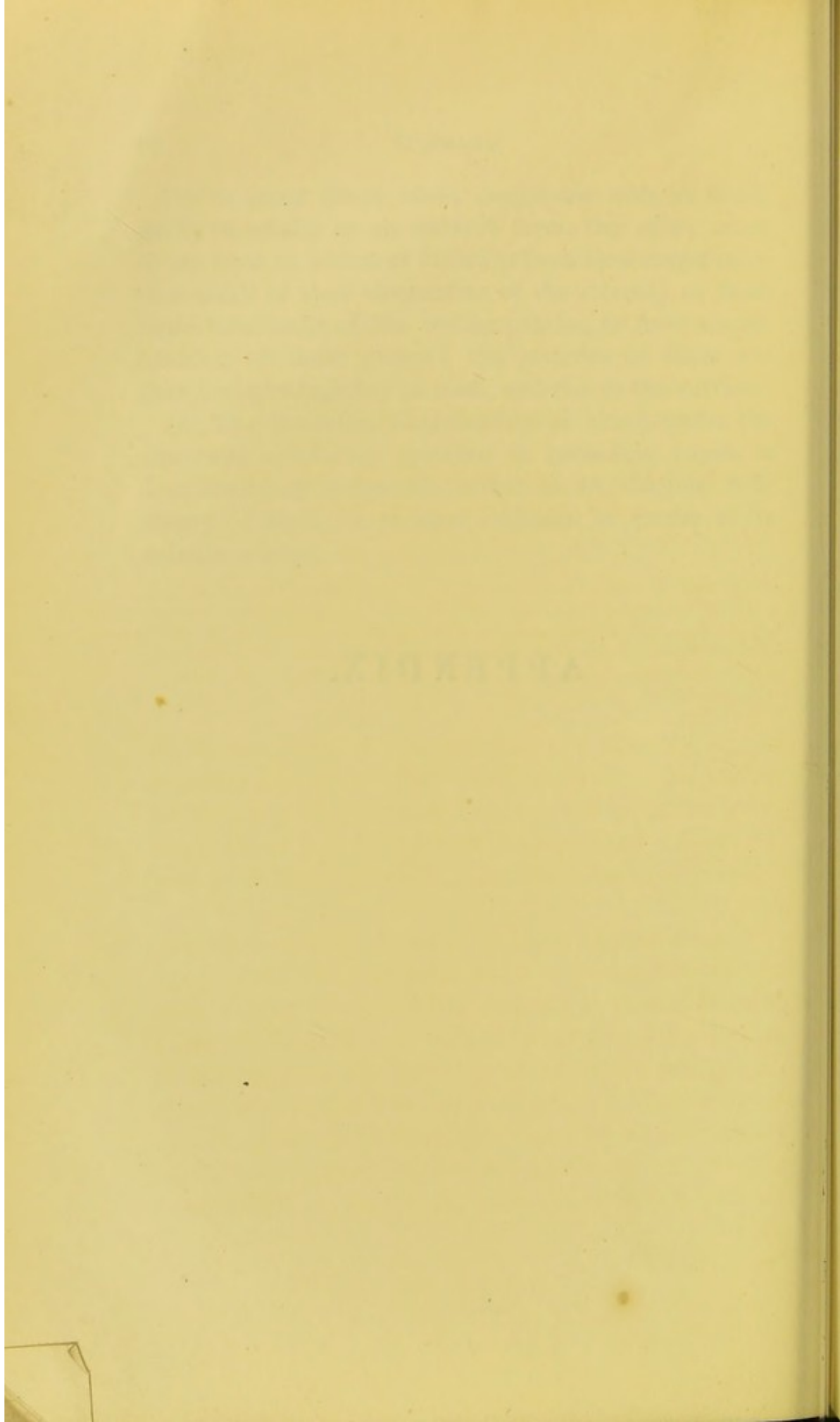
The minor propositions which spring naturally from the foregoing, are the following:

(a) As a result of the evolution of the volatile solvent from newly drawn and liberated blood, the fibrin, which has previously been held in solution in the serum by virtue of the alkalinity imparted by the ammonia, is transformed from the fluid to the solid condition; its particles, coming together, constitute with the blood-corpuscles and serum, in ordinary coagulation, the red clot; and the after separation of the serum is due to the contraction of the fibrin, by a continuance of the same process.

(*b*) In cases where blood coagulates with its fibrin partly or wholly in an isolated form, the effect arises either from an excess of fibrin, or from slow coagulation (the result of slow elimination of the solvent), or from rapid subsidence of the red corpuscles, or from a combination of these causes; the particles of fibrin are thus brought together in mass, and rise to the surface.

(*c*) The imperfect coagulability of blood, under the abnormal conditions specified in preceding pages, is due, according to the case, either to an absolute deficiency of fibrin, or to slow evolution or excess of its volatile solvent.

APPENDIX.



APPENDIX,

SHOWING SOME OF THE BEARINGS OF THE PRECEDING LABOURS ON PRACTICAL MEDICINE AND PATHOLOGY.

"But here I come upon a field where I might roam freely and give myself up to speculation. And, indeed, such a flood of light and truth breaks upon me here; occasion offers of explaining so many problems, of resolving so many doubts, of discovering the causes of so many slighter and more serious diseases, and of suggesting remedies for their cure, that the subjects seem almost to demand a separate treatise."—HARVEY.

In this appendix are included a few short papers on certain subjects which have occurred to my mind at different times, since first I took up these studies on the blood. Each subject thus introduced is discussed under a definite head, and forms in itself a special thesis.

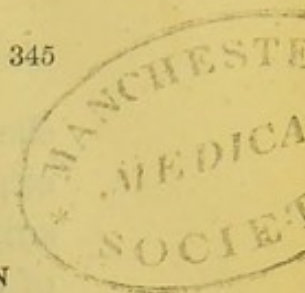
Those who have heard or read the various communications, which I have made since the year 1850, at the Medical Society of London, will recognize in the section on Depositions of fibrin in the heart and blood-vessels during life, a repetition, epitome, and confirmation of views already expressed. But, as I believe now, after further and deeper consideration of this question, that in all matters of practice the views previously advanced are essentially the truth; and as, to use a Shakespeare phrase,

"Truth can never be confirmed enough,
Though doubts did ever sleep ;"

no apology is required for the reintroduction of a series of natural facts which are equalled only in importance by the inattention which is paid to them.

The other subject matter of the appendix is entirely new.

It was my intention in the first instance to have published this appendix as a separate treatise ; but as many of the arguments adduced are based on the experimental data furnished by the labours of the preceding essay, I felt it best, in the end, both for reader and author, that the appendix should stand as it does, the corollary and, in some measure, the practical result of physiological research in its simplest representations.



I.

ON SUPERALKALINE CONDITIONS OF THE BLOOD IN
RELATION TO DISEASE.

THE existence of ammonia in the blood in some diseased conditions has been referred to by many writers. Mr. Herapath found carbonate of ammonia in the blood of cholera patients. Frerichs and Litzmann have shown its presence in uræmia. Dr. Blair, in a *Report on Yellow Fever in British Guiana*, remarks specially on the ammoniacal state of the breath, the blood, and the vomited matters in that disease. In some of his cases, he says, the blood was like to port wine as regards its fluidity, and the corpuscles were all dissolved; the blood in these cases was strongly ammoniacal.

I might extend such notices; but my object in this essay is rather to point out the possible fact that ammonia or its salts, existing in the blood in excess, may be considered as the cause of the leading and more serious symptoms in certain forms of acute and chronic disease.

We have seen by direct experiment what the effects of ammonia are when it is thrown into the body in large quantities. Thus introduced, it produces what may be unhesitatingly considered *typhoid* symptoms. The tongue becomes dry and dark; there is an involuntary action of the muscles, varying from subsultus to violent convulsions; there are insensibility, extreme sensitiveness to sound, obscurity of sight, and ultimately, if matters are pushed far enough, death by coma. The morbid anatomy is equally demonstrative. The blood is dark and fluid; the serous membranes

show petechial spots; the tissues are softened; and, in an experiment which I have lately performed on a dog, sulphide of ammonium being inhaled, there were patches of ulceration extending along the alimentary tract.

In marked cases of true typhus, the presence of ammonia in excess in the body is indicated by prominent and trustworthy signs. In a boy whom I attended a few months since, and who was suffering from this disease, the breath was so markedly ammoniacal, that it coated the acidified microscope glass with crystals of the chloride of ammonium, and restored the blue colour to reddened litmus. In this boy, the blood-corpuscles were misshapen, agglomerated, and partially dissolved, precisely as they are when weak solutions of the alkali are added to healthy blood. The symptoms, too, were those of alkaline poisoning; they were as I have described them above, from experimental data.

The superammoniacal condition of blood extends to other diseases, marked by the typhous or typhoid type. Suppression of the function of the kidney leads to this result. In cholera, the excess of ammonia in the blood is explainable as Frerichs has explained uræmia. The urea, uneliminated by the kidney, is possibly transformed into the carbonate of ammonia. This soluble salt, carried throughout the body, reaches the intestinal wall; it is there partly eliminated, and is hence found in the alvine excretion. The blood is not fluid in cholera, despite the excess of ammonia—a result arising from the deficiency of water; but it is thick and treacly, notwithstanding the absence of water—a result due to the excess of the alkali. Water added to blood of this kind dissolves it into a thin fluid, which on displacement of the ammonia coagulates. Newly drawn blood,

held fluid by excess of carbonate of ammonia, and gently evaporated down, may be brought to have all the characters of cholera blood. Thus reduced, it may be again made fluid by addition of the water lost, and may be induced, by displacement of the alkali, to coagulate firmly.

In cases where the blood is surcharged with alkali, and where the water is not deficient, cases of fever *par excellence*, the fibrin, held in too permanent solution by the blood-stream, is infiltrated into the structures of vascular organs. If the blood here congested remain locked up, a condition obtains somewhat similar to what occurs in the blood enclosed in the vessels after death. The alkaline solvent is gradually eliminated into the surrounding structures, and the fibrin is at length deposited or stranded in the infiltrated part. Thus deposited, it forms those semi-plastic exudations so common in many diseases of a low or asthenic inflammatory fever type; ultimately, if recovery takes place, it either undergoes transformation and becomes the basis of a morbid growth, or remains a firm fibrinous exudation, the more fluid parts of the liquor sanguinis, with which it was originally in company, being removed by absorption.

But while the considerations above noted lead to an explanation of many symptoms and pathological states commonly met with and recognized, they invite also to work at deeper strata. They are secondary to and dependent on the development of the agent which in excess produces them.

If we may allow ourselves to take a broad view of pathology, symptomatological as well as anatomical, we may look on every pathological state as a modified physiological process.

There is not, on strict scrutiny, a single feature in disease which does not bear such interpretation. What therefore leads to the normal development of the alkaline solvent of the blood, may lead in extreme instances to its development in excess. This recalls us to a physiological problem yet unsolved. But it is not in every case necessary to trace back the primary cause to its primary source.

By this I mean that there are conditions which may lead to derangements of the body from superalkalinity of blood, independently of the idea of the production of the alkali in excess by an exaltation of the physiological process by which it is normally produced. As a first example, there are external sources. In health, the blood is capable of absorbing but very limited quantities of ammonia by the lungs. We have seen an explanation of this fact in speaking of the rapid elimination of the alkali from drawn blood: *i. e.* there is, in the fixed alkaline property of the blood, as well as in the temperature of the blood, an admirable provision against excessive absorption. For, were ammonia capable of absorption by the blood as it is by water, there is not a foul place where decomposing organic matter delivers up its ammoniacal emanations, which would not be at once and permanently a very plague spot, the heart and home of fever, absolutely uninhabitable. I do not question, however, that an ammoniated air constantly inhaled is and must be injurious, despite the provision made for its exclusion. There may, moreover, be conditions of blood, otherwise brought about, such as an excess of water, which favour the absorption of the alkali, and may be accepted as so-called "predisposing causes" (a term often violently abused,) for the re-

ception of the alkali; and thus symptoms of disease may arise from simple exposure to the alkaline vapour. But these instances are rare; and the symptoms produced are either transient when they are lighted up, or, if permanent, slow and feebly defined.

In a close room, through which ammonia vapour is diffused so widely as not to be detectable by the sense, I know from personal experiment that the air thus feebly charged is for a time the cause of symptoms, to say the least of them, disagreeable. There are headache, nausea, giddiness, and debility. These symptoms pass away as fresh air is breathed; but, by frequent repetition, they at length produce a more permanent debilitating influence.

Hence I presume that much of the excitable anæmic feverish state, to which persons who live in foul localities are subjected, may have its origin in the cause thus specified. We must push this argument but little closer now; for that fever is ever actually lighted up in such way, there is as yet no satisfactory proof. But that fever once lighted up would find its course and its intensity favoured by the inhalation of an air bearing even one ten-thousandth part of ammonia, is an inference fairly derivable from the labours which have gone before.

But the matter here considered must not be left without a word of suggestion. Brooding in low and filthy localities, there is common to them a form of fever, endemic in its character, doubtfully contagious, and seeming to want *habitat* only to take form and live.

While some experimentalists occupy themselves in seeking in organic cells for the cause of this disease, others might, with equal chance of success, and with more precision, look for it in one of that numerous

family of volatile alkaline principles, coming from the death of the organic world, of which the common ammonia forms but a single representative.

Wherever there is an air containing such a trace of foetid vapour as to be detectable by the senses, and often when the senses fail to detect it, there ammonia exists in one or other of its varieties.

The microscope test is invaluable in such researches, since all the ammonias yield characteristic crystals of the chloride. Another delicate test for ammonia is the iodized paper for ozone; the merest trace of ammoniacal gas, such as would be inappreciable under ordinary circumstances, being a sufficient check on the action of the ozonometer.

In tobacco-smoke, an ammonia is given off in large quantities. If a microscope glass moistened with hydrochloric acid be held for but a moment over the fume of the weed, and be then dried, the glass will be found frosted with crystals of the chloride of ammonium.

The breath of all confirmed smokers is markedly ammoniacal; and I have shown in experiment XVI, p. 101, what the effects of inveterate smoking are on the blood. There is no doubt that some ammonia is absorbed from the pipe in prolonged smoking; the modification of the blood-corpuscles and the fluidity of the blood incident on prolonged inhalation of the tobacco fumes proclaim the fact; while part of the prostration, the anæmia, the nausea, and the hysteria to which great smokers who have not the lungs of Stentor, are subject, are possibly traceable to superalkinity of blood, and to tobacco as the source of the alkali.

In cases where the function of the kidney has been suppressed, we have a fair insight into the origin of

the ammonia salt with which the body is poisoned from the excess of the ammonia. We find the source here in the non-elimination and subsequent decomposition of the urea. In experiments where the kidney is extirpated, this superammoniacal state of the blood prevails. The blood is rendered fluid, the corpuscles are dissolved, and coagulation can only be induced by the addition of caustic lime, or the cautious addition of potassa or soda, so as to secure the elimination of the ammonia. The breath also before death is strongly ammoniacal. In fatal cases of scarlet fever, where the function of the kidney as well as that of the skin is suppressed, the foetid breath is loaded with the alkaline excreta, and the convulsions and coma are accounted for by a simple toxical cause. The same argument might extend to many other diseases, preceded in their later stages by an arrest in the action of the two great emunctories, the skin and the kidney.

During periods when the body is exhausted by over fatigue, and especially when to this prolonged abstinence is superadded, the excess of ammonia evolved by the breath is well marked; and impoverishment from imperfect diet is in itself a cause of diseases marked by great fluidity of blood, exudations, and flux. In these cases, the breath is alkaline, and the blood-corpuscles are more or less dissolved. The excreted matters thrown off by the stomach and bowels are foetid and charged with ammoniacal compounds; while the symptoms, the convulsions, and ultimate coma, are in a general sense identical with those of slow alkaline poisoning. In short, when the balance between the forces of regeneration and decay is broken, and the former kicks the beam, there is set up a decomposition,

or as the old men called it, a putridity or ferment, amongst the effects of which the excessive developement of the nitrogenous alkali leads to results which are typical as regards general phenomena in various diseases, and are known by symptom to every practitioner as the fatal and specific "typhoid" condition.

There is, again, a class of diseases in which the symptoms are induced by the introduction into the body of animal poison; such introduction being by medium of the lungs, or alimentary surface, or by direct inoculation. We know too little of the specific influences set up by each of these poisons after their entry into the body, to speculate on the changes which they individually produce in the animal organism; for, in this path of philosophical and experimental research, not a single traveller has as yet systematically set foot. But accidental observation has revealed a few facts which may serve as beacon lights to the wayfarer; and amongst the facts which have been thus chronicled, is the one that, in certain of these cases, extreme fluidity, together with an extreme ammoniacal condition of blood, prevails. These conditions, as I have already stated, have been found in yellow fever, and they have also been traced in cases of death from the bite of the cobra di capello.* Contagious typhus, the only disease of this class now being discussed, to which my own observations have been specially extended, is marked by similar manifestations.

In instances where an enfeebled or obstructed respiration precedes dissolution, extreme fluidity of blood

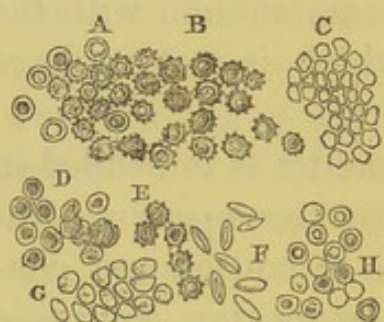
* My estimable friend and colleague, Dr. Cockle, opines that there is an identity between the poisons of yellow fever and the cobra—a view strictly original on his part, and which has lately received support from one or two other observers.

is often a *post mortem* fact. It has been already explained that this result may arise from a deficiency of fibrin. But, in the case of the child who died from cyanosis and tubercular deposit, page 127, and whose death was purely by asphyxia, the blood was fluid and contained a large excess of ammonia. In experiments where carbonic acid gas is inhaled so as to produce slow poisoning, the blood is slow to coagulate on simple exposure to the air. But, as the addition of potassa with extreme care, so as not to produce a new and fixed solvent, produces in such blood firm coagulation with evolution of ammonia, it is a fair inference that in this experimental example the carbonic acid, received into the circulation, enters into a combination with the alkali, producing a compound which is not at once eliminated when the blood is set free.

Lastly, in cases where putrid matter is imbedded in the system, as when deep seated abscesses, open by fistulous canals to the air, exist in the organism, and contain pus in a state of partial decomposition, ammonia is fully generated by decomposition in the putrid material, and is sometimes, I have reason to suspect, when the exit for the purulent matter is not free, absorbed by the surrounding tissues and taken up into the blood. Here received, the toxical effect is not slow in being developed, and the "typhoid" which succeeds is the result not of so-called irritation, not of exhaustion from the drain, but of poison generated in the cavity and conveyed from it to the body at large. In the lungs, when putrid abscess forms, the fœtid breath is charged with ammonia; and I found by direct experiment in one patient, under my care at the Royal Infirmary for Diseases of the Chest, that the fœtor arose from the sulphide of ammonium.

In such cases, the dangers arising from the organic decomposition are doubled, since the patient in respiration must constantly breathe an ammoniated air. Dr. Reuling believes that ammonia may be formed in the blood from the presence of pus, and also that it may be absorbed from the bladder when it has been produced there from the decomposition of retained urea.

Corpuscles of Superalkaline Blood. The modifications which occur in the blood-corpuscles under the influence of the alkalies have already been depicted and described. Whoever would see these modifications at once, has only to watch on a little of his own blood the influence of extremely diluted portions of ammonia. I



need not dwell on facts which many authors have referred to regarding the solubility of the envelope of the corpuscles in alkali. But it is well to recall that under the influence of the alkalies, and specially under the

influence of ammonia when the blood of a living animal is surcharged with it, the corpuscles undergo specific changes within the body, being easily soluble, becoming crenate at the edge (B. E.) (as sometimes may be observed when the corpuscles are losing the fluid around them from evaporation, but not in these cases from that cause) becoming many sided, colourless, transparent, collapsed, and loosely agglomerated, but not in rolls, (C. G.) or even taking the pure oval form (F.), so as to be undistinguishable from the corpuscles of birds. Such conditions of corpuscles may, it is true, occur under other circumstances; for I have seen the oval or bird corpuscle, for instance, which seems to be an extreme

modification, in jaundice (see experiment xvii, page 102), and also when water has entered the system in excess, (experiment xl, page 130); but the effect is most common to superalkaline blood.

The effect of an excess of alkali on the blood-corpuscles during life being, then, to effect a modification of shape, and even, in extreme examples, as in Dr. Blair's cases of yellow fever, and in my own experiments, (see especially experiment xxx, pages 118-21), to dissolve up the corpuscles generally, the influence of superalkalinity in this direction is a matter of great moment.

It is, indeed, as curious as it is interesting, to find how fully the microscopic observations of Dr. Jenner on blood in typhous fevers correspond with mine on the blood of animals poisoned by alkali. Amorphous heaps of red discs, according to Dr. Jenner, replace the normal rouleaux; and the adhesion of the red discs to each other, in the imperfectly formed rouleaux, is far less complete and long continued than in healthy blood. The red discs lose their colouring matter more easily, and dissolve more rapidly than they do in their normal state. This is shown by the red serosity formed in almost every serous cavity, and by the deep dusky red hue of the flesh and of every structure in contact with the blood. The blood drawn during life, or found after death, is loosely coagulated or absolutely fluid.

How far the more serious symptoms arising from superalkalinity—the convulsions, the subsultus, the coma—are due to destruction or modification of the blood-cells, is a point on which I have no data to guide to an opinion. But this, from demonstrative evidence, may be stated; that the corpuscles, after undergoing a

degree of change and partial dissolution from superalkalinity, which would seem altogether incompatible with existence, will, on withdrawal of the alkali, be renewed in the blood, and, becoming day by day more matured in character, will, after a lapse of some weeks, at last reassume all their normal attributes, such restitution being attended with restoration of the general health, either as a cause or as a coincidence.

The diagnosis of a superalkaline state of blood is easy. Usually the fact is shown by the exhalations from the lungs or skin, which yield the alkali in abundance. If with the evidence of the presence of alkali in these ex-

* For the examination of blood in disease I have been accustomed to use an artificial leech for its abstraction. But my friend Dr. Horace Dobell has lately shown me an instrument invented by himself, which plays so admirably, and which promises so much usefulness in the study of blood pathology, that I introduce both a verbal and a diagram sketch of it. The instrument is called the "*Hæmantlion*." It is constructed as follows.

A, a cylinder having a solid base, *b*, perforated at *n*, so as to communicate at that point only with *c*, a small glass receiver.

G, a piston to the cylinder *a*, worked by a rod *k*, which is four-sided, and moves in a four-sided aperture in *i*, to prevent its turning round, and having a ring at the end for the finger.

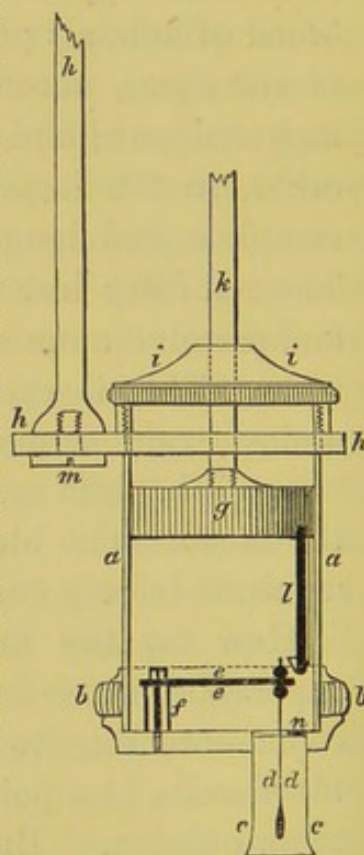
Attached to the piston is a slender rod *l*, having a spring trigger at its end, and descending through *n*, into the receiver *c*, when the piston is thrust down.

A spring, *e*, is connected with the needle *d*, which passes through the solid base of the large cylinder in the receiver below.

The needle, *d*, is so shaped at the point, that it shall cut an opening into the cuticle sufficiently wide to allow the blood, in its natural proportions of corpuscle and serum, to gush through, and is not long enough to reach the surface of the flesh until discharged by the trigger.

A pistol-shaped handle is attached to the cylinder at *h*, *m*, *h*.

In using the instrument the orifice of the receiver is placed upon the skin of the patient, the upper arm being the most convenient place. The piston rod is raised by the finger in the ring, and thus the receiver



halations, the blood-corpuscles are altered in character, such alterations being clearly not due to the mere physical result of drying or of admixture with fluids of different densities, and if the symptoms already described are present, the inference is fair that the blood itself is surcharged with an ammonia, by whatever name the preexisting disease may have been known and recognized, and that the symptoms are such as experiment would trace to the alkali as a toxic cause.

The effects of the fixed alkalies on the blood, or of their alkaline salts in excess, ought not to be omitted in considering the question of superalkalinity. That there may be an excess of fixed alkali, and that symptoms may arise from this cause analogous in character to those arising from the volatile alkali, and even more permanent, is an inference fairly deducible from the experiment recorded in chapter III, where the effects of potassa as a slow poison are strikingly brought out; and the possible influence of common salt in the production of sea scurvy is not difficult to understand, when the effect of the chlorides of potassium, sodium, and ammonium, in holding the blood fluid, is fully comprehended.

is sufficiently exhausted to draw the flesh up into its cavity. As the piston rises, the trigger, at the end of the slender rod, catches the spring and raises it, and with it the needle. The moment the piston has reached the top of the cylinder, the flesh being well up in the receiver, charged with blood, and insensible to pain, the spring slips from the trigger, and the needle is instantaneously darted into the flesh and withdrawn by the recoil of the spring, a drop of blood starting at the same moment to the surface.

II.

AMMONIA AS AN EXHALATION FROM THE BODY.

AMMONIA has long been known as an excrete from the skin. My friend, Mr. Thomas Taylor, Lecturer on Chemistry at Middlesex Hospital, tells me that, many years ago, Dr. Hue was accustomed to demonstrate to his class the presence of ammonia in the cutaneous exhalation by the following experiment, which in his time was not new. He exposed to a red heat fine glass sand, let it cool down, and showed by experiment that no ammonia was evolved from it. Then rubbing the sand with his hands, previously washed and dried, he again exposed the sand to heat, and showed the evolution of ammonia from it by the turmeric test. The objection to this experiment is, that in the friction of the hand with the particles of sand, organic matter may be removed, and may be decomposed on the second application of heat. This objection is however removed, at least in part, by the experiments of Berzelius and Anselmino, the former of whom found in collected cutaneous exhalation, chloride of ammonium, and the latter acetate of ammonia.

Some fifteen years ago, my esteemed and learned friend the Rev. J. B. Reade, F.R.S., Vicar of Stone, who, as a member of a sister profession, and at the same time a successful and unwearied experimental inquirer in matters of natural science, may be looked on as the Hales of this century, made the discovery that an ammonia is contained in the expired air of the breath. Extending his observations from himself to others, and to inferior animals, Mr. Reade deduced that the rule was general. His mode of testing was by the microscope and acid test; and a brief account of

his labours was laid before the Microscopical Society soon after they began, and was ultimately printed in abstract in the *Gardeners' Chronicle*.

Since the observations of Mr. Reade, Dr. Reuling, in 1854, published a paper which is epitomized by Dr. Day in his edition of Lehmann's *Chemistry*, vol. III, page 559. In this paper, Dr. Reuling points out that the expired air of every one contains ammonia, and shows that in certain diseases—as typhus, pyæmia, and uræmia—ammonia is in excess in the breath. He argues, however, that in health there is no exhalation of ammonia, nor absorption of it by the pulmonary membrane. Scherer has, if I mistake not, referred also to ammonia as a constituent of the expired air in respiration.

Independently of these inquiries, after the detection of ammonia in blood-vapour, I sought for evidence of it in the breath and in the cutaneous exhalation, using the microscope test as it had already been used by Mr. Reade, but without any knowledge of his labours. The result has been to confirm these previous observations to their fullest extent.

Up to this time, the experiments I have made on the breath amount to more than a thousand. They have been made on persons of both sexes, on animals of different kinds—dogs, cats, oxen, horses, guinea-pigs, and sheep. They have been made on myself under varying conditions, as regards temperature of body, times of day, repose, and fatigue. They have been made on individuals suffering from different kinds of diseases.

I shall attempt, as a condensation of these observations, to sum up the results under a few heads.

While I fully corroborate the deduction made by Mr. Reade and Dr. Reuling, that expiration of ammonia by the breath of persons in health is universal

as a rule, I have met with an exception, in one case, out of all which came before me.

This exception occurred in a gentleman who lived entirely on vegetable food, and abstained from alcoholic drinks. Time after time, and for intervals of an hour at once, I tested this gentleman's breath with the microscope glass for ammonia, without ever finding a trace of crystal; while at the same time, in the same air, and under every identical condition, the breath of other persons yielded abundant evidence of the exhalation of the alkali. Whether the same exception applies to all vegetarians, I cannot say.

In examination of my own breath I have found remarkable variations. On rising in the morning, after a sound night's rest, I have obtained no evidence of ammonia in the breath. Then, having gone through the day's labour, and returning home tired and exhausted, I have found, on repeating the same process under the same conditions, abundant evidence of the alkali. I once carried on this inquiry daily for three weeks, with the same results. I made experiments also on myself when heated with exercise and during hot summer weather, as well as at periods when the air was cold and my own body was cold, doing the experiment out of doors in frosty air in the latter instances. Here the rule was general; during the higher temperature the evolution of the alkali was free, during the cold weather the result was either very little marked or *nil*.

As previous remarks prove, I so far agree with Reuling as to opine that in health, and with no excess of ammonia in the air, there is possibly no absorption of the alkali by the pulmonary membrane. But I maintain that the evidence is demonstrative that ammonia is constantly *exhaled* by the pulmonary membrane, and

that what is found in the breath is not the mere return of the minute proportion inspired with the air. The single fact above referred to, where one gentleman did not throw off the alkali in respiration, while others breathing the same air did, is indeed sufficient evidence of itself of the truth of my position.

But to carry this argument further, I took advantage of times, when my own breath was yielding the ammonia so freely as to give a field of crystals after thirty or forty expirations over the microscope glass, to test the air which was being breathed by having it driven in gentle current from small bellows, during the same interval, over another microscope glass prepared in precisely the same manner. Then, drying the microscope glasses together, I examined them, and found, as an invariable rule, the presence of the ammonia salt on the glass which had been breathed on, and no trace of it in that over which the air had simply passed.

I found further by experiment, that the amount of alkali exhaled is greatest at the end of an expiration. If short expirations be made, intervals of four or five minutes will elapse without any production of crystals; while thirty prolonged expirations made in one half the time, will yield sufficient of the alkali to afford a fine field of the crystalline salt. This experiment removes satisfactorily an objection I have heard made, that the ammonia comes from the decomposition of organic matter in the fauces or about the teeth.

In one form of disease, simple anæmia, I have met with cases in which no evidence of ammonia could ever be detected in the breath. In the case of a young girl suffering from pure anæmia in its most marked form, this obtained so fully, that on two occasions, after making her breath pass through hydrochloric acid in a potash bulb tube

fitted for the purpose, for six hours consecutively, I obtained no evidence whatever of the formation of the chloride.

On the other side, a copious expiration of ammonia is common to many diseases. I have said that the breath of all inveterate smokers is ammoniacal, and this point in male subjects must always be borne in mind when the breath is tested. In both sexes I have met with excess of ammonia in the breath in chronic bronchitis, in typhus, in one well marked case of purpura, in various simple dyspeptic cases where the bowels were constipated, in uræmia, in a case of albuminuria, in the various stages of phthisis, and in abscess of the lung.

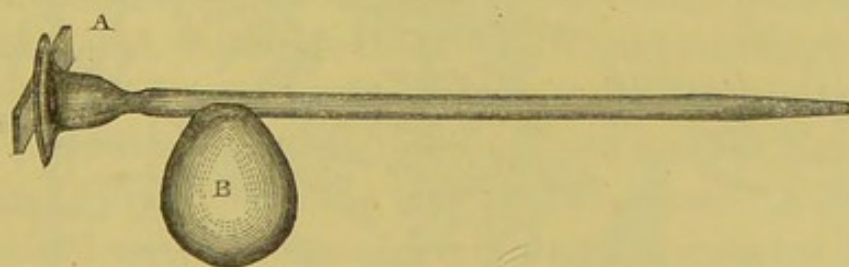
To arrive at an approximate idea as to the normal and abnormal amount of ammonia exhaled by the breath, practice is required, first with men in health and afterwards with men diseased. To attempt an absolute quantitative analysis in each case is impossible, not only from the time required for the task, but from the difficulty of calculating the amount of air altogether evolved in a given time by different persons. But simple practice with the microscope glass soon supplies the general fact.

For the detection of the expired ammonia, Dr. Reuling recommends logwood paper;* but the microscope test is as delicate as can be desired, is, after a little

* The action of ammonia on hæmatoxylin was pointed out by Erdmann (*vide* Handwörterbuch der reinen und angewandten Chemie, Band III, Braunschweig, 1848.) Hæmatoxylin, when brought into contact with ammonia, is dissolved, forming a rose-red or clear purple solution when the mixture is made over mercury. If an acid is introduced, the colour becomes yellow, but there is no precipitate; and, by adding sulphuric acid, crystals of unchanged hæmatoxylin are formed. If air is allowed to enter the ammonia solution, the colour immediately becomes purple, and ultimately dark red and almost opaque. A part of the hydrogen in the hæmatoxylin combines with the oxygen of the air; and a new body is formed which Erdmann calls hæmatein.

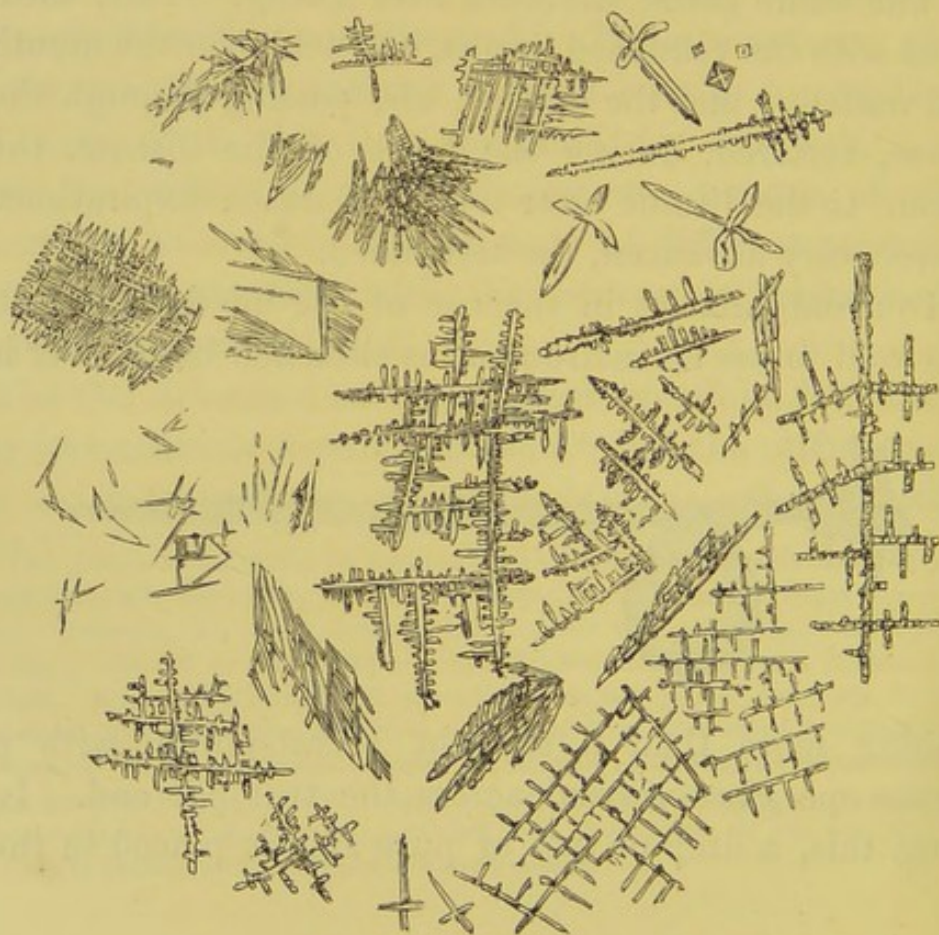
practice, most manageable, and gives a general knowledge of quantity. The mere holding of a rod moistened with dilute hydrochloric acid is not a sufficiently delicate test in the majority of cases; but if, when the rod is thus used, there is distinct evidence of white fumes, the test is sufficient to show that the amount of ammonia expired is far beyond the normal proportion; and, as at once proving this fact, it is simple and valuable. The reddened litmus and turmeric tests are also useless in most cases, because carbonic acid is thrown off in excess as regards the alkali; but if in any case these tests show the presence of alkali, they are valuable as proving at once a condition seriously abnormal, and as denoting excessive alkalinity of the blood. In one case of typhus in a boy, I used a piece of fine white gauze stretched over a ring. This, saturated with the reddened litmus, was held over the mouth and nostrils; and the expired air, passing through the gauze, restored, during the acme of the disease, the colour to the litmus after ten or a dozen expirations. As recovery advanced, the test failed.

To avoid fallacies in the use of the microscope test, it is well to use an instrument as sketched below. It is



nothing more than a straight breast-pump with a microscope glass carried across the trumpet end. In using this, a drop or two of pure acid is placed in the

bulb (B); the microscope glass (A) is secured across the trumpet end with a band of India rubber, and the patient is made to breathe through the tube by his mouth at the long and fine end. The air thus comes in contact with the acid is passing over it in the bulb, and a part of the alkali is there fixed; but some of the acid and alkaline vapours also pass on together, and, as there is condensation on the microscope glass, a field of crystals is deposited on drying. The acid in the bulb, containing also water which has been condensed with ammonia, may also be collected, if required, and subjected to experiment. In the subjoined microscopic sketch, the crystals were taken from a specimen derived in the manner above stated from a healthy man.



Ordinarily, the ammonia evolved by the breath is in combination with carbonic acid; and if the carbonic acid is removed, as I have found by experiment on my own breath, evidence of the free acid and of the alkali may often be obtained simultaneously. To show this, it is simply requisite to place baryta water in a Wolf's bottle, to breath through this, and to connect a long escape tube from the bottle with a potash bulb tube containing a solution of litmus, slightly reddened with acetic acid. While the expired air is passing through the baryta water, the Wolf's bottle is immersed in water at 200° Fahr., so as to raise the temperature of the baryta water and prevent the absorption and fixation of the ammonia. The expired air must be gently driven through the fluids in both containing vessels; and, if much time elapses, the baryta water must be changed. In the end, not only will the evidence of the carbonic acid be given in the baryta water, but the reddened litmus will have its colour temporarily restored.

The evolution of ammonia in cutaneous exhalation has been known, as I have already shown, for a long time. In seeking for its presence in this exhalation, I place the hand for a few hours in a large wide mouthed bottle, moistened on its inner surface with pure hydrochloric acid, and connected to the wrist by a broad India rubber band, so as perfectly to exclude the air. After the hand is withdrawn, the contained fluid is carefully poured out of the bottle into a watch-glass. A drop of it placed on the microscope glass and evaporated down, with the usual precaution to evaporate slowly that the salt formed may not sublime, yields full evidence of the crystals of the chloride.

In some diseases where the action of the skin is pro-

fuse, the amount of ammonia exhaled is very considerable. From the bodies of the consumptive, during and after the colliquative perspirations, this evolution is most marked. In one case of this kind, I found the acid rod giving white fumes when held near to the cutaneous surface; and, indeed, the peculiar odour which attends the perspirations of the phthisical, and is so marked when the bedclothes are raised, arises possibly from this cause, being faintly ammoniacal in character. In the critical sweats of fever there is a similar exhalation.

From fresh urine in health, ammonia rarely goes off *spontaneously*,—at all events, in sixty examinations of the vapour from healthy urine at the moment when it was passing, I failed to detect it with the microscope test; but in many of these cases the addition of a little fixed alkali or caustic lime with elevation of temperature to 98° secured its evolution. The normal amount of excretion by the urine of ammonia in combination as a salt, and the excess of such excretion in diseased conditions, are points on which, from deficiency of experimental evidence, I hesitate to speak.

In a paper read before the Royal Society, with a copy of which I have been favoured by the author, Dr. Bence Jones has endeavoured to show that, when salts of ammonia are administered internally, nitric acid in small quantities may be detected in the urine, a result due, as he opines, to oxidation of the nitrogen in the system. Lehmann has disputed this, on the ground that the mode of analysis pursued by Dr. Jones is calculated to mislead. Without entering into a discussion on this interesting topic, I would mention two facts. One is that, in an experiment where an animal was subjected to ammonia for a long time, until in fact death occurred, the

urine was not ammoniacal, but had often a feebly acid reaction. The other fact is, that where ammonia is largely administered, its removal by the breath is so rapid and immediate, that no argument as to its elimination or non-elimination by the urine can be satisfactory in the absence of observations as to the condition of the air thrown off in expiration, and of the exhalations from the cutaneous surface. So rapid, indeed, is the elimination of ammonia by the pulmonary membrane, that in an experiment performed and recorded by Mr. Blake, where a drachm of liquor ammoniæ was thrown into the jugular vein, ammonia was detected in the breath by the acid rod test a few seconds after the operation.

When the serous cavities, as the peritoneal cavity, of the body of an animal are opened directly after death, there is, for a few minutes, a free watery exhalation, which, according to my observation, always contains ammonia. In oxen, after a small opening has been made into the peritoneum, I have several times introduced a microscope glass moistened with acid, protected by a cylinder, (as in the cylinder B, p. 281), into the cavity, and, after withdrawing the cylinder, and carefully drying it and the contained glass slip, have found distinct evidence of the crystalline deposit on both. The coagulation after death of the serous fluid in these cavities may possibly be connected with this evolution.

I infer, then, as will be seen from the preceding, that ammonia is a normal excrete of the animal body. The inference is significant, apart from the mere consideration of the animal organism. It embraces the idea of a further and more intimate connexion between the

animal and the vegetable worlds. We have long recognized the carbonic acid excrete from man, and the water vapour which he exhales, as deposits in the air bank for the use of plants, and for elaboration by them into new food for the animal itself. To the magic circle ammonia may be introduced, not only as resulting from the decomposition of effete animal matter, but as given off directly from the animal organism.

In the transformations of the animal body, the evolution of ammonia is as necessary an act as its production; and the freedom of its evolution is secured by its volatility, equal diffusion, and easy excretion from every excretory surface. Had a fixed alkali been the blood solvent, not only would the required amount have been considerable, but the diffusion would have been less subtle, and the elimination less secure, since the arrest of the function of but one organ would lead to accumulation and to the dangers incident thereto.

The consideration of the evolution of ammonia by the body as an excrete, leads also to one or two observations bearing on practical concerns. I have shown that in consumption there is at times an abnormal exhalation of ammonia by the skin, while in some other diseases of a chronic nature there is also an equally abnormal elimination of the alkali by the breath. These cases must be carefully separated from those of the low fever class, in which the free elimination is but the result of superalkalinity. This separation made, the question naturally suggests itself, whether in those chronic cases where the elimination is so free, the fact of the elimination may not be intimately connected with the fact of the debility and waste of substance by which such exhaustive diseases are specially character-

ized. It is clear that an evolution of the two elementary representatives, nitrogen and hydrogen, cannot occur in excess, and over above their normal standard, without waste of substance, if the position be correct that such evolution is direct from the blood; and this position seems at once possible and obvious.

Lastly, the evolution of ammonia by diseased persons is suggestive of various hygienic points bearing on the treatment of disease. A number of healthy persons cannot be long entombed in an ill ventilated place, without respiring an air charged, not only with carbonic acid, but with the alkaline emanation in addition. An historian of the Calcutta black hole tragedy, himself one of the sufferers, tells us that what added intense suffering to the prisoners, was the intolerable irritation produced by the inspired air: the sensation being, as he said, as though the face were held over a vessel of hartshorn. In this catastrophe, one hundred and forty-six men were shut up in the dungeon, which was eighteen feet square, open to the west only by two small windows, which were strongly barred, and admitted but a feeble current of air. The difficulty of respiration commenced within an hour after this living interment; and in two hours, fifty were dead. In the morning, only twenty-three remained alive; and it is a matter of great interest, that nearly the whole of these suffered afterwards from putrid fever—evidently our malignant typhus, and many of them died.

Dr. R. D. Thomson has also shown that, in the air of ill ventilated cholera wards, sulphide of ammonium is one of the constituents. I have already indicated that the effect of sulphide of ammonium on animals is to produce symptoms strictly analogous to typhus; and

it is fair to presume that this gas is present not only in the air of cholera wards, but in all badly ventilated hospitals. In a wretched workhouse infirmary, which I had occasion to visit a few times during last year, the roofs of the wards being low, and the whole place a dungeon, the presence of ammonia in the air required no other test than the sense; and I understood that this was a common condition. The treatment of disease in this place was always unsatisfactory.

In these facts, we have set before us, in fuller light, the importance not only of providing free ventilation, but, in fever cases specially, of carefully isolating the patients, and of securing a rapid and complete removal of the emanations from their bodies. In the absence of these precautions, if nature, busy on her part in relieving the system of the poison which is destroying it, be not seconded by the practitioner, treatment must needs be a farce, and a farce the more solemn, as it apes the more profound.

III.

EXPERIMENTS SHOWING THE EFFECT OF LACTIC ACID
ON ANIMAL BODIES.

WHILST my attention was being directed to the effects of the alkalis, I thought it would be a point of great interest to change the line of experiment, and to inquire into the influence of the acids as administered in moderate and continued doses. I selected for experiment primarily the *lactic acid*; first, because it is a feeble acid; secondly, because it is an acid of the tissues; and, thirdly, in consequence of the theory advanced by Dr. Prout, and supported afterwards by the arguments of Drs. Todd, Williams, Fuller, Headland, and Mr. Spencer Wells, that lactic acid is the probable *materies morbi* of acute rheumatic fever.

I premise by stating, that the acid solution used in all the coming experiments contained ten per cent. of the acid itself.

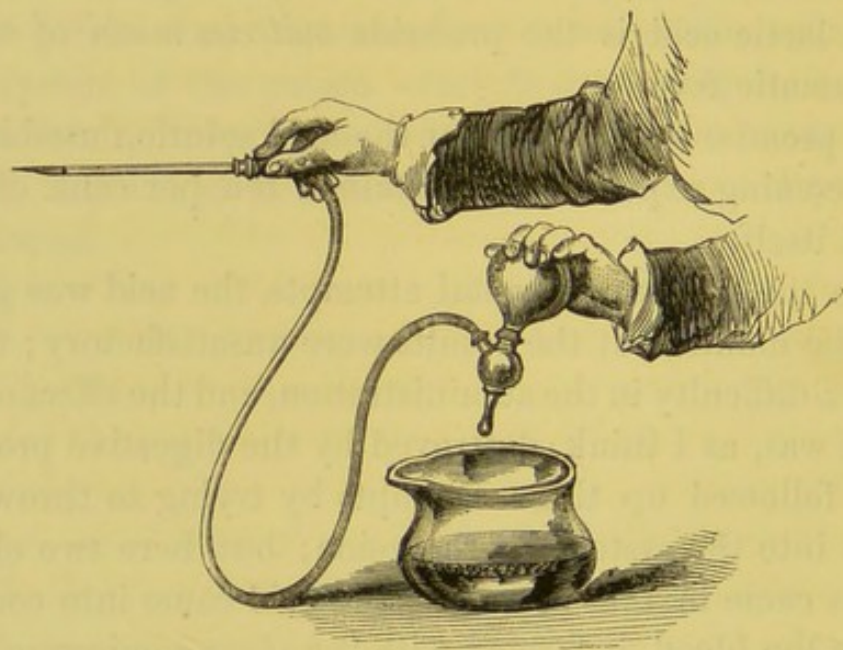
In the first experimental attempts, the acid was given by the mouth, but the results were unsatisfactory; there was a difficulty in the administration, and the effect of the acid was, as I think, destroyed by the digestive process.

I followed up these attempts by trying to throw the acid into the system by the veins; but here two objections came in the way. As the acid came into contact with the blood, it formed with it a slimy semicoagulated mass which prevented injection; and at the same time I foresaw that any effect on the endocardial surface, after such injection, might be reasonably construed as resulting from the direct action of an irritant.

In this dilemma, I turned to the experiment of injecting the fluid, well diluted with water, into the peri-

toneal cavity. Previous experiments of injecting simple water by this means, had rendered me familiar with the operation, and had taught me the fact that absorption into the blood, of fluids thrown into the peritoneal sac, is rapid and effective.

In the first experiments, the acid was introduced by making a small lancet opening through the abdominal wall, and then injecting the acid solution through a fine pointed syringe. The operation was objectionable, the opening being unnecessarily large, and two steps in the operation instead of one, being necessitated. To remove these objections, I got Mr. Weedon to construct for me the following instrument, which answers perfectly.



The instrument is a simple hollow needle, attached by its blunt end to a tube connected with an India rubber injecting bag. During the operation, the animal is held down on his side; the needle, charged to its point with the acid solution, is cautiously introduced through the abdominal wall in the flank; and the fluid, pre-

viously raised to a temperature of 96° , is slowly thrown in. Prior to the operation, the animal is kept for a few hours from food and drink.

I proceed now to the details of experiment.

EXPERIMENT CCCC. *Injection of Lactic Acid.* A full grown healthy cat was placed under the influence of chloroform. The external jugular vein was laid bare, a small tube was introduced into it, and an attempt was made to inject four drachms of the acid with the same quantity of water. The operation, for reasons I have explained above, as well as in experiment CCLX, p. 252, did not succeed. I therefore at once closed the wound in the neck, put a ligature on the vein, and making a lancet opening into the peritoneum, threw in seven drachms of the acid with eight of water. The operation was easily done, and no fluid was lost. The animal soon regained consciousness, and recovered from the effects of the chloroform. During the first hour after the operation, she was breathing at the rate of forty-five per minute; the surface of the body was cold; and she was restless. Two hours later the respirations were forty-two per minute, and the heart-beat so irregular and irritable that it could not be counted accurately. About six hours after the operation, she was left in the same condition for the night, being provided with a straw bed and food. In the morning she was found dead, and with the body in a state of intense rigidity.

Post mortem Examination. The peritoneal surface showed no sign of inflammation, and contained no trace of the injected fluid. The liver on its exterior was rather pale, but internally was congested. The kidneys and spleen were congested. The lungs were entirely free from congestion, but of a colour too much ap-

proaching to red to be natural. The blood in the veins and right side of the heart was of a dark, slimy, soft, and cheesy character, much as I have described as occurring when lactic acid is added simply to blood (Experiment cclviii *et seq.*) The right side of the heart was healthy. The left auricle contained a small coloured coagulum, which interlaced feebly with the muscular structure of the wall. The left ventricle contained some fluid blood. The mitral valve was greatly thickened, red, and (I am indebted for the term, as I shall afterwards explain, to my friend and colleague Dr. Halford) œdematous. On the surface of the valve there was a small fibrinous deposit, which adhered to its position by means of an under layer of a white glutinous fluid, the like of which I found afterwards could be made to exude from the valve on puncturing it with a needle. The surface of the endocardium lining the left ventricle had an intensely vascular appearance, resembling, in fact, bright red velvet. The pericardium was dry and slightly injected. There was no trace of mischief in the joints, and the brain was normal.

EXPERIMENT cccci. *Injection of Lactic Acid.* I injected into the peritoneal cavity of a full sized terrier dog, through a lancet opening, one ounce of lactic acid with two ounces of water, at eight p. m. The animal was not narcotised, and seemed to suffer but little from the operation. The fluid was all retained. Prior to the operation, the chest was examined with the stethoscope, and the respiratory and heart sounds were found quite normal. On the following morning, he was languid, and seemed to care little for food: there was no pain on pressure of the abdomen, nor fullness. The heart-beat was quick and sharp; the second sound seemingly

accented; the first obscure. The respiration was natural. At eleven a.m., I injected another half-ounce of the acid with an ounce and a half of water; the operation produced no expression of pain. At three p.m., Dr. Snow, Dr. Beck, Dr. Graily Hewitt, Dr. F. Webb, Mr. Spencer Wells, and Dr. Rogers, saw the animal. We distinctly made out, that the second sound of the heart was prolonged, and the first obscure; but we could not decide as to the existence of a *bruit*. The sclerotic vessels were greatly congested. The animal lived, with much the same symptoms, till early the following morning, when he was found dead, but lax and quite warm.

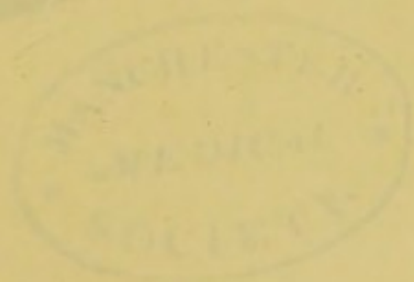
Post-mortem Examination. The cadaveric rigidity was less marked than in the cat. No injury to the intestines had resulted from the operation. The peritoneal lining showed no trace of injection or inflammation, but was rather paler than usual. The mucous surface of the intestines was in parts vascular. The liver was rather shrunken and pale, dense in structure, not inflamed. The spleen was normal. The kidneys were rather congested, and their capsules were intensely injected, the vessels being beautifully delineated. The bladder was contracted and empty, and its lining membrane was pale. The bronchial membrane was free from congestion; but the lungs were vascular, dark, and condensed, except the surface of the upper lobe of the left lung, which was of a bright red, contrasting strongly with the other parts. The pericardium contained no trace of fluid, but was unusually dry, and, like the capsule of the kidney, had its vessels finely injected. Held up to the light, the membrane had a bright vermilion tint. The heart was distended on both sides, but most on the left side, with clotted blood. The endocardial surface on

the right side was natural; but one segment of the tricuspid valve was swollen several times beyond its usual size from œdema, and was of a bright red colour. The thickening was irregular. The pulmonary semilunar valves were natural. On the left side, the endocardial surface lining the ventricle was throughout of a brilliant red colour, having a velvety appearance, and contrasting strongly with the lining membrane of the right ventricle. The segments of the mitral valve were thickened, œdematous, and also of a bright red colour; while, around their free margins, were several beads, varying from the size of a pin's head to that of a millet-seed. The aortic valves were of a deep red colour; their free borders were thickened and everted. There were no fibrinous coagula. The muscular structure of the heart generally was more than usually red. The external vessels of the brain were congested; but the brain structure was natural. Several joints were laid open, but presented no abnormal appearance.

The appearances presented by this heart on the left side have been admirably depicted by Mr. Tuffen West. (See Plate I). The drawing indicates what I shall afterwards designate endocarditis in the first stage.

EXPERIMENT CCCII. *Injection of Lactic Acid.* Injected into the peritoneal cavity of a very small dog, with the needle apparatus described at p. 372, one ounce of solution of lactic acid with two ounces of water. The animal had, very improperly, been fed just previously to the experiment; and, after the operation, vomiting succeeded. He soon became cold, tremulous, and feeble, and died within twelve hours.

Post-mortem Examination. The peritoneal surface was found intensely inflamed, and contained nearly as much



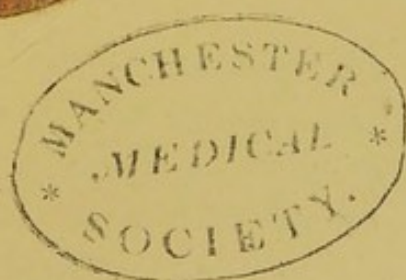
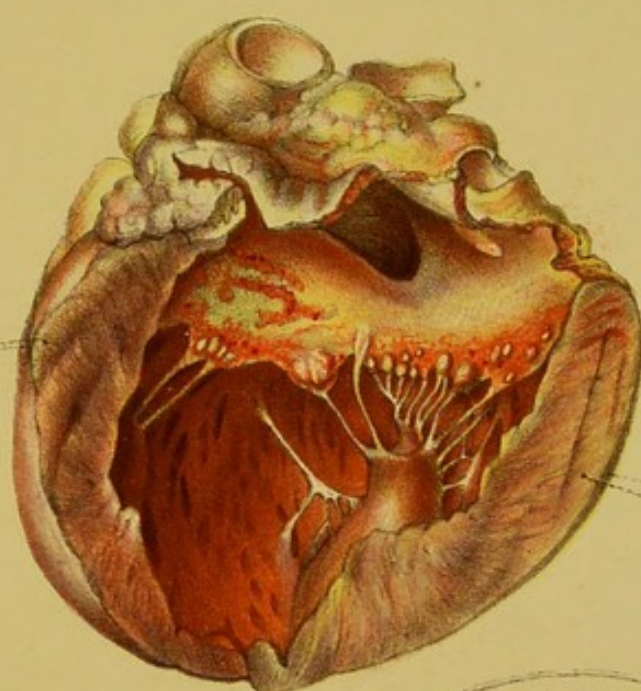
The right side was natural; but one segment of the thoracic valve was swollen several times beyond its normal size from edema, and was of a bright red colour. The thickening was irregular. The pulmonary emboli were natural. On the left side, the endocardial surface lining the ventricle was throughout of a brilliant red colour, having a velvety appearance, and contrasting strongly with the lining membrane of the right ventricle. The segments of the mitral valve were thickened, edematous, and also had a bright red colour; while, around their free margins, were several heads, varying from the size of a pin's head to that of a millet-seed. The aortic valve was of a deep red colour; their free borders were thickened and everted. There were no fibrous clots. The muscular structure of the heart generally was more than usually red. The external vessels of the brain were congested; but the brain structure was natural. Several joints were laid open, but presented no abnormal appearance.

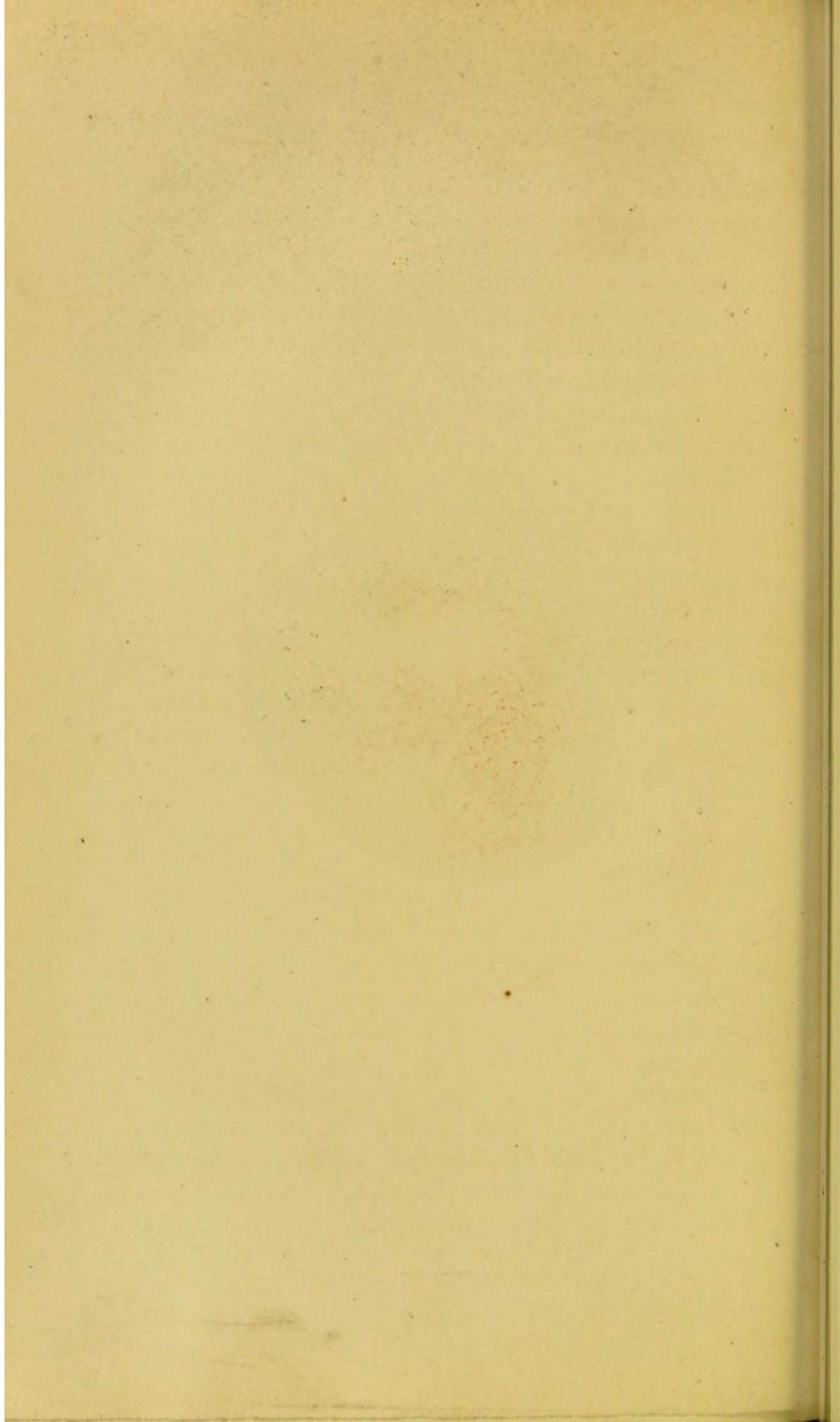
The appearance presented by the heart on the left side has been admirably depicted by Mr. Tuffen West. (See Plate I.). The drawing indicates what I shall afterwards designate endocarditis in the first stage.

Experiment 1. Injection of Lactic Acid.—A dog was put into the perfused cavity of a very small dog with the needle apparatus described at p. 372, and a solution of lactic acid with two ounces of water. The animal had, very improperly, been fed for previously to the experiment; and, after the operation, he soon became cold, trembled, and died within twelve hours.

Post-mortem Examination.—The peritoneal surface was found intensely inflamed, and contained nearly as much

PLATE I





fluid as had been injected, in which floated numerous flakes of coagulated lymph. The lungs were natural. The heart contained coagulated blood in all its cavities. One segment of the tricuspid valve was cedematous and red, but the lesion was slight when compared with the other cases. The pulmonary valves were normal. On the left side, there was no injection of the endocardial surface, nor any lesion of the mitral valve; but the aortic valves were reddened, and thickened at their free margins.

In this case, it will be observed that too large a dose of the acid was injected. The fluid was not absorbed, and rapid peritonitis was the result, with comparatively but little cardiac mischief.

EXPERIMENT CCCIII. *Injection of Lactic Acid.* At the same time when the last experiment was performed, one ounce of lactic acid with two ounces of water were injected by the needle apparatus into the peritoneal cavity of a very large dog. The operation was unattended with any manifestation of pain. Prior to the operation, the heart-sounds and the respiration were perfectly normal.

Second Day. The animal was very unwell; he frequently suffered from shivering, and his skin was hot. Pressure on the abdomen caused no pain. The heart's impulse was great. The second sound was intense and accented; the first sound somewhat obscure. There was no pain in the joints, nor limping.

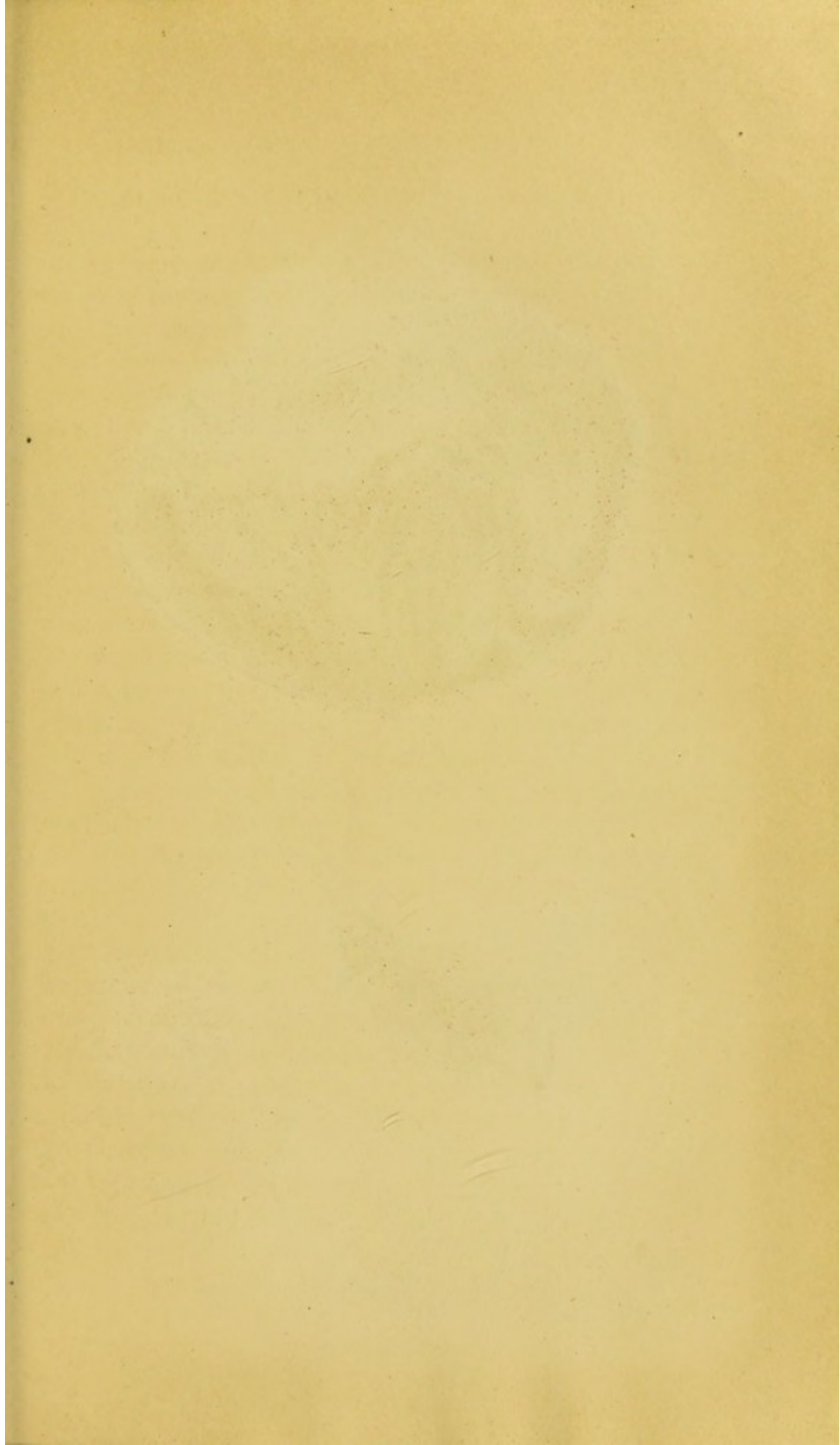
Third Day. The symptoms were much the same. The heart's impulse was considerable; the first sound was quite lost; the second was sharp and accented. There was no pain on pressure over the abdomen. An ounce and a half of the acid was now injected with four

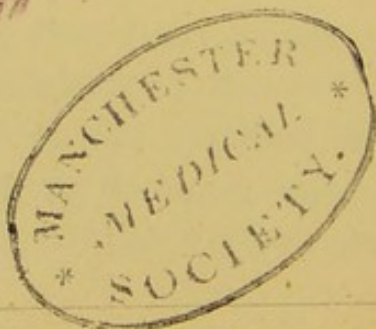
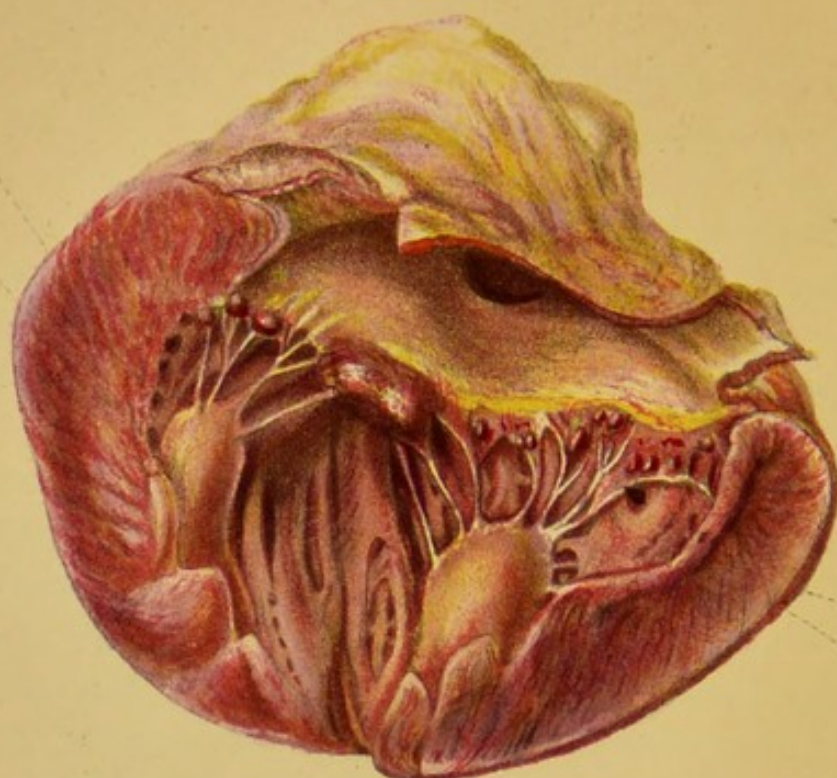
ounces of water. A few hours afterwards, he took his food as usual.

Fourth Day. The tremulousness was very great. There was no affection of the joints, nor evidence of peritoneal pain. The action of the heart was now irregular; the second sound was still accented; and, accompanying the first sound, there was a soft murmur, rubbing, as it were, into the second sound.

Fifth Day. The joints continued unaffected, and there was the same absence of peritoneal pain. The action of the heart was more irregular than before, and there was a loud systolic *bruit*, audible over a wide surface. The second sound was accented, as before. There was a slight constant hacking cough. An ounce and a half of lactic acid solution, with four ounces of water, were again injected into the peritoneum without any manifestation of pain. During the day, the symptoms continued unaltered; and, in the course of the night, death took place.

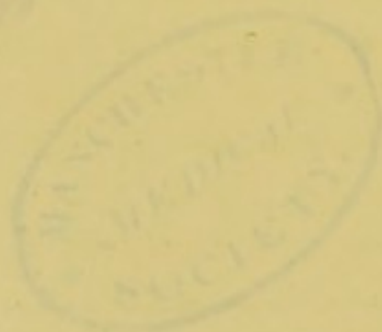
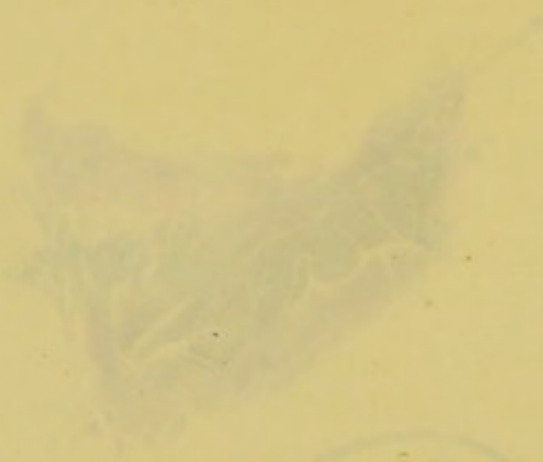
Post mortem Examination. The peritoneal cavity was filled with a brown glutinous fluid, having an alkaline reaction, and which had escaped, as was found, from a wound in the small intestine, opposite the point where the last injection had been performed, and evidently produced by the needle. There was peritonitis, but much less intense than in the last case. The abdominal viscera generally were congested. The lungs were natural, but in the left pleural cavity there was an exudation of lymph. The pericardium embraced the heart closely; its vessels were injected; the membrane was generally reddened; and, on the superior anterior part, over the left ventricle, there was an exudation of plastic lymph, of about the size of the surface of a shilling. At this





point, the membrane was a little thickened. The right side of the heart was filled with dark coagulated blood, and all the segments of the mitral valve were thickened, firm, and of a pearly white colour. (See lower sketch, Plate II.) The ventral segment of this valve was thickened more than the rest to its normal size, and was bound down by strong fibrinous adhesions to the side of the heart, and to the coronary artery above named. The endothelial wall of the ventricle was natural in appearance, and the colour of the blood. The segments of the aortic valve were thickened several times beyond their normal size, and of a pale red colour; their consistence was hard, and their free borders were studded with beads, whitish in colour, and pearly (see fig. 1, Plate II). On examination with a common lens, the pale appearance was seen in this valve, as in the tricuspid, to have arisen from exudation of lymph beneath the lining membrane. In the third drawing (Plate II.) the artist has depicted this appearance separately. The aortic valves were not thickened on their free margins, and everted. The brain and its membranes were normal. Some of the larger joints were opened, and in the ankle-joint the lining surface was a little more vascular than in the others.

Experiment cccv. *Injection of lactic acid.* Into the peritoneum of a healthy dog (the respiration and heart-sounds being perfectly natural) I inserted through a lancet opening one ounce of the lactic acid, and with two ounces of water. Two days after the operation F. Webb, and W. R. Rogers, Esqrs. of the University were present at the operation, and saw the result. As before, by any manipulation of the animal, or by any day, the dog was dead, and the lactic acid was found



point, the membrane was a little thickened. The right side of the heart was filled with dark coagulated blood, and all the segments of the tricuspid valve were thickened, firm, and of a palish white colour. (See lower sketch, Plate II). The anterior segment of this valve was thickened many times beyond its normal size, and was bound down by recent fibrinous adhesions to the side of the heart, as is depicted in the drawing above named. The endocardial surface lining the ventricular wall was natural, as were also the pulmonary valves. The left ventricle contained a small quantity of treacly blood. The segments of the mitral valve were thickened several times beyond their usual size, and were of a pale red colour; their consistence was firm; and their free borders were studded with beads, whitish in colour, and pearly (see fig. 1, Plate II). On examination with a common lens, the pale appearance was seen in this valve, as in the tricuspid, to have arisen from exudation of lymph beneath the lining membrane. In the third drawing (Plate II.) the artist has depicted this appearance separately. The aortic valves were red, thickened on their free margins, and everted. The brain and its membranes were normal. Some of the larger joints were opened, and in the ankle-joint the lining surface was a little more vascular than in the others.

EXPERIMENT CCCIV. *Injection of Lactic Acid.* Into the peritoneum of a healthy dog (the respiration and heart-sounds being perfectly natural) I injected through a lancet opening one ounce of the solution of lactic acid with two ounces of water. Drs. Snow, Graily Hewitt, F. Webb, and W. R. Rogers, and Mr. Spencer Wells, were present at the operation, which was unattended, as before, by any manifestation of pain. On the following day, the dog was dull, heavy, and cold, suffering from

repeated shiverings. There was no pain on pressure over the abdomen.

Third Day. The temperature of the body had very much risen. He was thirsty, and suffered from great pain in all the limbs, shrinking whenever he was touched. There was also well marked injection of the vessels of the sclerotic. The pressure of the stethoscope over the region of the heart seemed to produce great pain and anxiety. The first sound was obscure; the second sound accented. The action of the heart was irregular and quick. On this day, another ounce of the acid was thrown into the rectum, but was returned.

Fourth Day. The injection of the sclerotic vessels was intense, and the pain in the limbs seemed to have entirely disappeared, except about the shoulders. The heart-sounds were as on the previous day. One ounce of the acid was administered by the mouth, and was retained. The animal was much purged this day; the faecal matter had a strong acid reaction.

Fifth Day. The purging continued, and the faeces still had an acid reaction. The animal seemed greatly relieved; the heart-sounds being clear, and the beats regular. An ounce of the solution of the acid, diluted as before, was injected into the peritoneum.

Sixth Day. The pain in the shoulders had returned, being most marked in the left shoulder; so that, when the animal was led about, he rested the left fore-leg entirely, and moved on the remaining three. He was exceedingly thirsty, and the skin was hot. The first sound of the heart was again obscure; the second strongly accented. The alvine evacuation was still very copious, and manifested the same acid reaction as before.

The animal took his food freely. An ounce of the acid was added to his drink.

Seventh Day. The pain of the limbs had passed away, and he moved about on all four legs. There was no pain of the peritoneum; but the small opening, through which the fluid was last injected, was unhealed, and had a fistulous appearance, so that a probe could easily be passed into the cavity. The first sound of the heart was lost; the second sound seemed to me intensely accented; but Dr. Halford, who examined the heart on this occasion, thought that the intensity of the second sound was simply relative—that is to say, arising from the loss of the first sound. The animal passed urine freely; the fluid was intensely acid. Through the fistulous opening in the abdominal wall, a full ounce of the solution of lactic acid was injected without difficulty.

Eighth Day. The pain in the left shoulder returned; the animal moved again on three legs. The first sound of the heart was now heard as a soft blowing murmur; the second sound was sharp, as before. Another ounce of lactic acid was thrown into the peritoneum by the fistulous opening; but some returned at the time, and most of the remainder afterwards.

Ninth Day. He was better, and free from pain in the limbs. The heart-sounds were clearer, but not well defined. The urine was neutral; there was no purgation. On probing the fistulous opening, it was found closed at the lower part. A small opening was therefore made on the opposite side, and two ounces of the acid, diluted with the same quantity of water, were injected.

Tenth Day. The animal was dull and very thirsty.

The action of the heart was quick and tumultuous, but both sounds could be distinguished. There was slight hacking cough.

Eleventh Day. The animal was in the same state. He passed large quantities of strongly acid urine. There was free alvine evacuation. The dry hacking cough continued, and there was great indication of pain over the heart. The heart's action was quick and irritable.

Twelfth Day. The symptoms were generally the same. The urine was copious, and strongly acid. There was great pain excited when the stethoscope was placed over the heart, and the heart-beats were still quick and irritable. The first sound was again obscure, and the short cough was constant; but the respiratory murmur was clear. The alvine excretion was free.

Thirteenth Day. The symptoms were much aggravated. The application of the stethoscope produced great expression of pain. The heart-beats were still quick and irritable; the first sound was obscure; the second accented. The animal vomited several times to-day, and refused food, but drank water freely. The urine in the morning was strongly acid; at night neutral. In the evening, he was so snarlish, and winced so much when the stethoscope was applied to the chest, or when the joints of the shoulder were moved, that only an imperfect exploration of the heart could be made. The first sound could not be detected, and there was great irregularity of action.

Fourteenth Day. The general symptoms were the same. The urine was copious and intensely acid. The short cough continued. There was much thirst, and occasional vomiting of a little mucus. There was still

considerable pain over the region of the heart, and a loud and pure systolic *bruit* was now heard. In the evening, Dr. Cockle examined the heart, and confirmed the diagnosis of the systolic *bruit*.

Fifteenth Day. The general symptoms were the same; the cough continued. I noticed, for the first time, a little fulness of the abdomen. Drs. Fuller, Cockle, and Meredith saw the animal this day, and listened to the systolic murmur, which was extremely well marked, and could be heard generally in the cardiac region. In the course of the day, the tension of the abdomen increased rapidly, showing that there was some effusion; and, in the evening, I drew off by puncture six ounces of a thin darkish fluid.

Sixteenth Day. The general symptoms were the same. The systolic *bruit* was very loud and harsh. There was a little exudation from the wound. The urine was strongly acid. Drs. Hawksley, F. Webb, and Cockle examined the heart this day, and confirmed the diagnosis of a systolic *bruit*.

Seventeenth Day. On visiting the animal this morning, I found a return of the pain in the limbs, together with considerable exhaustion. When his limbs were touched, he grew angry, but could not stand nor move his head without great pain and difficulty. When food and drink were brought, and placed conveniently for his mouth, he raised himself slowly, so as to eat and drink, which he did with great avidity. During the whole of the day, he could not move his limbs, and cried when they were touched. The systolic *bruit* was still well marked.

Eighteenth Day. Early on this morning, the tenderness of the limbs entirely disappeared. He ran about

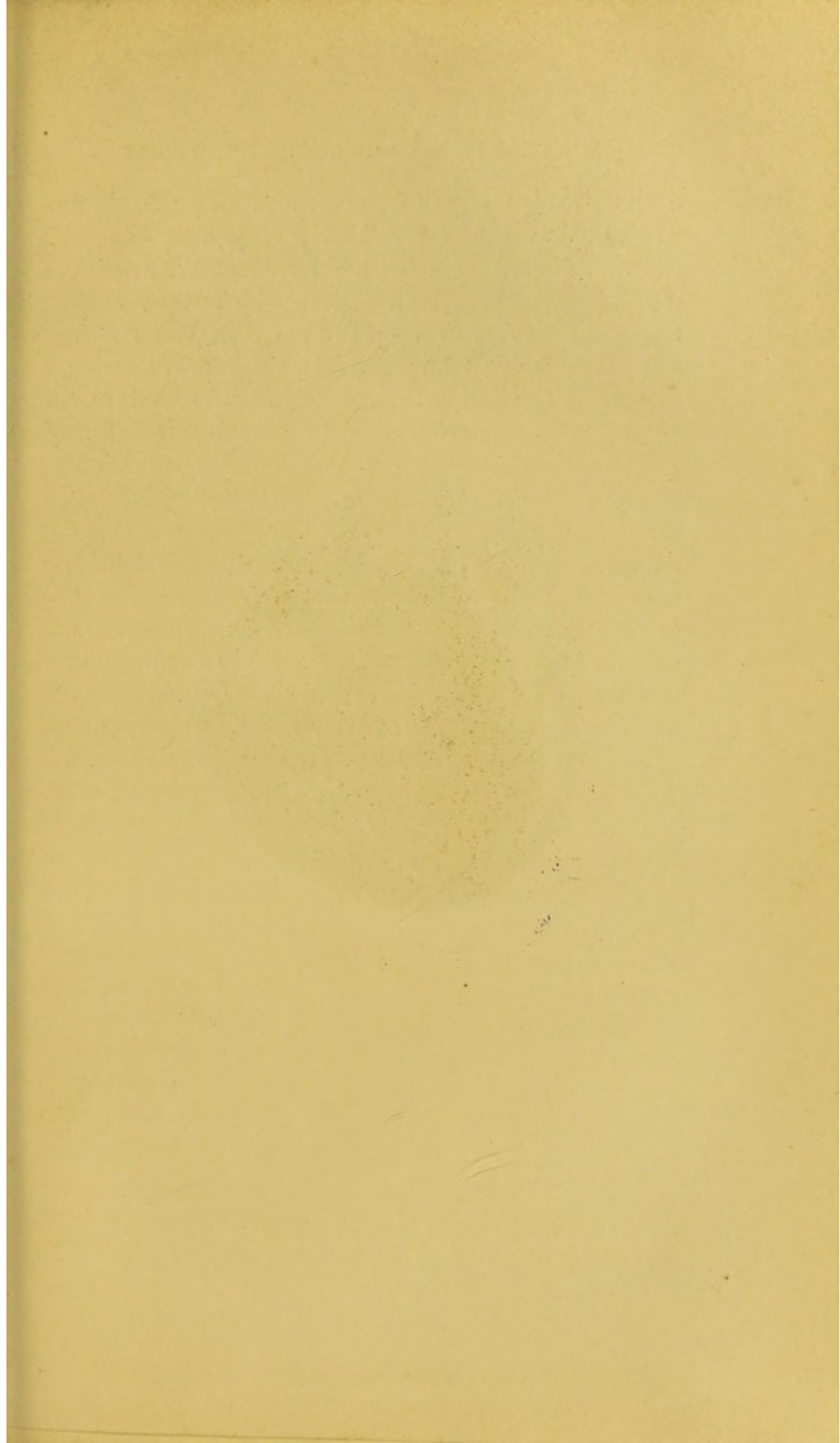
freely, and took his food and drink as though in perfect health. At ten a.m. Dr. Todd saw him, and confirmed the fact of the systolic *bruit*. There was, however, some little tenderness over the region of the heart when the stethoscope was applied. A few hours later, he suddenly relapsed into his previous condition, becoming violently enraged whenever his limbs were touched. He vomited a little once, and was freely purged two or three times, the excreta having a neutral reaction; but he passed a large quantity of strongly acid urine. After this, he seemed greatly relieved.

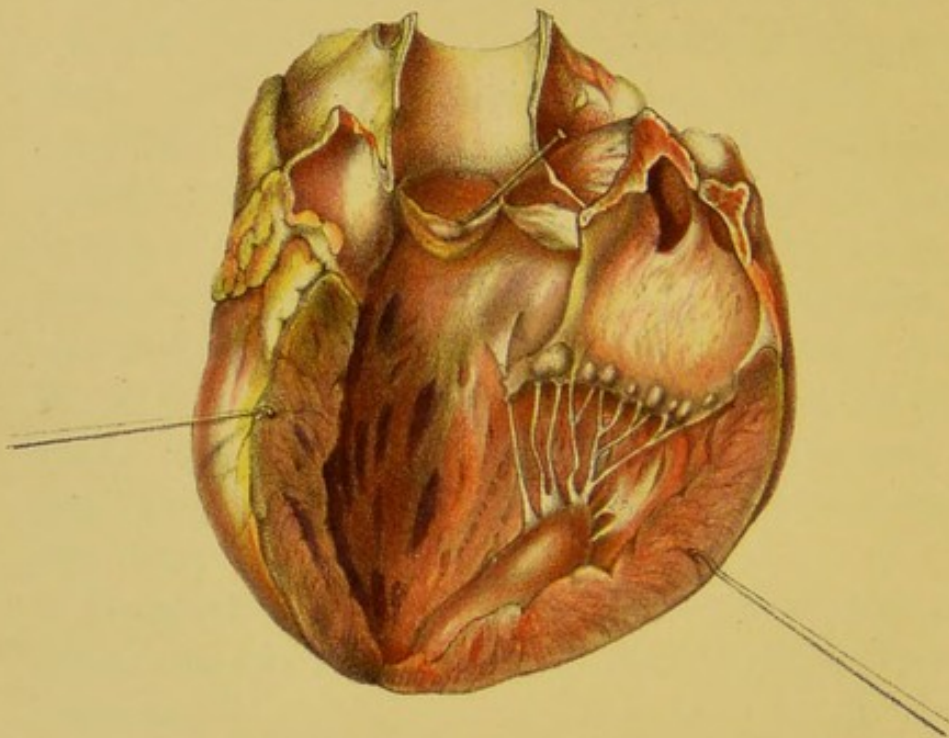
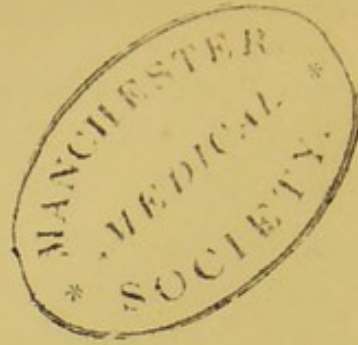
Nineteenth Day. He was more lively, and took his food heartily. He was frequently purged, the excreta having a yeast-like appearance and acid reaction. The urine had a strong acid reaction. The systolic *bruit* was loud and prolonged. Mr. Haynes Walton and Dr. W. R. Rogers saw him this afternoon, and heard the *bruit*. The body of the animal on this and several days past had a peculiar sour smell, which scented the whole of a room very quickly.

Twentieth Day. The animal continued the same. There was free purgation; the excreta still had an acid reaction.

Twenty-first Day. He was better. The purging had ceased altogether. He ate and drank well, and ran about without any difficulty; but he gave evidence of pain when the stethoscope was firmly placed on the chest. The systolic *bruit* was very loud, and was heard over a large surface. Drs. Camps, Henry, and Seaton saw him this day, and confirmed the existence of the systolic murmur.

From this time, recovery rapidly took place; and, day by day, the systolic murmur became more feeble,





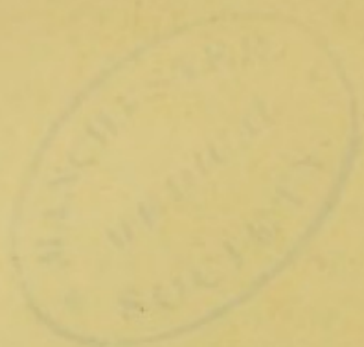
and the pure first sound more obvious. After three weeks, the murmur being now almost extinct, I narcotised the animal to death with the fumes of the *Lycoperdon giganteum*, and opened his body in presence of several of the gentlemen who had seen him during life. All that remained of the endocardial lesion was a series of fibrinous beads along the border of the mitral valve (see Plate III.) The beads were firm and pearl-like. One of the aortic valves was slightly thickened, and quite opaque.

The joints showed no pathological evidence of the disease to which they had been subject.

Experiment XXV. Injection of Lactic Acid. A fine healthy carrier was the subject of experiment. His respiratory and heart-sounds were natural. Into his peritoneal cavity I injected, through a lateral opening, one ounce of the solution of lactic acid with two ounces of water at 96°. The operation seemed to give him little pain. Half an hour after the operation, the pulse was 45. It conveyed to the finger a gentle thrill, and intermitted occasionally. Five hours later the pulse remained the same, and there were marked fits of shivering. He was left for the night with food and drink, and well bedded.

Second Day. The shivering had passed away, and the body was hot and feverish. The heart-beats were quick and sharp, but both sounds were audible. He took but little food.

Third Day. He was moving about on three legs, holding up the left hind leg, and evincing much expression of pain when the limb was moved. The heart-beats were sharp and irritable, the second sound was accented, the first was scarcely audible. He was still disinclined for food, but drank freely.



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The joints showed no pathological evidence of the disease to which they had been subject.

EXPERIMENT CCCC.V. *Injection of Lactic Acid.* A fine healthy terrier was the subject of experiment. His respiratory and heart-sounds were natural. Into his peritoneal cavity I injected, through a lancet opening, one ounce of the solution of lactic acid with two ounces of water at 96°. The operation seemed to give but little pain. Half an hour after the operation, the pulse was 45. It conveyed to the finger a gentle thrill, and intermitted occasionally. Five hours later the pulse remained the same, and there were marked fits of shivering. He was left for the night with food and drink, and well bedded.

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Fourth Day. The joint affection had spread to all the limbs, but the right shoulder was more affected than the others. This joint was much hotter to the touch than the rest; and when it was handled, or when the dog was laid down reclining upon it, the expression of acute pain was intense. The action of the heart was quick and sharp; the second sound was accented; the first sound was accompanied by a soft blowing murmur. There was a general feebleness, but this possibly arose from the inability to move the limbs with freedom, and from the instinctive desire for rest. Pressure on the peritoneum caused no pain.

Fifth Day. The general symptoms were relieved, and the systolic murmur had disappeared; but the first sound was obscure, and the second less accented.

While these symptoms were progressing, the lancet wound in the peritoneum remained open externally, and on this day there was some amount of cellular inflammation about the wound.

Sixth Day. The wound in the flank had a fistulous character, but the inflammatory action had subsided. The general symptoms had also subsided, but he still limped on three legs, the right hind leg being now the one affected. The heart-sounds were both audible and clear. An ounce of the acid solution, with water as before, was injected into the fistulous opening, but the greater part flowed back.

Seventh Day. He was still lame in the right hind limb, and the heart's action was irritable, but altogether he seemed more lively, and better.

As the fistulous opening closed but slowly, I did not reinject this animal, but allowed him to recover. For a few days the joints were at times affected, the lame-

ness moving from one joint to the other. At last recovery was perfect; and, twenty-one days after the operation, he was running about in perfect health.

EXPERIMENT CCCCVI. *Injection of Lactic Acid.* I injected into the peritoneum of a healthy puppy, with the needle injecting apparatus, one half ounce of the lactic acid solution with an ounce and a half of water at 96°. The operation seemed to cause but little pain.

Second Day. There had been slight shivering, followed by heat of surface, and a sharpness and irritability about the heart-beat, but no abnormal character in the sounds. The joints were unaffected. He ate and drank freely, and seemed all alive.

Third Day. He was quite lively, and showed no indication of disease. One half ounce more of the acid solution, with water as before, was injected with the needle apparatus.

Fourth Day. The shivering, followed by heat of surface, and irritability of the heart, had returned; but he continued lively, and took food and drink freely.

Fifth Day. The heart-beat was sharp, but both sounds were audible; the second was slightly accented. The joints remained free, and he moved actively about. There was throughout no indication of peritoneal mischief.

The animal was now allowed ten days respite, during which he made complete recovery. At the end of that time, I injected into the peritoneum an ounce of the acid solution and two ounces of water.

During the operation an accident occurred. The animal struggled, and the needle, being for a moment partly withdrawn while the pressure of the fluid was on, the cellular tissue was injected with the fluid, and an

œdematous tumour was formed round the needle opening. On the following day the animal was prostrated, and the surface of the body was very hot. There seemed to be no affection of the joints. The heart's action was quick and irritable, but both sounds were clear. The animal refused food, but took liquids. His inclination was to lie perfectly at rest. The skin over the injected part was still œdematous, ecchymosed, and showed indications of cellular inflammation. In the evening of the day the animal died.

The *post mortem* examination was made twelve hours after death. There was feeble cadaveric rigidity. The skin round about the injected part was ecchymosed. The intestines and the peritoneal surface presented no redness, nor unusual vascularity; still the intestines were bound together, more or less, by recently deposited lymph. The spleen on its anterior surface had been torn by the injecting needle. There was no congestion of the kidney or liver, but the spleen was soft in structure and much congested. The lungs were in every respect normal.

The right side of the heart was filled with dark and clotted blood, in which were two portions of separated fibrin. The anterior curtain of the tricuspid valve was thickened, pale, and bound down firmly to the heart wall. The other curtains and the lining membrane were healthy, and there were no beads. The left side of the heart was but little affected; it was filled with dark coagulated blood. The curtains of the mitral valve were opaque, but not vascular. Beads were not present, and there was no injection of the surface of the lining membrane. The aortic valves were slightly thickened, opaque, and everted. The pericardium was

normal. The peritoneal mischief was the probable cause of death.

As it is my chief wish, in recording these experimental facts, to leave them with the reader, that he from them may draw his own inferences, I have described them with all the precision as to detail which constant observation could supply, and without comment. Such comments, therefore, as are now about to be made, are to be considered only as those of a mere looker on, and as open to the same criticism as the deductions of a stranger.

The first inference deducible from the experiments, according to my reading of them, is, that lactic acid has the power, when existing in an animal body in excess, of producing a class of symptoms attaching themselves mainly to the fibro-serous textures, and which, regarded in all points of view, are essentially the symptoms of acute rheumatic inflammation.

The symptoms also are obviously dependent on the presence of the poison. Experiment ccciv, which is, in fact, a series of experiments, tells this fact definitely. By giving time for the elimination of the poison, symptoms could be made to disappear; on the re-supplying of the poison, the symptoms returned; the alternation was as marked as night and day, and was as clearly in the order of natural sequence. There was also what the old school-men would call "metastasis" of symptoms; now one joint suffered, then another, again the heart.*

* It also will be observed, in looking over the particulars of the experiments, that in the examples where the heart suffered most, the peritoneum suffered least, and *vice versa*. An exception would at first sight seem to have occurred in Experiment ccciii; but here the bowel was injured, and the intestinal contents were poured into the peritoneal cavity. Regarding this peritoneal mischief, when it was present as the mere effect of the injection of acid, its characters were peculiar. Its cause was evidently connected with slow absorption of the

Thus it is clear that lactic acid has the properties of a rheumatism-producing poison; but that in the human subject it is the veritable cause in every or any case of rheumatism, is only an inference. As yet, there are wanting many experiments to make the matter a demonstration. But this seems to me clearly proved; that if not lactic acid, yet some acid of analogous character is always *the* cause. It has yet to be learned by experiments what formic, acetic, lithic, and butyric acids will do under the same circumstances.

Again, if by after experiment it should be proved that various acids have the same influence, or if it should be proved that the lactic is the one simple representative of this class of special poisons, the experimental argument will have to move back another step towards the primary cause of the disease. The question will next be, Where in the body, and in what manner, is the poison generated?

We are not without a flickering light calling us towards the way in which to pursue this latter inquiry. To understand better the point of origin, is to understand better the process of oxygenation in animal bodies.

In some of my experiments, where animals were subjected many hours to an over-supply of oxygen, the general symptoms were those of an acute inflammatory attack. True it is, that as yet I have never obtained joint-affection by this means; but in one or two cases a vascular condition of the left endocardial surface, closely approaching to endocarditis in the first stage, was clearly

acid, or with a too concentrated dose. Its atphology was not, strictly speaking, the pathology of acute structural membranous inflammation, but rather conveyed the idea that the normal serous and plastic secretion had undergone direct coagulation from contact with the acid fluid. This view is supported in some measure by the facts that acute pain of the abdomen was never present, and that the absorption was least effective when the dose of acid was most concentrated.

present; and in the human subject, I believe endocardial mischief to be a more common complication than is generally conceived of pneumonia, which is the disease *par excellence* of hyperoxygenation.

It will be observed that, in the experiments with lactic acid, the right as well as the left side of the heart was sometimes affected. This was to be expected; for as the poison was thrown ready made into the body, it was taken up at once by the absorbing vessels, and carried into the right heart by the venous current, and afterwards by the pulmonary veins into the left heart, and so to the body at large through the arterial currents. The poison, therefore, of necessity passed through both cavities of the heart, and both were affected. But if by experiment, instead of injecting the acid ready made into the venous current, I could inject into that current an agent which, in the pulmonic circuit, and during the process of oxidation, should be transformed into lactic acid, then the inference is fair that the left side only of the heart would be affected.

In rheumatic endocarditis, occurring from the formation of the poison in the body itself, the left side only is affected as a general rule. Hence I infer that the chemical change whereby the *materies morbi* of acute rheumatism is produced, is completed in the pulmonic circuit; that in the respiratory act the *acid* quality of the poison is produced; that, thus formed, the poison is carried by the arterial circulation to be disposed of by decomposition or elimination, or both; and that it does not return as an acid by the veins, but simply as a product which admits of re-transformation in the pulmonic circuit into the acid state.

If this view be true, it is easy to connect further the

origin of the rheumatic disease with the digestive system, or with the arrest of special secretions. In either case, the basis of the poison may be generated and carried into the returning venous current, thence into the pulmonic circuit, and finally, after oxidation, into the left heart and through the arterial system.

This, as far as inference as incidental to experiment is allowable, is the only explanation of the peculiar fact that in rheumatism the left side of the heart usually suffers alone, and always most severely.

Regarding the origin of lactic acid in rheumatism, a view has been advanced by Dr. Headland, to the effect that ordinarily the starch of the food is first converted into lactic acid, which afterwards is decomposed into carbonic acid and water, and so is excreted by the lungs; but that under conditions unfavourable to this series of changes, the lactic acid accumulates. This view, if it should eventually be proved that lactic acid is *the* unit cause of rheumatism, may offer an explanation of the argument now on hand; for on this hypothesis the starting point of the acid poison would be the pulmonic circuit.

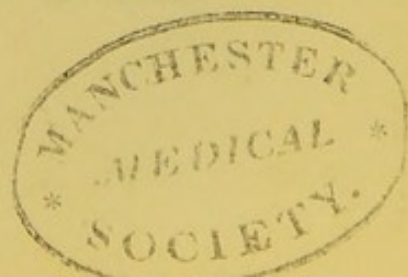
The considerations here introduced lead, moreover, to two other deductions. The first is, that it is vain to look for the *materies morbi* of ordinary rheumatism in venous blood, but that it may be looked for with possible success in arterial blood. The second is, that the action of the poison in ordinary rheumatism is local, *i.e.* by direct application to the endocardial surface; for if the poison were conveyed by the blood to the membrane *à posteriori*, *i. e.* through the coronary circulation, both sides of the heart should suffer alike, which is contrary to the natural fact.

Returning to the experiments, and leaving the argument from inference altogether for matters of fact, there are certain truths, pathological and practical, taught by these experiments, which deserve consideration.

From the circumstance that the animals operated on either died, or were killed, at certain different and well marked phases of the disease, an opportunity was afforded of observing, perhaps for the first time, the course of endocarditis through each successive stage. I find from these observations that endocarditis has three well marked periods of progression.

1. The primary stage is one of congestion and œdema.

In this stage (see Plate I, p. 376), the endocardial surface is intensely vascular, approaching in colour to bright vermilion. The membrane has also a soft fleecy character, giving to it a velvety appearance. The curtains of the valves are in a swollen and vascular state, which my colleague Dr. Halford has very appropriately called an "œdematous condition". If the swollen valve be pricked with a needle, a clear lymph oozes from the puncture, and the valve collapses. In the heart depicted in Plate I, the valve, several times larger than it is shown in the drawing, had lost its fulness before it reached the artist, in consequence of its having been punctured in this fashion. Occasionally during this stage, if the congestion and œdema is very great, there is a transudation of this lymph through the membrane on to its free or ventricular surface. When this occurs, there is laid at once the basis of a fibrinous deposit from the blood. In Experiment cccc, this occurrence was beautifully marked, and as a positive result its value cannot be well over-estimated. For, as in the process here described, there is laid a basis for a fibrinous de-



posit, so is there also a basis for an organised product ; the connection between the deposited matter, and the matter effused on beneath the membrane, being direct.

While these changes are progressing in the curtains of the valves, around their margins, as shown in the drawing, small beads are abundantly developed. These primarily are œdematous points also : they yield a clear coagulable lymph when pricked or compressed, and shrink at once after the operation. In this stage the aortic valves are also vascular.

The general symptoms which mark this stage of the disease are characteristic. There are reduction of the animal temperature, distaste for food, shivering, and then continued feverish excitement, thirst, heat of skin, quick and short inspirations, and rapid sharp pulse. In this first stage, the heart's action is irritable ; the first sound becomes muffled, and eventually is lost altogether. This condition marks the time at which the mitral or tricuspid valves are in the swollen or œdematous state ; and this circumstance has special interest as proving the fact first experimentally shewn by Dr. Halford, that the first heart-sound is dependent on the tension of the auriculo-ventricular valves. During this stage also, the second sound is sharp and accented. Dr. Halford opines that this sharpness or accentuation of the sound is relative only, that is to say, is brought out more strongly from the loss of the first. To my own ear there is, however, always conveyed an intensity of the second sound ; and considering that in all the cases where I could trace out the signs to their pathological origin, the aortic valves were red, and slightly thickened, the intensity here spoken of is accounted for. Lastly, this stage is marked by a short irritable cough, which

is not dependent on mischief in the lungs, but is connected with the condition of the heart.

2. In the second stage of the disease (see Plate II, page 379), the pathology is modified. The endocardial surface loses its intense vascularity, but presents points at which the tendinous cords are bound down to it by loose adhesion. The intense redness is shaded down to a pale pink, the membrane superficially being of the pink colour, while beneath it there is a pale film which shades through it. The curtains of the valves remain thickened, but less red. Their surface externally is pink above, while beneath the membrane there is a pale fleecy appearance, evidently from the presence of clear and semi-solid lymph exudation. With a small magnifying power, this is brought out very beautifully; and in the lowest sketch on Plate III, the artist has depicted this condition with considerable effect. Sometimes, as in the middle sketch of the same plate, the thickened valve, in this instance the tricuspid, is firmly bound down to the heart-wall by firm exudative bands. In this stage, the beads around the margin of the valves have assumed the same characters and appearances as the curtains of the valves themselves; they are firmer, pink on their external surface, with a curtain of pale exuded lymph as the back ground.

The symptoms of this stage are equally characteristic. The heart-sounds are modified. The ventricular valves having lost their spongy or œdematous state for one in which their structure is firmer, a sound results from their attempts at closure, but this sound has become a murmur, which varies in intensity. At first it is wavering, dull, and obscure; then soft, and almost musical; next, loud, harsh, and prolonged. Ultimately, if recovery is

permitted, it gradually melts with the same series of modifications which introduced it, but in reversed order. The general symptoms are peculiar. The acute febrile condition passes away, and there is an obvious elimination of the poison from the body. The amount of urine passed (see Experiment ccciv) is far above the normal quantity, and the secretion is strongly acid. The bowels are freely purged, and this secretion is strongly acid. The exhalations emitted from the body of the animal are intolerably sour to the smell.

3. The pathology of the third stage, or that of resolution, is simple. The vascular character of the membrane externally is removed entirely. The exuded product beneath becomes firmer, and both curtains of valves and beads have for a time considerable firmness, and a pearly whiteness. Later, these parts soften down, as if from absorption of the exuded matter. The curtains of the valves recover their normal characters first; the beads remain longer, and often give rise to a loud musical systolic bruit, which conveys the idea of a much more serious amount of valvular disease than is really presented on inspection. In Plate III (p. 383), the condition of the heart in this stage of the disorder is given with the utmost possible accuracy.

In this stage the general symptoms of the disease disappear, and the animal runs about, eats, drinks, and sleeps in every respect in apparent health.

Such is the sum of the observations I have made on the influence of lactic acid on animal bodies. The recorded facts I leave as facts, independently of any or all the inferences. The inferences I leave as correct or incorrect, according as they are logically deducible from, or opposed to, the actual and observed phenomena.

IV.

DEPOSITION OF FIBRIN IN THE HEART AND BLOOD-
VESSELS DURING LIFE.

IN Chapter III., pp. 64 to 90, I have referred to the subject of the separation of fibrin during life, under certain abnormal conditions. Those observations were recorded merely for physiological purposes. In the present chapter I shall take up in detail certain points which would have been out of place there, and which refer specially to pathological and practical studies.

Simple coagulation of blood in the vessels of the living body, although an occurrence of great rarity, has been observed. At a meeting of the Academy of Medicine in Paris, in 1828, M. Ferris related an instance in which he had endeavoured to perform venesection in a woman, whose arm had suddenly become intensely swollen and of a livid red colour. He found the vein filled with a simple coagulum of considerable length.

But depositions of fibrin in the separate form in the circulatory system during life are of much more frequent occurrence. A word or two on the history of this subject will not be without interest.

In the past literature of medicine, an amount of knowledge is to be found on the subject of fibrinous depositions in the body during life, which would somewhat surprise such members of the medical profession as are unacquainted with the medical literature of the period extending from the time of Malpighi, about the middle of the seventeenth century, to that of Chisholm in the latter part of the eighteenth.

The surprise would moreover be increased by the observation that the many questions involved in the study

of polypoid, or now called fibrinous formations in the circulation, gave rise to a form of discussion, strictly analogous to, and in many respects identical with, the disputes on this matter which have been held in our own times. Whence do these masses come? Why are they found after some kinds of death, and not after all? Are they formed before or after death? If really formed previously to death, are they to be considered as the mere effect of the process of death, or as the causes themselves of the dying symptoms? These, and many other topics of a similar character to those which have been discussed of late, were warmly debated in the period I have named, by Kerkringius, Pasta, Gould, Burserius, Templeman, Queye, Brown, Cullen, Chisholm, Huxham, not to mention many less illustrious names. The process either of learning or of teaching by disputations is never very satisfactory during the time that it is proceeding. It causes, not uncommonly, an overstrained and unguarded enthusiasm; leads to many displays of superficial argument and observation; and rarely succeeds in convincing those who dispute as to the truth of any other thing than the principle to which they have pinned the symbol of their faith. Yet out of the chaos thus produced, knowledge often gleams; but the eye that catches it stands afar off, watching the tumult and appropriating the result.

It was thus with our learned Esculapian friends to whom I have alluded above. Each of them seems signally to have failed in convincing his opponents of error; but their discussions appear nevertheless to have led to some results, and to have thrown a general influence over the practical views of their age. If I might be allowed to express, in a very few words, the general

nature of that influence, as it exists spread over at least a mile of ancient paper in imperishable folios, I should say:—

1. That although the writings of Pasta and Kerkringius were well calculated to lead to a contrary supposition among the advanced Esculapians in the seventeenth and eighteenth centuries, the opinion was pretty general that polypoid concretions were formed in the heart and blood-vessels *previously* to death.

2. That the presence of these concretions in the living body could often be diagnosed.

3. That they were formed out of the blood.

4. That they were peculiar to certain diseases, and to certain stages of those diseases; exhaustion and debility being the most favourable conditions for their development.

5. That they might either form suddenly and destroy life as by one check the circulation, or form slowly and give rise to a peculiar class of chronic symptoms, continued over a lengthened period. *

6. That the concretions were more frequently found on the right than on the left side of the heart.

7. That there were sometimes, though very rarely, and only under peculiar circumstances, epidemic visitations, in which persons seemed peculiarly liable to the development of cardiac polypi.

8. That the concretions were susceptible of undergoing organic changes, such as organisation and vascular adhesion to the walls of the heart, and softening.

9. That cardiac polypi, instead of being substances requiring but little consideration, were of the greatest importance; and that they were the absolute cause of death in many forms of disease.

10. That, in some cases where these formations were attached to the walls of the heart and remained there for a time, while the blood continued circulating, portions of them might be carried away into the other parts of the system, and block up the circulation at its extreme ramifications.

From these statements (the truth of which may be readily confirmed by a reference to those books of this period which are mentioned in the list of authors) it will be gathered that the ancient physicians held views not very dissimilar to those which are held by many living practitioners; and that modern investigations on the subject of fibrinous concretions in the heart are rather to be considered as a continuation of the labours of a past age, than as the original productions of the present period, as is too often presumed.

That the generally improved state of knowledge on medical matters in these days has led to an improved and refined order of writing and of thinking in relation to the subject of fibrinous concretions, there cannot be a doubt. Still, as I have before intimated, the main points of discussion which existed in the past age exist now; and, in discussing the subject in the forthcoming pages, it will form the chief portion of my labours to confirm and elaborate the ten leading principles which I have described as having been held by writers of the seventeenth and eighteenth centuries.

It will probably be asked by some, how it has happened that statements and opinions so generally believed in in the course of the last century, could have become obsolete in the earlier part of this; *i.e.*, if they possessed any approach to the truth? The solution of the question is easy. In the period named, the practice of me-

dicine, which always is modified by new theories either in practice or in physiology, was diverted briefly from the study of the circulation of the blood, towards a method which endeavoured to explain everything in disease by dogmatical, but often incomprehensible, references to the functions and derangements of the nervous system. As each discovery in relation to the nervous system was made, a series of hypotheses were woven about it, in relation to diseased conditions, which tended much more to embarrass and mystify medical practice than to rationalise it. Thus it came about that, whatever the cause of death might be, little or no differences were made; for men could only die suddenly from "apoplexy", or "shocks to the nervous system", or "nervous exhaustion"; and in the *post mortem* room, the brain was examined for microscopical causes of dissolution, to the almost total neglect of other parts and organs. In short, to use the language of my former distinguished Professor, Dr. J. A. Easton, "the nervous system was made the convenient beast of burthen, on which observers of all diseases saddled all their peculiar little difficulties."

In a preceding chapter (III), I have already pointed out facts, which prove to a demonstration that fibrinous depositions may occur during life. It has been there shown that the fibrinous deposit may positively be removed from the heart of an animal, while yet that organ is contracting briskly. Further evidence of this kind is not required.

I shall, therefore, in this place, confine my observations more closely to the mode in which fibrinous depositions are laid down, and to the symptoms by which their presence is characterised.

Construction of Fibrinous Concretions.

An attempt has been made by some authors to determine the parts of the vascular system in which fibrinous concretions are most commonly formed, as though some law regulating their formation might be learned from such observations ; and a few years since (in 1850), when the subject now under discussion was beginning to attract my earnest attention, I attached great importance to this inquiry. But as time has gone on, and opportunity for reflection has been afforded, based on a broader and more comprehensive experience, I infer that this question of frequency, as regards the situation of the concretion, is a matter of less moment, since the fact has come out that the position of the concretion depends on physical causes, having their origin in the disease of the system which gives rise to the formation itself. Thus, from physical causes which I shall eventually explain, taking all cases into consideration, the heart is the most common seat of these concretions ; but they also form in the veins and arteries, and in the right side of the heart as readily as in the left. But wherever they may be found, the arrangement, shape, and position of the fibrinous concretions are subjects very important. In the following pages, I shall discuss all these points leisurely, with some others which may spring up incidentally, recording chiefly such observations as I have myself conducted.

The position of a concretion in relation to the blood near or around it, requires to be well considered. Many writers, looking at these formations hastily, have stated that the concretions are invariably found existing as the upper strata of clotted blood, as though they were

merely formed during coagulation of the blood in the body after death, as the buffy coat is formed in the cup after venesection. In regard to this question, it must be admitted, that occasionally clots of blood are found coated with a layer of fibrin, which has obviously been produced by coagulation of the blood during or after death. Fibrinous layers of this kind are, as a general rule, found in the right auricle, and more rarely in the right ventricle. The layer lies in these cases upon the blood; and, as the body usually lies horizontally during the time that coagulation is taking place, the surface of the clot is not directed toward the base of the heart, but toward the anterior wall of the auricle or ventricle, and parallel with the anterior wall of the chest. The concretion in this case takes the shape of the ventricle, being convex anteriorly, and flat or concave where it lies in contact with the blood. It is thin, varying from the thickness of a shilling to that of a half-crown; and it may be easily raised from the clot of blood beneath, into which it is gradually shaded.

Such is the description of the only kind of fibrinous concretion that is formed, as I believe, after death from simple coagulation of the blood. Compared with other concretions, it is rare; but it may exist either alone, or together with other concretions, which present unmistakable evidence of a formation previous to death from blood in motion.

The purest form of a concretion formed during life is that which absolutely fills one of the cavities of the heart, and with which few traces of clotted coloured blood are to be detected. I have three such specimens before me at this moment, all of which have been exhibited at the Medical Society of London. One is from the heart of

a child who died of acute laryngitis, the second from a child who died of pneumonia, and the third from an infant that suffered from hypertrophy of the spleen and purpura. In each case the concretion was removed from the right auricle, the cavity of which it completely filled, sending a prolongation into the inferior cava. Surrounding these concretions, there were lines of coloured blood; from which it would seem that the manner in which the fluid blood found its way into the ventricle past the obstruction caused by the concretion, was by flowing round it. In instances of this kind, there can be no doubt of the concretion having existed previously to death, for there could be no sufficiency of fluid blood in the auricle at death to yield such a concretion by the ordinary process of coagulation.

I have also met with three instances of concretion in the right auricle, in which a kind of double concretion was present, the division having been caused by the current of blood from the superior vena cava. In these specimens, the concretions have originally commenced to form from two points,—one from the appendix auriculæ, the other from a part of the auricular wall between the openings of the superior and inferior cavæ. As time goes on, and the fibrin is laid down, layer upon layer, on each point of attachment, the concretion increases; the upper one deriving its substance from the blood of the superior cava, the lower one from the blood of both the superior and the inferior cavæ. The current of the inferior vessel now passes between the wall of the heart and the inferior surface of the lower concretion; the current of the superior vessel, between the upper surface of the lower and the inferior surface of the upper concretion. In this way the circulation

will often go on until the spaces left for the current of blood through the auricle are reduced to a few lines in extent; and the two existing concretions seem almost as one, their parallel surfaces being separated merely by a film or band of coloured blood-clot.

Wherever situated in the heart, a fibrinous concretion, if pre-existent to death, has an attachment more or less firm to some favouring point in the cardiac wall. The degree of firmness varies with the nature of the surface. In the appendix auriculæ, the rough muscular structure affords an excellent *point d'appui*; and here, therefore, a concretion forms a firm connection. The connection is, however, as a general rule, mechanical only; the fibrin, divided into filaments, entwining itself round the muscular columns. In other instances, where the surface is less irregular, the fibrinous matter is laid down in a fine delicate stratum, which may be raised with the forceps; and in some inflammatory cases I have found the internal cardiac surfaces lined with these transparent layers, which resemble so closely the endocardial membrane itself as not to be distinguished from it without careful examination.

A concretion sometimes extends from the right auricle into the corresponding ventricle. Thus extending, it generally passes as a loose body, suspended as it were from the superior, into the inferior chamber. But I have also met with a concretion taking the same course, but adherent all its way to the side of the heart. In the first case of this class which came under my observation, the concretion seemed to have taken its origin in the extremity of the appendix auriculæ, to which it was firmly attached; it then swept down by the cardiac wall, and passing out of the auricle through the auriculo-

ventricular opening, and over part of the tricuspid valve, ran down into the ventricle, and curved upwards into the pulmonary artery; thus describing in an unbroken manner the exact course of the blood from the superior vena cava into the pulmonary artery. It adhered more or less firmly to the wall of the heart through the whole of its course, and its surface facing the cavities was coated with coloured blood.

In another case (*see* drawing, page 66), the concretion, having its root lower in the auricular wall, presented a large body which nearly filled the auricle, terminated in a lower limb which ran over a part of the tricuspid valve, and attached itself to the muscular wall of the ventricle at the root of the pulmonary artery.

In both these cases, the action of the tricuspid valve was quite destroyed by this fibrinous deposit; and it was with great difficulty that, in the first named case, one section of the valve was set at liberty, for I was obliged to divide the concretion and dissect it cleanly away to accomplish this end. It would, of course, be absurd to suppose that concretions thus placed and arranged could be formed after death.

The most common point at which concretions form in the right ventricle is the tapering part that runs up toward the pulmonary artery—the infundibulum. The concretions here found are often more or less cylindrical—the cylinder being tubular, and made up of distinct longitudinal layers. This fact of the cylindrical tubular character, sometimes assumed by fibrinous concretions, is of vast importance, as proving incontestably the existence of these masses previous to death. I believe I was the first pathologist whose attention was turned to these hollow cylinders of fibrin. The cylinder is peculiar to the round or tubular portions of the vascular

machinery, and the pulmonary artery and the infundibulum are excellent points for finding them. To see them properly, the artery and ventricle should be divided together perpendicularly. If a concretion then be present in the canal thus laid bare, it may be found in various forms. 1. It may lie as a semi-cylinder around part of the canal, attached firmly by its base to the muscular wall of the ventricle. 2. It may exist as a pure hollow cylinder, completely coating the vessel, and filled in its interior with red coagulated blood. 3. The concretion may lie loose like a plug of a conical shape—its base in the ventricle, and its apex tapering and running into the artery; its body being modeled sometimes by the semilunar valves, and its external surface being separated from both artery and heart by coloured coagulated blood. Sometimes the deposition is formed, in the first instance, as a hollow cylinder; but, from the force of the blood-current, and from an imperfect adhesion of its lower part to the cardiac walls, it is torn away from its attachment, and left loose in the artery. Thus placed, it contracts on the blood in its centre; and the current of blood rushes between it and the wall of the vessel, and thus finds its course into the lungs, so long as life continues. Virchow has pointed out, that occasionally, when a concretion exists as a plug in the pulmonary artery, the blood forces its way between the concretion and the vessel, taking a spiral course around the concretion. I have observed this in more than one instance. It occurred, however, most strikingly in the cat experiment, page 73. The spiral character of the concretion is given in the drawing here reintroduced.



Concretions formed in the right ventricle very often have attached to them long filaments which extend into the smaller pulmonary vessels. These filaments are also tubular in some cases, but not in all. Of late, I have been in the habit of examining the ramifications of the pulmonary artery in all cases of death, a piece of pathology which has been much neglected. In these inquiries, I have once or twice found fibrinous cords existing in the smaller branches of the artery without any mass of concretion in the ventricle; and I believe that in some instances, where the circulation is exceedingly feeble, the extremities of these vessels are slowly plugged up with fibrin, the deposition commencing in this instance at the extreme points of the pulmonary arteries, just as in the case of an artery that has been tied by ligature.

In the left cavities of the heart, concretions are formed after much the same principle as in the right cavities. I have, however, rarely met with a large concretion in the left auricle; never with one large enough to obstruct seriously the passage of blood through that cavity. Here, generally, they merely line more or less of the auricular wall, to which they are firmly attached in many cases, and slightly in all. In the left ventricle they are to be met with,—1. lining its walls in coats of various thickness, as on the right side; 2. in irregularly shaped masses attached to the valves, and as cylinders in the infundibulum; 3. in filaments and cords stretching across and entwining around the chordæ tendineæ and other portions of the valvular machinery.

These, in general terms, are the forms and varieties of fibrinous concretions found in the heart after death. Whenever one concretion is found in a heart, it is in-

teresting to look for more, and sometimes the search will be crowned with peculiar success. Behind the columnæ carneæ, beneath the surfaces of the valves, deep in the interstices of the muscoli pectinati, shreds, filaments or layers of fibrin may often be found, all affording demonstrative evidence of an existence previous to death.

Fibrinous concretions sometimes found in the arterial system. I have already said something of the existence of fibrinous concretions in the pulmonary artery, and of their mode of formation in that vessel. In the arteries of the general system, fibrinous masses have an importance not easily described in words. The arch of the aorta is a very common point at which they form. Here existing, they are almost always hollow cylinders; and it was in the examination of a concretion removed from the dilated aorta of an aged woman, that I first observed the hollow cylindrical nature of a concretion. A concretion in the aorta varies considerably. Sometimes it has its root in the left ventricle, extends up the ascending aorta, over the arch, and for some distance down the descending trunk. When this is the case, there are always some branches, passing off from the concretion into the vessels arising from the aortic arch. A concretion may also be found, having its commencement above the aortic valves, and unconnected with the ventricle. In these cases there is generally some diseased condition of the aorta; it is either dilated, or roughened on its inner surface; or else the concretion, having commenced in the ventricle, has been broken off from its attachment and been carried past the semilunar valves into the vessel.

Dr. Crisp, in his valuable practical work on the arteries, has described a case in which a fibrinous con-

cretion was found attached to a hardened cartilaginous aortic valve. The membrane covering this valve internally was ruptured in a perpendicular direction. Dr. Crisp attributes the sudden death to the mere rupture of the valve; but my own impression is, that the tearing of the valve was secondary to, and a result of, the plugging up of the aortic orifice by the concretion. This, however, is the only instance I am acquainted with, in which a concretion could be assumed to have given rise to a visible recent lesion in the circulatory organs.

It is quite remarkable how large the concretions situated in the aorta sometimes are. In relation to the blood they may hold three positions. They may be found as cylinders, or semi-cylinders, with blood within them; as detached cylinders with a vein of blood running through them, but bathed also in blood on their outer surface; and, lastly, as detached solid cylinders, representing, in fact, mere plugs or cords.

Occasionally a fibrinous cord, and sometimes a semi-cylinder of fibrin, is found lying in the thoracic aorta. Such development has always some point to which it either has been or is attached; such as the mouth of one of the small branches of the intercostal arteries, or some roughened point in the vessel.

In the more extreme parts of the arterial system, fibrinous concretions may likewise present themselves. Here they may plug up a main trunk for a considerable length, or may merely close up a vessel at its terminal part; and, as in the branches of the pulmonary artery, they may either be tubular or solid in structure. The most extensive development of fibrinous concretion in the arteries that I have ever read of, is given by my friend Dr. Fuller, in the *London Medical Gazette*

for 1847. In this remarkable case, the whole of the arteries in the inferior half of the body seem to have been choked with fibrinous masses; and I once saw a case myself, in which the brachial and femoral arteries were blocked up in a similar manner. In another case which I examined, I found the basilar artery and several other branches of the circle of Willis plugged up with fibrinous concretions; these arteries were very much diseased, they were dilated and unyielding tubes from atheromatous and bony deposit.

I have never yet been able to positively satisfy myself as to the construction of concretions found in the smaller trunks of arteries. In the case named above, where the concretions were found in the arteries of the brain, they were distinct hollow cylinders; and I suspect they are so in many other cases.

It were impossible to leave the discussion of this subject without a word on the deposition of fibrin in aneurismal tumours. In these dilated chambers we see represented, on a large scale, what is much more frequently met with on a smaller scale in more ordinary cases of disease. The position of the fibrinous mass in an aneurismal tumour is in no way specially related to any peculiar position of the blood-current. It may lie beneath the current, above it, or completely around, so lining the tumour throughout. In a most interesting case, which I reported to the Medical Society of London, of aneurism of the aorta, in which the root of that vessel measured six inches in circumference, and the *arteria innominata* was lost in the expansion of the ascending aortic trunk, an immense fibrinous deposit, firm, dense, in layers, and of the size of a large orange, lay in the upper part of the tumour, its convex surface

being applied to what was originally the inner and upper surface of the arch of the aorta, so that the mouth of the left common carotid was quite sealed up; while opposite to this mass, that is on the lower surface of the aortic arch, which was roughened from osseous deposit, lay a large and very distinct half tube of fibrin of recent formation, which served effectually, in combination with the mass above, to block up the blood-channel. Some blood, it is true, had forced its way along the vessel, between the two fibrinous deposits, for each one was grooved by the current, and some blood still remained in the groove thus formed.

In the venous trunks fibrinous concretions sometimes form. Dr. Burrows records a remarkable case (Croonian Lectures, *Medical Gazette*, August 15, 1835), in which a mass of yellow looking coagula was found to fill the inferior vena cava and the iliac veins, the obstruction giving rise during life to great enlargement of the veins of the inferior extremities, and to œdema. In Dr. Fuller's case also, the vena cava inferior was blocked up by coagula at its point of junction with the iliacs; and Morgagni has related the history of a woman whose body previous to death had been universally tumid and of that livid hue which the skin usually presents when a great number of the subjacent veins are tinged with blood. In examining the body of this woman, John Anthony Stancari found the vena cava and emulgent veins dilated; the coats were partly cartilaginous, and in other places bony; and they, as well as the iliac and other veins, were nearly filled with a hard and polypous substance. Various similar cases have been given by modern writers.

I confess myself unable to speak satisfactorily as to

the construction of fibrinous concretions situated in the venous trunks. I refer the reader to the distinguished Virchow's researches on this point, because he has studied this subject from nature, and I have not. His writings on this point were, indeed, perfect but for one fault; viz., the use of terms, such as "thrombus" and "emboli," which are quite unnecessary, and will only add more confusion to the Babel of medical literature.

Considerable attention has been paid by different observers to the manner in which fibrinous concretions are placed in relation to the blood-current. I have met them with the elongations opposed to the stream of blood, or bending with it. The difference depends on the manner in which the concretion commences and progresses. If it commences in the face of the blood-current, as, for example, in the right auricle, or in the extreme points of the pulmonary arteries, the deposition takes place, layer upon layer, in the face of the current; and the free end of the concretion points necessarily into the current, and is often coated with red blood-clot. If, on the other hand, the concretion, commencing at one point, is laid down with the stream, it usually assumes the tubular character, and the free end of the deposit goes with the current.

Modifications of structure in fibrinous concretions. The difficulty of distinguishing between a true fibrinous concretion and other growths or formations which may form in the heart, and the confusion arising out of this difficulty, were fully recognised by Morgagni; who says, in speaking of polypus of the heart (*Seats and Causes of Diseases*, translated by Cooke, vol. 1., page 364), "Concretions found in the heart have been compared by different anatomists to marrow, fat, and sometimes to

flesh; and their appearance bears an accurate resemblance to these substances. But those who imagined that they really were of this nature were satisfied with a very superficial examination of them, and were consequently deceived. Those, however, who were not under a deception, and who really saw that blood-vessels had extended into these substances, a circumstance which I have never seen, did not then meet with the polypi of which I now speak, but with excrescences of the heart. *The principal and peculiar substance of these polypi is the same as the crust which often forms on the surface of coagulated blood.* These concretions, however, are sometimes begun and completed in the living body."

The difficulty which the prince of pathologists here glanced at, is not removed even in this day; for it still remains a disputed question whether mere fibrinous concretions can really become organised, or whether any of the organised growths which are sometimes found attached to the internal surface of the central organ of the circulation have at any time been mere fibrinous deposits. I met with a very interesting case some time since (see *Association Medical Journal*, April 14th, 1854, p. 340), in which a peculiar growth existed in the left ventricle of the heart, and adhered to the mitral valve. This growth had obviously been there for years; and from the manner in which it was interlaced with the muscular columns in the ventricle, had all the appearance of having been originally a fibrinous concretion, and of having subsequently undergone some form of organic change. The microscope proved that this mass was made up of white corpuscles embedded in a network of areolar tissue, with no trace of vascularity. At page 88, I have recorded an example of an organised concretion.

The mere fact of a concretion having a firm hold on the cardiac walls, has been set down by some authors as a proof of the possibility of an organic change in these developments. This, however, is possibly a fallacy when applied to the majority of cases in which these intimate mechanical adhesions occur, and of which I have given some illustrations (page 89). But we have seen, in referring to acute endocarditis, that an exudation of plastic matter may form the basis of a deposit, and it is possibly in such manner that true organised concretions are produced.

A concretion was once shown to me by a medical friend, which he supposed to be organised because of its peculiar red and fleshy appearance; it certainly resembled a piece of muscular structure very closely. But I found that the red colour depended merely upon a tinge derived from the colouring matter of the blood, and the symptoms of the case indicated that the mass had been of very modern formation.

Fibrinous concretions are occasionally found having in their centres a fluid resembling ordinary pus in appearance. This circumstance was at one time put forward as proof that these formations were capable of organisation, this fluid being mistaken for pus resulting from disorganisation, as in ordinary living structures. The researches, however, of Mr. Gulliver have proved that this fluid, found in fibrinous masses, simply arises from internal softening of the mass itself, and is no proof of organic adhesion.

Weight, size, and consistency of fibrinous concretions.
There is a concretion preserved in the College of Surgeons, which filled up nearly the whole of the thoracic and abdominal aorta, and which must have

weighed several ounces when removed from the body. One dense tubular concretion which I removed from the aortic arch and ascending aorta of an aged man, weighed no less than 170 grains in the fresh state, the ventricle behind being engorged with firmly clotted blood.

Their consistency varies. In the auricles of the heart fibrinous concretions are, as a general rule, softer than those found in the ventricles. This is easily accounted for, by a reference to the fact that the contractile power of the auricular walls is very much less than that of the ventricular. The concretions, consequently, are less compressed in the auricles; indeed, I have seen the right auricle distended to nearly twice its natural size by a concretion.

The consistency of concretions depends upon the amount of watery matter which they contain. They are most dense when most fibrous. They are all more or less elastic; but the elasticity is shown best in those which are long, and are dense in structure. They rapidly contract when removed from the heart, but swell out again if immersed in water, in this respect resembling ordinary fibrin removed from blood by whipping it with a bunch of twigs. When a tube of fibrin is detached from its hold on the cardiac wall and is left perfectly free, its two ends contract, like the mouth of a divided artery, giving the concretion the appearance of a solid cylinder with conical ends, and completely concealing the blood in the interior. From this cause, these kinds of concretions have often been mistaken for solid plugs or cords.

Some authors have described fibrinous masses of a granular friable kind. In these instances the masses must

have existed for a long period in the heart, and have passed through some form of chemical or degenerative change, under the influence of the blood-current and the contractile motion of the central circulatory organ. I have never myself met with concretions of this type.

The breaking up of a concretion under the influence of the blood-current, and the sealing up of fine vessels by the fragments, has been suggested. Gould was a very decided advocate of this supposition. In the course of these last few years, the same theory has been advanced originally by Dr. Kirkes. That from a fibrinous clot in the heart, which has undergone some sort of change rendering it soft or friable, small portions may be detached and be borne into remote parts of the arterial system, is a circumstance as probable as it is possible ; and I once saw a case, in St. Mary's Hospital, through the kindness of my friend Dr. Sibson, in which this event had occurred. A man came under Dr. Sibson's care, suffering from a peculiar embarrassed condition of the heart. This continued for several days, when suddenly the embarrassment was relieved, but was followed almost instantaneously by numbness and coldness in the right arm, which continued more than a week. The man, it should be added, had old standing valvular disease. Dr. Sibson's diagnosis in this case was, that the embarrassment of the heart resulted from a concretion formed on the left side ; that the sudden relief arose from the detachment of the concretion, which, being carried into the brachial artery, sealed up that vessel, and produced numbness of the limb, until a re-supply of blood was ensured to it by the establishment of the circulation through anastomosing branches.

But the occurrence of such cases as these must not lead

the medical observer to the conclusion that all masses of fibrin found in the arterial system have been thus carried out of the heart. For, as fibrinous concretions form in veins quite independently of any such process, it is clear that they may form in arteries after a manner equally independent, *and that concretions in arteries, as in veins, may be formed at the places where they are found.* I once found a *tube* of fibrin placed in one of the cerebral arteries. This could only have been formed where it was found. Whenever the circulation is rendered excessively feeble, whether from debility of the heart or from the presence of a concretion, thus rendering the course of the blood through the capillaries slow, it is just as easy for the fibrin to be laid down in the extreme arterial branches as in an artery whose calibre has been diminished by the pressure of a ligature; and this, I believe, is what often occurs in the pulmonary artery, when the flow of blood into it is slackened by a concretion obstructing the right side of the heart. Thus the existence of a concretion in the heart may coexist with a similar concretion either in the veins or arteries, or both, and yet each concretion may be formed quite independently of the other.

In a case of gangrene of the fingers in an anæmic woman, reported by myself in the *Medical Gazette*, 1852, there existed in the veins small pultaceous masses, which could be felt and could be pushed along in the course of the blood-current. The woman recovered, and is still alive.

Appearances of other organs. Whenever a large fibrinous concretion blocks up some important part of the circulation, for any considerable period antecedent to death, it gives rise invariably to certain pathological

changes in neighbouring structures. If the right auricle be filled with a concretion, as it often is in cases of croup or acute bronchitis occurring in young children, the abdominal veins and organs are congested to a remarkable extent, while the right ventricle is deprived of blood: the lungs are absolutely blanched and often emphysematous, and the left side of the heart and the arteries are comparatively empty. These conditions are easily accounted for. If a concretion exist on the right side of the heart, but only of such proportion as but partially to obstruct the blood-current through the pulmonary circuit, there may be, and often is found, not only a congested condition of the abdominal veins, but of the right side of the heart, of the pulmonary artery, and of the lungs, with fulness perhaps both of the left ventricle of the heart and of the arteries. I once saw general anasarca caused by the partial blocking up of the right auricle by a fibrinous concretion. Again, should the concretion be situated in the left cavities of the heart, or in the aorta, more or less of congestion of the lung occurs, according to the size of the concretion and its exact position in the cavity or vessel; while the venous system and right cardiac cavities also present indications of congestion. Lastly, when an artery or vein is plugged up with fibrin at a point distant from the central circulating organ, there may be general disorganisation of the structures beyond the concretion, if the obstruction is arterial; or œdematous swelling of veins if the obstruction is venous.

To resume: the evidence from a fibrinous concretion itself, that it has been laid down during life, is supplied in observing whether its construction accords only with the idea that it was formed while there was yet living

action for its special construction. If it assume the tubular or semi-tubular character ; if it line a cavity, as an added layer ; if it be made up of distinct layers ; if it have a firm attachment, mechanical or by vessel ; if it have impressed on it a model of valve-structures ; if it assume a spiral character : under all or any of these circumstances, it has been formed before death.

Again, a concretion may commence in the course of the circulatory canals, and may be built up in opposition to the current ; in which case it will be a plug or solid cord. Or, commencing on some point of obstruction, as the side of the auricle, it may go with the stream, and be deposited with it ; in which case it will be deposited in layers, and assume, more or less, a tubular character.

Lastly, a portion of concretion dislodged from the heart, may be carried into the finer ramifications of the systemic arteries ; or a portion detached from a vein may (but this is rare) be carried into the right heart, and thence into the pulmonary artery and its ramifications. At the same time, concretions admit of being formed at the actual points where they are found ; and in many cases are thus formed and deposited.

Conditions which lead to Deposition of Fibrin.

In chapter III, there are briefly sketched out the leading physical conditions which favour the deposition of fibrin in the circulation ; viz. actual increase of fibrin, relative increase, and impeded motion. We are prepared now to see a little better the way in which these conditions assist in the act of deposition.

The simple fact of deposition from absolute increase of the fibrinous constituent is very simple. The excess of fibrin cannot be held in solution ; it is out of pro-

portion to its solvent, and deposition becomes a mere mechanical result, taking place at such parts as afford most resistance, such as a point of exuded matter, or a thickened valve. When the excess is relative, the effect is virtually the same; except in special cases, cholera for instance, where the diminution of water is attended with increase in the amount of alkali; or in cases where the respiration is much impeded. In the third class, where an obstruction to the current of normal blood gives rise to the deposition, the deposition is the result of partial stasis of blood at the obstructed point. The blood, thus checked, yields up its solvent to the blood-current which does pass along the tube, as the blood in the test-tube beneath a current of blood-vapour yields up its solvent to the upper and fluid stratum, and straightway solidifies. In the aneurismal cavity, this process of separation is exceedingly simple. Lancisi, and also Dr. Baillie, were aware that the deposition in the aneurismal tumour is most marked at the point where the current is most feeble. But Lancisi attributed the effect to a mere statical cause; and stasis is, after all, the primary element. But stasis in itself would never lead to deposition if the fluid were permanent; nay, it does not even lead to the final deposition of blood-corpuscles, for these are washed away with the stream; but it is sufficient to lead to the deposition of the plastic fibrin, held as it is but temporarily fluid by a solvent which, under favouring physical conditions, is diffused and borne away. In instances where the fibrinous deposition is the mere result of an enfeebled circulation, there may yet be other conditions favourable to deposit. There may be, for example, as in phthisis pulmonalis (in which disease these depositions

in the heart ordinarily are found in the last stages of life), an absolute loss of the blood-solvent, either by its rapid elimination, or by an arrest of the process by which it is normally supplied to the blood.

The effect of some septic agents in inducing fibrinous deposition is a point which must not be overlooked, however little we may know concerning the influence of such agents. I presume, but on this I have not sufficient experimental data to lead to any positive conclusion, that a poison having weak acid properties, or having the power of giving rise to the formation of an acid on being introduced into the circulation, would by its presence lead to a deposition of fibrin. Experiments differ in regard to poisons thrown into the blood. Gaspard and Lee found that the injection of pus gave rise to fibrinous deposit. Magendie injected putrid fluids, and produced permanent fluidity. All may depend on the condition of the fluid used at the time of its injection. Pus having an acid reaction, as sometimes obtains, produces, when added to blood newly drawn, instant coagulation. A little more of the same specimen of pus, allowed to stand till decomposition has commenced, and it has acquired an alkaline reaction, on being added to blood in the same proportion, retards coagulation, or stops it altogether.

Lastly, there is a condition which has long been known to favour coagulation and fibrinous deposition. I mean loss of blood, and syncope or exhaustion during impoverished states of body. The explanation here is, that these states are attended, as a general rule, by an excess of fibrin in the blood as well as by an excess of water. The fibrin solvent is thus widely distributed, the density of the blood is reduced, the fibrin super-

abounds, and stasis only is required to give all the circumstances favourable to deposition.

Symptoms and Diagnosis of Fibrinous Concretions in the Heart.

The symptoms produced by fibrinous deposition in the heart are strikingly characteristic when they are once understood. But as they are commonly super-added to other symptoms, and appear at the acme or near the end of a disease, they occasion great perplexity to all who are not prepared to read them off, and whose attentions are bent to some mere local mischief, by which the disease perchance is misnamed, rather than to the grand changes which are occurring in the body as a whole.

Whatever be the disease, the effects of a fibrinous deposition are in the main the same, according to the manner in which the deposit itself is laid down. In other words, the symptoms depend on the position, form, and character of the deposit, less than on the pre-existing malady.

Whenever fibrinous deposition takes place in the heart during the course of a disease, the pure symptoms of the disease are lost or masked by the new symptoms which are set up, and which take to themselves a general representative position.

The advantages which I have had for tracing out the symptoms produced by concretion, and for confirming by dissection the diagnosis instituted, have been confined mainly to cases where active inflammatory mischief (hyperinosis) has been the forerunning disorder. I write, therefore, from these sources of natural information.

All symptoms of acute inflammatory disease are attended with some risk of fibrinous deposition. Taking the majority of such cases, the risk certainly is small ; but it is present in each case, and what renders the risk more serious is, that such risk or tendency to deposition cannot be measured by the local indications of inflammatory mischief in any given case, nor yet by the general symptoms which accompany the local. The symptoms of concretion may supervene in the mildest as in the severest cases. They may creep on insidiously ; they may take effect in a sudden and unexpected outbreak. The following is an outline of a case in which the symptoms are unexpected. I write as I have seen, and as others have seen.

A patient is suffering from an acute inflammatory attack. The local mischief, be it pneumonia, bronchitis, erysipelas, peritonitis, rheumatism, is not in itself such as to cause immediate alarm. The symptoms go on from visit to visit, and the patient is left on one of these occasions not apparently in imminent danger. Unexpectedly, there is a sudden call for the practitioner. He goes, and in the universal change that has occurred he reads off the death-signals. The man will sink. The fact as it is written in the patient is not to be described in words, but is easily learned from experience ; it is written in the face of the sick man, in the restlessness, in the expression altogether. Whoever knows disease, knows at once, without further comment, what I mean. It is my business to show how far this *finale* of inflammatory disorders results from fibrinous deposit, and to indicate how the symptoms, when studied in detail, yield the diagnosis of concretion.

If my observation of the last symptoms and of the

pathology of the cases thus referred to be correct, the origin of the symptoms is connected with obstruction on the right side of the heart, in the majority of instances. The obstruction may be on the left side ; but the occurrence is comparatively rare, and the symptoms themselves are modified in detail by the difference in the point of obstruction.

Taken generally ; the symptoms of fibrinous obstruction on the right side are those which might be anticipated on *a priori* physiological reasoning, as necessarily incident to obstruction of blood-making towards the pulmonic circuit. They are the symptoms of arrest in the nutrition and life of the body. They are characterised primarily by a peculiar and distressing dyspnœa. This occurs, not because the respiration is checked, for the respiratory murmur may be audible enough, but because the current of blood to the lungs is in part cut off. As an addendum, emphysema of the lungs, especially in children, results, and the physical signs of this lesion are often a valuable corroboration of the presence of concretion on the right side. The dyspnœa depends on the deficiency in the supply of blood to the lungs and the nervous centres. The left side of the heart being imperfectly supplied with blood, the arterial circulation is weakened ; the pulse is small and intermittent ; the surface of the body is cold, and generally white as marble ; but, as there is stagnation of blood in the venous circuit, the more vascular parts, as the lips and centre of the cheeks, are often of a leaden hue. There is general muscular prostration ; and, as the brain is not supplied normally with blood, the muscles are not under the control of the will, but are in a continued restless motion. The mind loses its power ; the acts of excretion are per-

formed involuntarily; and death sets in, the gasping respiration outliving the paralysed and obstructed heart.

The symptoms thus portrayed are applicable to cases in which they last for several hours: in such examples the concretion is either lodged in the right auricle, or is being laid down as a tube in the infundibulum and pulmonary artery, or is commencing at the extremities of the pulmonary circulation.

But other cases occur, where the course of the symptoms is suddenly cut short. There may have been some slight premonitory symptoms, but the suddenness of the end is the great fact. The patient, previously exhausted, is rising in bed or making some muscular movement or strain, when suddenly he reclines or falls, breathless, faint, feebly convulsed, dead.

I have met with two illustrations of this last event. The cause in both cases was the same, and the cause is ordinarily the same; the pulmonary artery is suddenly blocked up with a fibrin cylinder. In each of the cases observed by myself, this cylinder had been hollow, and had conveyed a stream of blood like a tube. Its base had commenced in the infundibulum; its apex had ascended into the pulmonary artery. The concretion had suddenly been torn from its attachments, and carried up into the artery. In its centre was a column of red clotted blood; externally it was encased in a thin layer of blood, the result of a rush of blood past the concretion after its detachment.

Once more: there are instances where the symptoms are unusually prolonged. In one instance which I observed, the symptoms of dyspnœa extended over many days, and anasarca supervened as a result of the obstruc-

tion. The concretion, in this instance, commenced in the auricula, where it had a firm attachment, and sent a prolongation downwards into the ventricle. In the case supplied by Dr. Sayer, and described at page 89, the symptoms of dyspnœa extended over many months; and Mr. H. Lee has recorded an instance in which a similar extension of symptoms occurred.

When the concretion is deposited on the left side of the heart, the ventricle, the infundibulum, and the ascending portion of the aorta, are the most common positions. The symptoms which characterise the presence of concretion here situated are different in many respects from the preceding. There is tumultuous action of the heart, a symptom which is strikingly indicative that the deposit is on the left side. There is congestion of the lungs, and suffocative dyspnœa, with expectoration sometimes mixed with blood. The surface of the body is of a leaden colour, and the body is cold. The muscular perturbation lapses into powerful convulsions, and coma precedes dissolution. These symptoms may extend over many hours.

But, as in the preceding class of cases, the symptoms may also occur in a sudden manner. The patient, in moving or making a straining effort, suddenly falls back, is seized with a violent convulsive fit, and so expires.

I once saw these symptoms and this sudden form of death in an old lady, who had previously suffered from no other symptoms than a slight attack of cold. In rising from bed she fell, as I have described, and died before medical assistance could be obtained. In this case, the concretion had formed as a hollow cylinder in the infundibulum of the left ventricle, had become dis-

lodged, and had been carried into the aorta, which it entirely occluded.

Again ; the symptoms of the concretion may extend over a long period. The concretion may, as I have shown, become organised. In such case the symptoms are those of valvular obstruction on the left side. Such cases often end suddenly at last.

Cases may be met with in which concretions exist on both sides of the heart at the same time. In such instances, unless the concretion on the right side be small, or placed out of the direct course of the circulation, the symptoms partake of the characters which belong to deposition in the right cavities.

The pre-existence of disease of the heart, either acute or chronic, favours materially the deposition of fibrin. We have seen in acute endocarditis how this obtains ; it is easy to see, and cases abundant are on record for illustration, to what extent dilatation of the heart, feebleness of its walls, or induration of its valves, favour the formation of concretion.

I have often been asked, whether there are no reliable physical diagnostic signs of concretion ? I think not. There are sometimes abnormal sounds, but it is difficult to distinguish these from murmurs, the results of valvular lesion. The tumultuous action of the heart, taken with the general symptoms, is always a valuable diagnostic mark of concretion of the left side ; but this is compatible with other diseased conditions. The weak irregular action is, with the general symptoms, a valuable diagnostic sign on concretion of the right side ; but it is equally compatible with other causes. In some cases, where the concretion interferes with the action of either the auriculo-ventricular or semilunar valves, there

is a muffled character with the sounds, dependent on the obstacle to the play of the valves, by the tension of which the sound is produced. But, as it is scarcely ever the fact, that both sets of auriculo-ventricular valves, or both sets of semilunars, are affected simultaneously by concretion, loss of either sound is of rare occurrence. In short, the only physical signs of moment are, feebleness of action, tumultuous action, or occasionally a peculiar rumbling, fidgety, jog-trot motion, with which the two sounds are heard in natural sequence as regards each other, but irregularly and lispingly.

The diagnosis must therefore rest on the general symptoms, rather than on the physical. The nature of the case must first be considered. All acute sthenic inflammations form favourable pre-existing conditions; pneumonia foremost of all. The puerperal state, before and immediately after parturition, stands in the same category, and this without the absolute necessity of acute inflammatory disorder. The puerperal state is second to none in this particular, and the symptoms of concretion are often as insidious as they are sudden. I do not speak here of puerperal phlebitis, and of deposits in the veins, but of cases where there has been no untoward sign, either during pregnancy or after parturition, and where the woman suddenly succumbs, without any preliminary indication of acute disease.

I have met with but one example of this kind, and my notes of it are defective. My friend, Mr. Edenborough, has, however, given me a note of an unpublished case which occurred in his practice, in May 1849, which illustrates the argument too painfully. The patient was delivered of her sixth child, after an easy labour of three hours, on May 1st. On the following day, lactation was

established, and the lochia were natural and moderate. On the 6th, "I saw her," says the writer, "quite well, as I thought; she had not one bad symptom. On the following day I was sent for in haste, and found her sitting up in bed, suffering from violent spasm in the region of the heart, with insufferable dyspnœa. She was evidently dying. I gave ether; but, within ten minutes after my arrival, she was dead. I examined the body thirty hours after death. It was well developed—all the abdominal viscera and vessels were healthy. The uterus was firmly contracted. The lungs and pleuræ were normal. The pericardium contained five ounces of a pale, greenish coloured serum. The heart, of normal size, was pale and somewhat flabby. The right auricle and ventricle were normal. The left auricle contained three small fibrinous bodies. In the left ventricle lay a large mass of the same kind. It was not adherent, but, stretching diagonally across the mitral valve, obstructed the blood-current, and was evidently the immediate cause of death.*

In these instances, unattended with pre-existing changes in the venous trunks, or evidence of inflammatory lesion, we can only, in the present state of our knowledge, assign as a cause of the deposition, excess of fibrin in the blood, arising from absorption of the thickened uterine walls, or suppressed lacteal secretion; or neutrality or deficiency of the fibrin solvent.

I have, more than once, seen a sharp inflammatory attack, without direct evidence of organic inflammation,

* See an interesting case, described by Dr. Edward Smith, in the "Medical Times and Gazette" for 1854, in which a pregnant lady died suddenly. In this case, there was contraction of the arteries—malformation; but the immediate cause of death was occlusion of the pulmonary artery by a hollow cylinder of fibrin.

end fatally by the deposition of concretion. Many cases of so called "simple inflammatory" or perhaps "continued fever," are of this character. After death, it is found, that there has been an inflammatory affection of some organ, but that such affection has not been diagnosed. In these examples, the spleen is often the organ which has suffered the local lesion, but the symptoms have not been sufficient to be readily detectable during life.

I have, in a former part of this work, described cases where, from a relative increase of fibrin, or from a disproportion between the fibrin and its solvent, concretions are produced. In phthisis pulmonalis, this event is common, and the last stages of the disease are often cut short in this manner. A sharp colliquative diarrhœa, profuse sweating, or hæmoptysis, is sufficient to establish a relative disproportion in the constituent parts of the blood; and the result is a deposition of fibrin.

In any case, whatever be the producing cause, the symptoms of concretion in the heart, as I have given them, would remain the same; for, as has been explained, when the symptoms of concretion are present, they supersede and mask those which were preexistent.

By some observers, who admit that the fibrinous deposit may be formed before death, an argument is sometimes used that such concretions are always formed in the last hours of existence, and that they are rather the sequences of the dying state than its precursors and final cause. To some extent this argument has weight; for there are cases certainly in which these concretions are found, where the inference is fair that death would have occurred, though the concretion had not existed.

On the other side, various instances have been given where both the symptoms and the pathology show that the concretion was the veritable cause of dissolution. In other words, the patient would not have died, if the concretion had not been formed. Moreover, in all cases where the deposit occurs, this is clear, that in the majority of cases it is the final seal and bond to the death claim.

The question may be asked, Of what good is this knowledge regarding concretions in the heart? Why be anxious to learn the existence of a cause of death, which by its irremediability may be considered death itself? I answer, Great good. I am not without hope that the day may come when science shall show to us, how the dissolution of these concretions may in some cases be effected; for I have seen them partly dissolved as an effect of alkaline treatment. But, irrespective of this matter, the correct diagnosis of concretion is a guide to prognosis, and is a guide against many forms of meddlesome and mischievous, because useless, practice. Take one or two examples.

In the latter stages of inflammations, bleeding is notoriously bad practice. The reason is obvious; and, I regret to say, I have seen the evil too obviously and practically explained. In these cases, the tendency of the disease is towards fibrinous deposition; and the tendency of hæmorrhage is towards the same event. Therefore, as the practitioner bleeds, the balance of the blood-constituents, already disturbed, is disturbed the more: all that was wanting to secure deposition is secured; the circulation is enfeebled, and the proportion of water and of fibrin is increased. The deposit forms, and the patient sinks. In one instance of pneumonia, I saw the

fatal symptoms of concretion on the right side follow the free abstraction of blood, as clearly as the symptoms of narcotism can ever be observed to succeed upon the administration of an opiate.

For the same reason, in the later stages of acute inflammatory affections, it is equally dangerous to carry the depressing system by medicines to an extreme, or to produce too free an elimination from the body: of all medicines, in such stages, purgatives and opiates should be alike avoided.

Lastly, the correct diagnosis of concretion in the heart may prevent unnecessary surgical interference, and explain the reason why some measures, conducted on the most scientific surgical principles, miss their intended object. This is strikingly illustrated in the disease, true inflammatory croup. In this affection, as I have proved by repeated inspections, concretions definitely formed from blood in motion, and long before death, are often found in the heart after death has occurred. Further, I have been able in this disease to trace the symptoms of concretion as clearly as I had previously traced the special local or inflammatory symptoms of the disorder. Thus, in croup, there may be death from one of two sources; from the obstruction in the larynx—asphyxia; from the obstruction in the heart—syncope; or from the combination of these.

If, then, the symptoms are clearly those of pure asphyxia, dependent obviously on the obstruction in the air-passages, the operation of tracheotomy is the grand remedy. But if the stethoscope tells that the air enters the lungs with moderate freedom at each inspiration; if indications of emphysema are present; if the symptoms are those of obstruction at the heart—

syncope, then is the operation of tracheotomy as useless as would be that of phlebotomy for removing a solid plug from the windpipe.*

As a concluding remark, I would observe that there seem to be periods during which, owing to some general external cause, possibly atmospherical, the development of a diseased condition of blood characterised by increase of fibrin, and tendency to fibrinous deposition, is markedly present. I know not what special meteorological states are connected with these diseased manifestations; but an epidemic catarrh is often an accompanying phenomenon. Sometimes also, as one or two interesting narratives go to prove, a similar tendency to fibrinous deposition assumes an endemic type. A most curious and valuable illustration of this type is supplied in an account in the *Edinburgh Annals*, by Dr. Chisholm, under the title, "An Epidemic Polypus in Granada in 1790." Here a number of negroes, working in a position which exposed them, at one and the same time, to excessive heat, a blast of cold air from a ravine, and a marsh-vapour, were seized with a fatal disease, the essential symptoms and pathology of which consisted in the formation of fibrinous concretion in the right cavities of the heart, extending into the pulmonary artery.

* In the remarks which have been made in this section, I have entered into few details of cases by way of illustration; my feeling being that, over and above those given in chapter III, details were not strictly in character with this work. Suffice it to add, that every description has been drawn from direct observation of cases, and that the history of these will be found in the last ten volumes of the *Lancet*, under the head "Reports of the Proceedings of the Medical Society of London."

V.

THE ALKALIES AND ACIDS AS REMEDIAL AGENTS.

The Alkalies. The resolvent effects of the alkalies in general, and of the volatile alkali in particular, have long been empirically known. Hartshorn and oil is the common external resolvent used by all classes of people, both for man and beast. In the early days of the chemical school of medicine, the volatile alkali had a great reputation. It resolved humours, neutralised acidities, stimulated the heart and arteries, and was a panacea for epilepsy and a host of maladies.

The remedy, softened down in its specific pretensions, has retained its good name generally, both as a resolvent, a stimulant, and an antacid. The Hon. Robert Boyle, of whom a word anon, took great credit to himself for being a leader in the introduction into this country of this remedy. From what I have gathered from experimental data, all the alkalies have many properties in common. They are all, according to the old language, "resolvent," *i. e.*, they lead to solution of nitrogenous tissue. But the volatile alkali differs from the others, in that it excites the heart and circulation and muscular system primarily, when given in a large dose, and in that its effects quickly pass away, owing to its volatility.

It may seem strange, at first sight, but it is equally true, that there is a striking analogy as regards pathological effects between the alkalies and the salts of antimony. I have dissected, with great care, the bodies of animals slowly killed by the alkalies, and also of those killed by antimony; and my feeling is, that in ignorance of the symptoms preceding death, and with-

out the aid of chemistry afterwards, I should feel a difficulty in diagnosing, from bare pathology, between death from antimony and death from an alkali. The same fluidity, or partial fluidity, of blood obtains; the same dissolution of blood-corpuscles; the same softening of the soft parts; the same absence of cadaveric rigidity; and the same extensive but simple vascularity of mucous surfaces and of vascular organs.

A similar analogy also exists between the action of the alkalies and the action of many of the alkaloids. The condition of blood after poisoning by strychnia, morphia, belladonna, and arnica, is almost identical; there are partial or complete fluidity, more or less dissolution of corpuscles, and injection of this fluid blood into the soft tissues. But I have lately observed, in relation to the microscopic character of blood after poisoning by belladonna and arnica, one essential difference; viz., that while there is an almost entire deficiency of blood-corpuscles, the field is crowded with crystals of hæmato-crystallin. It seemed, indeed, in two cases of belladonna poisoning in cats, which my colleague, Dr. Francis Webb, and I examined together, as if the blood-corpuscles were altogether replaced by these crystalline bodies, the bundle or fibre-groups being by far the most abundant. I point out this curious fact, in connection with belladonna and arnica, incidentally, but as having a direct bearing on their actions as medicines and as poisons.*


There is, further, an analogy between the action of the alkalies and the effects of water thrown into the

* For the student, anxious to pursue these or the preceding physiological researches, Pillischer's admirable students' microscope, which is within the reach of all inquirers, answers every practical purpose.

body in excess. This was well brought out in the experiments where water was thrown into the peritoneum. Here, too, the blood is fluid, the corpuscles are more or less dissolved, and the tissues are injected with fluid blood. The last symptoms, also, are much the same; viz., prostration and coma.

The application of the alkalies as medicines seems pretty clearly defined. It includes cases of the inflammatory type, where fibrin is in excess, and where there is rapid oxidation. It includes cases where there is acidity of the excretions; and in these respects the alkalies are now specially recommended in acute rheumatism. It includes cases where there is induration of tissue; and, in fine, cases generally, where resolution or fluidity of the blood and plastic tissues are required. As on the dead tissue, so in the living, the alkalies are the solvent or resolvent agents.

But from this very fact, there arises a caution which I would specially name; viz., that the alkalies as medicines may be carried to a dangerous extent. Of this I feel, from observation, quite sure. At page 122, I have related a case of the inflammatory type, in which, during the last stages, the use of ammonia was pushed to so great an extent, that after death the blood was found surcharged with the alkali, and the blood-corpuscles were dissolved. This is putting the remedy to an extreme past all reason. The event might be avoided by care in observation. As a diagnostic mark that the use of alkalies has been carried far enough, the blood-corpuscles afford the best indices. When these begin to take irregularities of form and character, such as I have already described, the indication is clear that, for the time at least, the remedy had better be discontinued.



Thus we come back, by physiological argument, to the old established practical fact, based on empirical observation, that the alkalies, the alkaline salts, antimony, opium, and simple water are, in reality, *the* remedies for diseases of the acute inflammatory type, since their effects on the blood are nearly the same in the long run. The points in practice are, to begin their use early in the disease, and not to carry the administration of them too far; and especially not, by an unhappy routine use of the word *fever*, to class cases of an acute inflammatory kind with the true typhus fever group, so as to confound under one head two classes of disease of characters precisely opposite to each other, and to treat them by the same general remedies.

It is also equally necessary, in studying the pathology of these different diseases, or the pathology arising from the medicinal agents above specified, not to confound simple vascularity of vascular parts, arising from mere fluidity of blood, with those plastic exudations which characterise the pure inflammatory condition. From thus confounding these two opposite pathological states, innumerable fallacies have crept into our science, and a handle has been given to unscrupulous and shallow men, to give to ridiculous dogmas an appearance of scientific meaning.

One illustration of this fallacious mode of argument is here in place.

The homœopathic charlatans, to carry out their foolish dogma of "like curing like," have seized on an unfortunate remark by Magendie, that the administration of antimony produces pneumonia. Upon this they argue that antimony, because it produces pneumonia, cures it. But the true fact is, that the condition

of lung produced by alkali, is the mere infiltration of tissue with abnormally fluid blood. It is a kind of blood-œdema, if such a term is allowable, and is as far removed from inflammation as the scurvy blot or the fever petechia. So far from antimony causing inflammation of tissue, I believe that the continuance of inflammation, in its legitimate sense, is impossible in a body under the influence of antimony.

Neither I, nor any other scientific practitioner, pin any faith to verbal dogmas, nor practise by the absurd rule "*contraria contrariis curantur*." But if we did, we could not have a stronger argument in our favour than the true influence of antimony on the true inflammatory condition.

Concerning the special use of each of the remedies I have named, in the treatment of acute inflammation, I have no experimental data for argument. I infer that any one of them, judiciously used, would have an equally good effect; while they are alike chemically compatible in combination. In prescribing the alkalies, I prefer, for my own part, the simple thing rather than the salts. Well diluted with water, both simple ammonia, potassa, and soda, are more quickly absorbed, and give their effects more rapidly.

In some experiments with oxygen on rabbits and guinea-pigs, in which the pneumonic inflammatory mischief was strikingly developed, I allowed the animals on removal from the gas to have plenty of fluid, milk and water, and nothing more. They drank freely, and recovered as favourably as could be desired. In the experiments with lactic acid, after endocarditis had fully set in, the natural process of cure was permitted, and was as satisfactory as could be wished. But it is to be

remembered that the causes of the symptoms thus induced, were administered temporarily, and then withdrawn; a condition which does not apply so definitely, when diseases spring up in the human subject.

Returning to the alkalies, a word about the stimulant and restorative effects of ammonia is required. Ammonia, as an assumed restorative, is often very injudiciously used. Its use as a stimulant and excitant frequently prompts its application, when it is just the time and case not to prescribe it. In poisoning by opium, I have known ammonia recommended. But the effects of ammonia and opium are, in the main, identical, when given in a large dose.

In cases where danger arises from the administration of chloroform, I have seen the patient made to breathe ammonia vapour, not as a mere excitant to respiration, (for in this sense it may be used legitimately, with due care), but as a supposed general restorative. As the effects of ammonia in a large dose are, however, the same as those of chloroform in their leading particulars, the free introduction of ammonia into the narcotised patient is the addition of one volatile narcotic to another volatile narcotic.

In the last stages of low typhus, ammonia is often given freely, though the breath be already ammoniacal, the blood surcharged and entirely liquefied with the alkali, and the blood-corpuscles dissolved. In these cases, no treatment can be more inappropriate. The same applies to the true typhoid sinking of uræmia, and to diseases arising from the introduction of animal poisons, and ending fatally by typhoid symptoms.

In syncope, the administration of ammonia has long been practised. Here its use is legitimate and invaluable.

able. Acting as an excitant to the heart and respiration, it whips on the circulation, while the blood is supplied with its own normal solvent.

Dr. Ogier Ward, in a very able paper on the action of Ammonia, read before the Medical Society of London last session, drew out certain analogies between the action of some salts of ammonia, especially the chloride of ammonium, and the preparations of iodine. There are some points of analogy. In the course of last and the present year, I made a long series of observations on the action of iodide of ammonium, a salt now largely used for photographic purposes. The cases in which I prescribed it were such as would have been selected for iodide of potassium; viz., cases of secondary syphilis, and of chronic glandular swellings. I have thus prescribed it in about one hundred cases. It is unnecessary to tabulate these, because one or two remarks will contain the pith of all that occurred. The medicine was applied locally as an ointment when the case was fitted for it, or given internally in doses of from one to two grains, with bitter infusion. In the main, the effects obtained were essentially the same as those of iodide of potassium. But the salt requires to be given with a little more care. Its action is rather more rapid, and externally applied it produces absorption of glandular swelling with great rapidity. In a child suffering for a long time with enlargement of the tonsils, I had a drachm of the salt dissolved in glycerine, and with this solution had the tonsils painted over each day. The result was, the entire removal of the enlargement, and apparently complete recovery. A few months later the enlargement returned, and was treated again in the same way with similar happy results. Mr. J. F. Wells, Surgeon to the Royal Infirmary for

Diseases of the Chest, also used an iodide of ammonium ointment as an external application in a case of goître with great success.

I leave the use of this medicine in the hands of the profession, without any further remark on its properties, and claiming for it no specific virtue over the potassium compound, saving that its action is more speedily effective.*

The Acids. The action of the acids on blood has been abundantly shown in preceding experiments. The mineral acids all quicken coagulation; some of the weaker acids such as citric and acetic, retard coagulation, and in sufficient quantities stop it altogether. Lactic acid does not produce normal coagulation, but a viscid dark semifluid condition. Formic acid produces

* Mr. Hunt, at my suggestion, has been kind enough to use the iodide of ammonium as a substitute for the iodide of potassium, in several cases at the Dispensary for Diseases of the Skin. He opines in favour of the latter compound. The relative feebleness or activity which he observed on the part of the iodide of ammonium, arose from the small doses in which he prescribed it; viz. one grain to an adult.

In the year 1851, Dr. Ubaldo Daveri, chief physician of the Hospital of St. Orsola, in Bologna, made some experiments on iodide of sodium, of which the following is a *resumé*, as published in the "Chemist", from the "Corrispondenza Scientifica di Roma", No. xxxii, 1852.

1. Soda being a common ingredient in our organisation, the iodide of its base seems best suited to the human system.
2. The taste of the iodide of sodium is less disagreeable than that of the iodide of potassium.
3. It is less likely to occasion iodism.
4. It is better borne than the potassium salt, and in consequence its dose can be almost daily increased; it thus becomes a more efficient remedy.
5. It has sometimes succeeded where iodide of potassium has failed.
6. We may commence by giving daily, in three equal doses, a scruple of this salt dissolved in three ounces of distilled water, increasing the strength of the solution every two or three days by six grains. Some patients have in this way been able to take two drachms a day, without suffering the slightest inconvenience.
7. The iodide of sodium is admirably adapted to cases in which the corresponding salt of potassium is indicated.
8. The iodide of sodium is the best substitute for mercury.

an effect somewhat similar to that caused by lactic, but more decisive.

We have seen that the effect of lactic acid on the systems of living animals, is to produce endocardial inflammation and plastic effusion.

As medicines, the acids have been used as styptics, astringents, and in the treatment of scurvy and fever.

Their use in these respects is in accordance with experiment. But experiment teaches demonstratively, that discretion is required in the selection of acids for such administration.

As styptics, the mineral acids are the true agents. Their effect is immediate in producing coagulation. As styptics, the acetic and the citric acids are objectionable. They both retard coagulation, and, applied to cut surfaces, have no influence in stopping loss of blood. The same rule applies to their internal administration in cases of hæmorrhage.

In the year 1852, a new styptic was brought before the notice of the profession by Dr. Pagliari of Rome, and raised a great amount of discussion. The composition of this styptic was as follows:—gum benzoin, eight ounces; alum, a pound; water, ten pints. The alum and benzoin were directed to be boiled for eight hours in the water; fresh water being added to make up for loss by boiling. The supernatant liquor afforded the styptic, the virtues of which were said to be such, that if one minim were added to a pint of newly drawn blood, instant coagulation resulted. I had some of this styptic carefully made, and tried it both on animals and on the human subject. In experimenting with this solution on blood, I used the mixed blood from the neck of a sheep; but by comparing each time for several occa-

sions, blood to which the styptic had been added, with other blood from the same animals to which no such addition had been made, I could detect no decisive difference in the periods of coagulation. After separation into clot and serum, the blood which had received the styptic was much the darkest in colour; and the serum yielded much less precipitation of albumen on the application of heat. In other experiments, I applied the solution to incised surfaces in the ears of sheep. Thus applied, it clearly possessed some styptic powers, but less marked than nitrate of silver or mere alum solution. A case also occurred in my practice, of excessive hæmorrhage from leech-bites, in which I tried the three styptic solutions named above. They were all three only partially successful, and the new styptic least of the three.

The experiments thus conducted led me to inquire a little further into the general subject, and on various occasions I tried the effects of numerous substances as styptics; viz., the mineral and vegetable acids, the actual cautery, and congelation. The results of these experiments lead me definitely to the following conclusions:—

1. That the actual cautery is the most effectual styptic. It acts in two ways; by producing coagulation of the blood, both of the albuminous and fibrous parts; and by astringing the vessels.

2. That, after the actual cautery, nitric acid is most decisive, most permanent, and least injurious in its effects.

3. That of the vegetable acids, the gallic acid is a true and admirable styptic, while the acetic, citric, and lactic acids are useless.

4. That cold, carried to the point of freezing the part to which it is applied, temporarily stops hæmorrhage. That cold acts like pressure, *i. e.* simply by producing contraction of the vessels. But that it is not a safe styptic, inasmuch as the hæmorrhage sometimes returns as the reaction commences.

In experimenting on dogs or sheep with styptic solutions, immense care and quickness of observation are required, in distinguishing between the real and the supposed effects of the solution. If the femoral artery of a dog, a vessel often experimented on, be laid bare and divided, either by transverse incision, oblique incision, or puncture, it is astonishing with what rapidity the hæmorrhage will cease spontaneously. As I have been deceived myself before instituting comparisons as to the assumed effects of styptics, I point out this warning with more earnestness and force.

As astringents, the use of the acids is well known and recognised. From the observation of the influence of acids, both as applied in disease and by experiment, I incline to the opinion that the mineral acids are the only astringent remedies of this class which are to be relied on, with one exception in favour of the gallic acid, which, in its effects on blood, on bleeding wounds, as an internal remedy in averting hæmorrhagic flux and profuse excretion, is scarcely second to either the nitric, nitrous, or sulphuric acids. For all these astringent purposes, the acetic and the citric acids are inadvisable, both on practical and experimental data. I remark strongly on this, because I have known acetic acid prescribed as an internal remedy in phthisis, for the arrest of hæmoptysis, and as a check on the colliquative sweats and pulmonary excretions. But I have shown that acetic and citric

acids dissolve fibrin, and that acetic acid holds blood fluid. Further, I have specifically used the acetic acid in several cases of phthisis and hæmoptysis to test its astringent value in arresting these discharges, but with unsatisfactory results. It does not arrest hæmorrhage, while it encourages excretion. Diarrhœa was no uncommon result under the continued use of this acid.

In using the mineral acids as astringents, the effect is best ensured by selecting those which are most fixed. Hence, for this purpose, the sulphuric and the nitric hold the first place. The gallic acid nearly approaches them in its efficiency, and is preferable in cases where an astringent has to be repeated for great lengths of time.

The action of such acids as act as astringents is exceedingly simple. They correct the superalkaline state of the blood, and increase its plasticity. Their effect, possibly, extends even further, *i. e.* to the healthy deposition of the nitrogenous tissues. In this sense, they are tonics as well as astringents, and, in this particular, have long been recognised as admirable adjuncts to quinine and to the tonic plan of treatment in general.

In true "typhus" and "typhoid," and in all diseases marked by superalkalinity (the typhoid type), the mineral acids are the remedies. I think, in these cases, that hydrochloric acid, from its less fixed character, holds the first place. Of late, in cases of this class, I have given the acid from the first, and with the best success. Pure air, dilute hydrochloric acid, and supporting diet, without any over-dosing with wine, form the tripod of treatment in low fever and its analogues. The point to be remembered in these cases, is the general condition of the blood, not the special manifestation of

symptoms, such as the dry tongue, and quick feeble pulse. The diagnostic signs which demand the acid treatment, are the alkaline breath, the partly dissolved blood-corpuscles, and the feeble power of coagulation. In such cases, the physiological practical argument disposes of all application of the alkalies, the alkaline salts, and the narcotic alkaloids. The elements of treatment are, in fine, reduced to one or two simple axioms. Encourage the elimination of the volatile excreta of the fever-patient, by free and constant ventilation; encourage the healthy oxidation of the body by the same means; meet the alkaline state of blood by the administration of a mineral acid; and supply a diet in which the nitrogenous and carbonaceous elements of food are correctly proportioned, and in which the introduction of alcoholic stimulants takes no excessive share.

These are the leading principles in the treatment of true fever, which physiology teaches; and I believe that their application at the bedside will confirm their efficacy more and more, as they shall be relied on by practitioners of the healing art.

VI.

APPLICATION OF AMMONIA TO THE OPERATION OF
TRANSFUSION OF BLOOD.

Since the time when Lower first performed the experiment of transfusing the blood of one animal into the vessels of another (1666), and Denys of Montpelier gained unenviable notoriety for pushing this operation into practical operation with too much enthusiasm, it has been felt a difficulty in the steps of the operation to hold the drawn blood fluid, for a time sufficiently long to secure its free transfusion into the animal body. It is true, that several ingenious instruments have been devised, which in some measure meet the difficulty, but not effectually. In this section I shall show that the cautious addition of ammonia to the drawn blood answers every practical purpose for sustaining fluidity, and for simplifying the operation.

EXPERIMENT CCCCVII. *Transfusion of Blood.* On one occasion, I had in my laboratory twenty ounces of sheep's blood held fluid by a solution of five grains of ammonia in a drachm of water. The blood had been kept fluid, for several hours, in a closely stoppered bottle. I had placed a dog under the influence of chloroform for an intended operation, when I perceived that the heart was stopping from the effect of the narcotic. I instantly laid open the external jugular vein, and blood escaped copiously; but, nevertheless, death took place. Prevented from following out the original operation, I thought it would be interesting to see how the sheep's blood would run in the vessels of this animal. I therefore warmed a portion of it to 98°, put a tube into the jugular vein, and injected four ounces

with great ease. I then laid bare the common carotid, and performed the same experiment with equal facility. The facility with which the operation was done, suggested the plan of transfusing blood into a living animal after a similar manner. I have now performed this operation several times with excellent results. As examples, I shall give two representative experiments; the one showing the dangers which are to be avoided; the other, the operation as it may be safely practised.

EXPERIMENT CCCCVIII. *Transfusion of Blood.* I laid bare the jugular vein of a healthy dog, and drew from it into an evaporating dish two ounces of blood, in which were four grains of ammonia with a drachm of water. The blood was set aside for a brief interval. Next, I drew two other ounces of blood from the same vein into another evaporating dish, in which there was no ammonia, and set this aside that it might coagulate; the vein being meantime secured above the opening by a firm ligature. When the blood in the second cup had firmly coagulated, an event which occurred about four minutes after its abstraction, I drew into a two ounce syringe the blood charged with ammonia, and which was still quite fluid, and, introducing into the vein the nozzle of the syringe, threw in slowly the ammoniated blood. The syringe was withdrawn, and the vein was tied below the opening. For a few moments after the injection there was but little change; then suddenly the action of the heart became so bounding and intense, that it seemed to heave up the chest-wall. Almost coincident with this, general tetanic spasms occurred, with rigid opisthotonos; and, in fine, symptoms so strictly analogous to those produced by strychnia, that

the action of the two agents could not have been distinguished by a stranger ignorant of the cause of the symptoms. The chest was fixed; and death took place in four minutes. An hour after death, the body was opened. The right side of the heart and the whole venous system were charged to distension with dark blood, which was perfectly fluid, and remained so for three hours on exposure to the air. In the left side also there was blood, of a bright red colour, and fluid. Set aside, this arterial blood coagulated in fifteen minutes, on exposure to the air at a temperature of 70°. The corpuscles were very much modified. In this experiment, the first of the series on a living animal, the ammonia was added in a poisonous dose, and the results were strikingly marked.

The analogy between the actions of ammonia and strychnia is so striking when the former is thus thrown in excess into the circulation, that I cannot dwell too strongly on the fact, since it may have an ultimate bearing on the mode in which strychnia destroys life, and the means to be adopted in cases where this alkaloid is fatally administered. In an experiment in which Dr. Halford lent me his assistance, the same results were observed, under the same circumstances.

EXPERIMENT CCCIX. *Transfusion of Blood.* I laid bare the jugular vein of a healthy terrier dog, and drew off two ounces of blood into an evaporating dish containing three minims of liquor ammoniæ (specific gravity .880) with thirty minims of water. Other two ounces of blood were drawn off into another dish containing no ammonia, and set aside to coagulate. The vein meantime was tied above the opening. After four minutes, the blood in the second cup had firmly coagu-

lated. The ammoniated blood was still completely fluid. After five minutes more had elapsed, the nozzle of the injecting syringe was introduced into the vein of the animal, and the ammoniated blood was injected. Dr. Halford, who managed the syringe, took great care to introduce the fluid slowly, and a full quarter of an hour was taken up in this way. Then the syringe was withdrawn, and the vein was tied beneath the opening.

In the course of this operation, not a dangerous symptom supervened. The blood ran easily. As it first reached the heart, that organ, which had been flagging, beat with a little more force, and sustained this activity, without abnormal increase. The animal recovered without the slightest indication of injury, and it is alive and well now.

A small portion of the ammoniated blood left in the evaporating dish, was observed to coagulate thirty-five minutes after the blood was first drawn; it formed into a firm clot. The temperature of the day was 75° Fahr.

In performing the operation of transfusion by this simple means, in the human subject, in the extreme cases adapted to the operation, a few precautions are required. The amount of ammonia first added to the blood about to be transfused, should not exceed two minims of the stronger liquor ammoniæ to the ounce of blood; for it is quite easy, if a diluted solution of the ammonia be ready at hand, to add a little more in course of the operation, if the blood should show a tendency to coagulate. The ammonia diluted with water, in the proportion of one part of the alkali to ten of water, should be placed in the vessel in which the blood is caught from the vein; and the blood as it falls into the vessel should at first be very gently stirred. When

sufficient blood is obtained, and the injecting syringe is at work, the injection should be made with the greatest care and slowness. Indeed, scarcely any pressure on the piston is required, and there is no cause for haste. This is a great advantage; for, I take it, one of the dangers of transfusion is the rapid distension of an empty and enfeebled heart with a full charge of blood. Harvey, whose shrewdness seems to have let nothing in his way escape observation, refers to the syncope which sometimes occurs in bleeding, not as a result of the hæmorrhage, but on the removal of the fillet; or, as the vulgar say, "from the turning of the blood." Harvey thought that this occurred from the coldness of the blood which retreated on the heart; but I think that I have demonstrated by experiment, in another place, that the effect is due to the sudden load of blood thrown upon the enfeebled organ.*

With these precautions the operation of transfusion by the process I have described, is at once as simple as it is effectual; and in sinking from loss of blood it has this advantage, that to the new charge of blood there is added an agent having the property of stimulating the flagging heart into renewed force and activity.

* Physiological and Practical Studies. On the Effects of the Horizontal Position of the Body in Syncope. Association Medical Journal, July 7, 1854.

VII.

ON SOME CONDITIONS OF THE BLOOD AFTER DEATH, IN
RELATION TO MEDICO-LEGAL INQUIRIES.

In sudden death from shock, as by a fall from a height; in instant death from chronic disease of the heart (rupture of the heart excluded); in death from blow on the stomach; and from syncope, the result of terror or emotion, the blood is often found fluid after death.

The cause of this fluidity is simple. It depends, when it is present, on three conditions:—

1. That death took place instantly, so that, after absolute death, the blood still remained fluid.

2. That the circulatory system was fully charged with blood, both in the heart and in the vessels belonging to it.

3. And this is most important, that the circulatory system remained, at every part, unopened and perfect.

These three conditions present, the blood will remain more or less fluid, until it is exposed to the air by the dissector's knife; then it will coagulate, as speedily as under any condition, if it is raised to a temperature of 98° Fahr.

The sustainment of the fluidity in these cases depends on simple physical causes, as I have already explained. Consequently, a modification in these conditions may lead to a modification in the condition of the blood, although the cause of death may be virtually the same—that is to say, by shock.

For example, if death occur from a fall, and in the fall a wound be inflicted laying open the circulatory canals, the blood will not remain fluid, as it would if no

such complication had happened. Or, if the death is not instantaneous, so that the circulation and respiration feebly continue for a time, the fluidity will be less marked. Again, if the vessels or chambers of the heart are, at the moment of sudden death, but partly filled with blood, as when death takes place during contraction of the ventricles, the blood will not retain its fluidity. Hence, also, when it so occurs, and this is not uncommon, that the right side of the heart and the venous trunks are left at death distended with blood, while the left side and the arteries are comparatively empty, the blood on the right side remains fluid, that on the left side is firmly coagulated.

After death by the alkalies as poisons, the blood is fluid, and the corpuscles are modified in the way already described. The poison of the cobra di capello is followed by similar results. In slow poisoning with antimony the same general rule obtains, both as regards fluidity of blood and condition of corpuscles. If the blood in these cases is coagulated, the coagula are dark and very loose.

In poisoning by chloroform, hydrocyanic acid, opium, carbonic acid, belladonna, arnica, tobacco, and narcotics generally, the blood is dark, and either fluid or loosely coagulated. Belladonna and arnica exert an effect on the corpuscles, seeming to reduce these in number, and to lead, in some cases, to the excessive development of particles of hæmatocrystallin.

In death by hanging or strangulation, if the fatal result be suddenly brought about, there is left a fluid or semi-coagulated condition of blood.

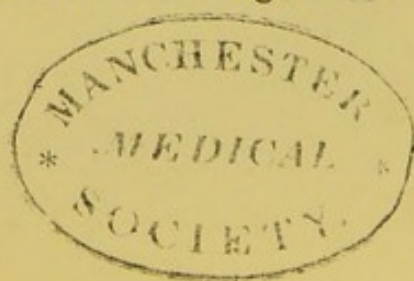
There are three modes in which death may be produced by hanging. 1. Pure asphyxia, from pressure

on the main air-passage. 2. Dislocation of the vertebræ. 3. Arrest of the circulation in the brain, from compression of the vessels of the neck.

In the first two modes, the death is almost immediate, and the blood is ordinarily fluid. In the last named mode, life may be long sustained with comatose symptoms; and the blood, after death, may be found not only coagulated, but with distinct deposition of fibrin, laid down during life, and leading to the fatal termination.

The following example is in point.

On Wednesday, 30th November, 1853, I was called to a man who had attempted suicide by hanging. He was tall, and the beam to which he had suspended himself was low, so that his feet touched the ground, while his shoulder rested against a wall. He had on his neck a stiff stock, and the cord rested anteriorly on this, but laterally pressed on the neck. He was hanging several minutes before he could be cut down, as the door of the room was secured within. When he was relieved, his face was congested, and he was profoundly insensible, but soon commenced to breathe, and when I arrived he was breathing well. I had him laid in bed, and bled him freely; once from the arm, and once from the temporal artery. The blood flowed readily, and the arterial blood was of bright red colour. The bleeding had no effect. The man reclined like one in catalepsy. He was quite unconscious; and wherever his limbs were placed, there they remained. After a lapse of eight hours, the temperature of the whole body, the head and face excepted, became greatly raised; the pulse got hard; and all the acute general symptoms of an inflammatory fever were manifested. Through the



succeeding twenty-four hours he remained in this state, having no power to swallow. The dry heat was followed by profuse perspirations, which bathed the whole body, except the head and face; these remained cold as marble. Through the succeeding twenty-four hours he continued much the same; the pulse 120, and hard; the breathing forty per minute; the skin hot, with occasional free perspirations. On the third day, the heart began to intermit, and the symptoms of obstruction on the right side of the heart from concretion, such as I have described, were so obvious, that both Dr. Willis and myself predicted the existence of fibrinous deposition and its results. Never becoming in the least conscious, the man gradually sank, and died late in the night of December 2nd, the respiration outliving the heart's action.

At the *post mortem* examination, which Dr. Cormack and Dr. Willis attended, we found that the main air-passage had altogether escaped injury or compression, and that the first symptoms were purely due to extensive congestion of the brain. The brain was found intensely vascular, with free exudation of serum beneath the arachnoid. The lungs were somewhat congested. The right side of the heart was distended to an incredible size with firmly coagulated blood, on the upper surface of which lay a fibrinous layer. Attached to the wall of the ventricle, at the commencement of the infundibulum, was the base of a large fibrinous tube, which ran upwards into the pulmonary artery, and extended into its branches. The deposit was laid down in distinct strata, and formed a perfect hollow cylinder, containing in its central axis a column of red blood. There was no trace of active disease in any

other organ, but some congestion of the liver, spleen, and kidneys.

In death from the excessive imbibition of water into the circulatory system, the fluidity of the blood is sustained; while, after death by the electric shock, there is not merely fluidity of blood, but, as it would seem, general disintegration.

In instances of slow poisoning, as by the alkalies or antimony, where the blood is found fluid, and the corpuscles more or less disintegrated, there is found also extensive congestion of the soft tissues. This condition must be scrupulously disconnected from all idea of inflammation or its upshot. The congestion has two sources. First, the blood being abnormally fluid, easily flows, as Plato has it, "through the thin structures." Secondly, when the more solid parts of the blood, as the fibrin and blood-corpuscles, undergo extensive liquefaction, the volume of the mass of blood augments and exerts a passive pressure from within upon the vessels, in addition to the active forces pertaining to the normal circulation.

After death from starvation, the blood is semi-coagulated (see case, page 126). This rule is not strictly absolute; for in a late instance of death from stricture of the œsophagus, in which the patient swallowed no solid food and but little fluid, for the long period of twenty-three weeks, and in which death arose from pure inanition, I found the blood, both on the right and the left sides of the heart, separated into a thick fluid part and a distinct fibrinous layer.

Fluidity of blood in the sinuses of the skull of the adult, is rather a normal than an abnormal indication; for, in the closed cavity of the skull, if there be no

breaking down of the brain-substance, the blood remains fluid much longer than in the other parts, even after hæmorrhagic death.

Fœtal blood, according to my observations, is always either fluid or but semi-coagulated. Even if the fœtus be healthy, the force of coagulation is low ; if the fœtus be the victim of syphilis, the blood is uncoagulable, and the corpuscles are misshapen and easily soluble. A very few independent respirations, however, on the part of a healthy new-born child, give to the blood plasticity and firm coagulating power. Hence firm coagulation of blood may be added as an accessory sign that a child has breathed.

In a placenta, however, which has undergone softening or destruction of tissue, blood may be effused, and coagulate : in which case the fœtus dies, as from syncope. Hence, in cases where a fœtus, apparently healthy, is born dead without any obvious disease, the condition of the placenta should be carefully observed.

In cases of sudden death in women, after or before parturition, it is important always to examine the pulmonary artery and aorta for fibrinous deposits.

In *all* cases of mysterious sudden death, where the cause is not at once obvious on dissection, the pulmonary artery ought to be carefully examined ; and this observation ought not to be confined to the main trunk, but extend to its ramifications.

If, in making a *post mortem* examination, in which the reason of sudden death is obscure, the right as well as the left sides of the heart are found full of blood, the inference is fair and almost demonstrative, that the death was not due to arrest of the circulation in the lungs, but to death commencing at the heart—syncope. If, on the

other hand, the right side of the heart is distended with blood, and the left side is found quite empty, the inference is fair and almost demonstrable, that the arrest of the circulation commenced in the pulmonic circuit—apnœa. There are indeed, according to strict rule, only two real causes of death ; death commencing at the heart—syncope ; and death commencing at the lungs—apnœa ; though these two modes admit of combination. Other so-called modes of death, coma and asthenia, are but forerunners, or, as it were, preceding diseases. If the heart and circulation continue in play, together with the respiration, there can be no death. This is a truism ; but it is necessary to state it, that the forms of death may be reduced to their proper number in a physiological point of view. A man may lie comatose for hours, or even weeks, but he need not therefore of necessity die ; nor does he, thus lying, begin to die until such time as his circulation or respiration begin, one or other, or both, to fail.

Much has been said and written about the differential diagnosis of the blood of man and of other mammalia. For my own part, I am free to say that, if specimens of blood from man, from the sheep, ox, pig, guinea-pig, dog, cat, or rabbit, were placed before me, I should be utterly unable to say with precision, from any examination which I could institute, chemical or microscopical, from which of these animals the different specimens were derived. The size, and to some extent the shape, of the blood-corpuscles, are not, indeed, alike in the same individual or in the same animal at all times. A mere difference in the specific gravity of the blood is alone sufficient to cause modifications of the corpuscles.

VIII.

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Amongst the works which have been consulted, there are some to which I would especially refer.

Mr. Turner, the respected President of the Royal College of Veterinary Surgeons, by a series of physical experiments very much resembling some of mine, but preceding those, came to the definite conclusion that coagulation occurs from the escape of volatile matter from blood. Mr. Turner's labours were independently conducted; and I have sincere pleasure in claiming for him a successful and original place in this interesting inquiry. At the same time, as has been shown, Scudamore and Polli had already taken a similar position.

Reading, some months since, one of Lancisi's papers, I was surprised to find him speaking of the volatile spirit of blood, and referring to the works of the Honourable Robert Boyle as his authority on this subject. The observation led me to Boyle's Essays, and to the perusal of his remarkable papers on the "Natural History of the Humane Blood; especially the Spirit of that Liquor." This "spirit" was ammonia; and although the mode in which Boyle obtained the volatile alkali, viz. by distillation of blood, is not in accordance with modern chemical knowledge, and although he never refers to coagulation, yet it is fair to him to say that he was acquainted with the facts that the addition of an ammoniacal salt to blood preserved it from putrefaction, and sustained its fluidity; and that, had his labours been carefully followed up, a much greater advance would have been made in the physiology of the blood.

In writing this work, I owe especial thanks to the labours of Mr. Ansell. To his papers I am indebted for many historical references, and for a masterly epitome of the whole subject up to the time when his labours were concluded.

To Mr. Gulliver's edition of "Hewson" I am equally

indebted. Gulliver's "Hewson" may, indeed, be compared to Pope's "Homer"; in it the expositor equals, and in some points surpasses, the master. If Hewson could for a moment look into the world of science as it is in these days, he could have no greater happiness than to see his able works brought before the age by so great a commentator and advocate as Mr. Gulliver. I write this without any knowledge whatever of the author of Gulliver's "Hewson," and with no other impulse than such friendly admiration as the study of his writings has inspired.

From Dr. John Davy's "Original Researches" many important facts have been gleaned. What he and his immortal brother Sir Humphry have each (and, as I think, equally in their respective spheres) done for science needs no note from me, except in an inadequate recognition of the extent to which I have been personally assisted by their experimental works.

The paper on "Ammonia evolved in Respiration," by Professors Latini and Viale, referred to in the Table of Authors, is of moment, as corroborating many of the views adduced in this work. These gentlemen, by a series of independent labours, arrived at the fact that ammonia is thrown off in the expired air. I need scarcely say, that their labours, original as far as the authors were concerned, were many years before fully anticipated by the researches of our countryman, the Reverend J. B. Reade.

Lastly, to the labours of Scudamore, Polli, Remak, Franz Simon, and the learned Lehmann, my deepest obligations are expressed.

THE END.

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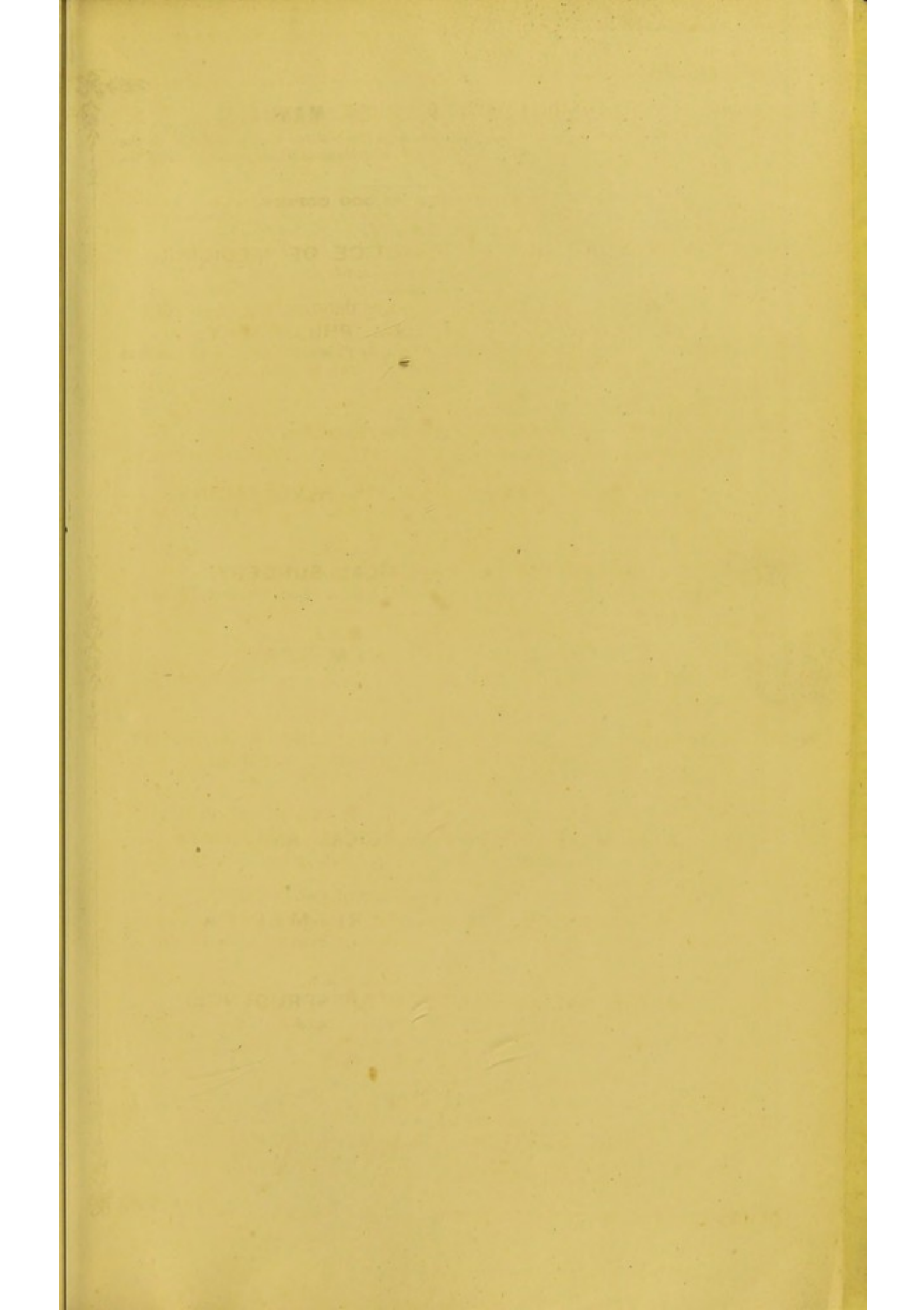
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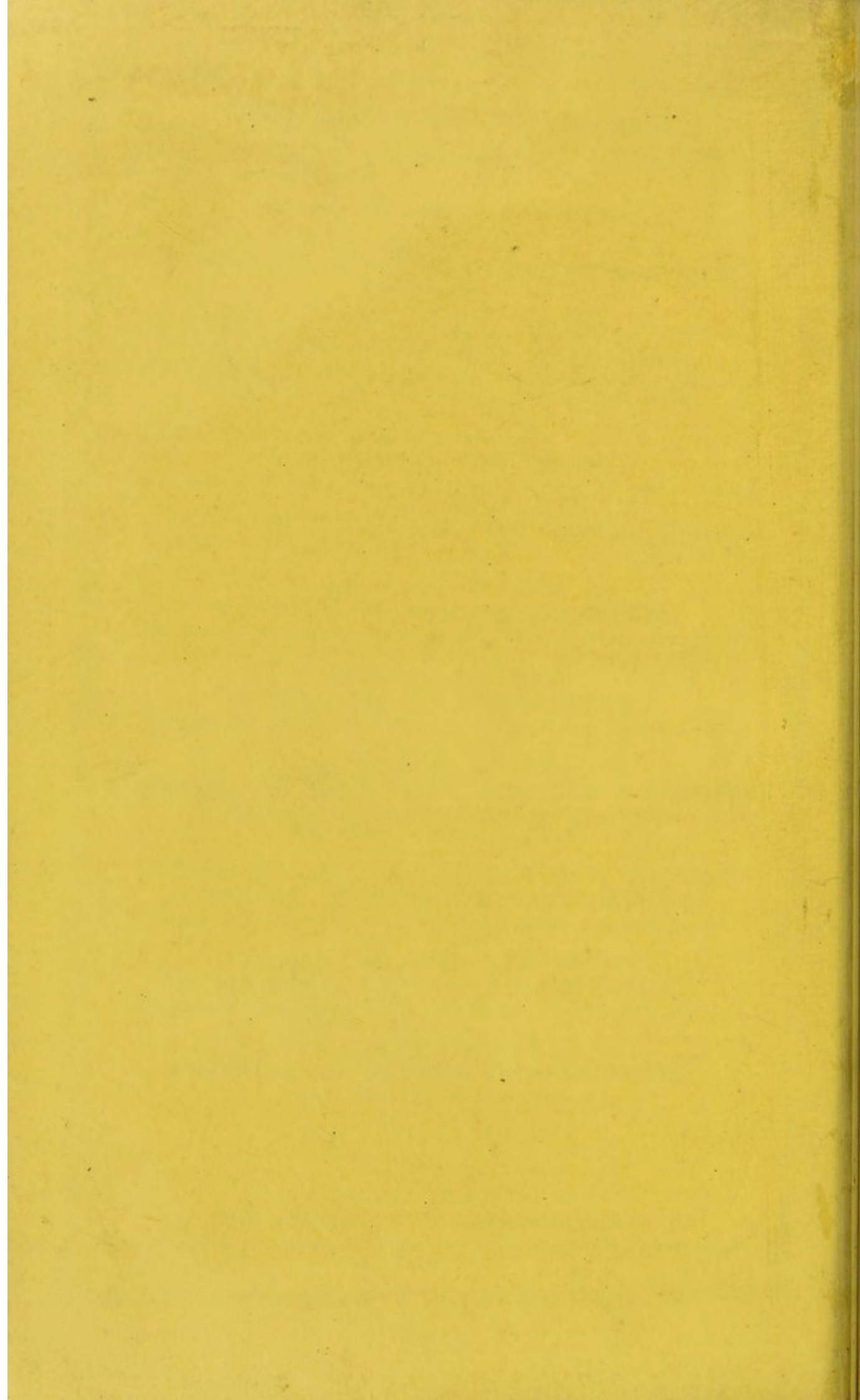
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