each method requires to bring it to perfection; and, in comparing the two methods, those of us who advocate the examination on the back have, at all events, this advantage over those who examine on the side, that we have tried both methods, while all our opponents can claim is that they find no occasion to make any change. It would, indeed, I think, be evident, from an unprejudiced survey of the mere mechanics of the question, that that position should be chosen which enables you to examine both halves of the pelvis equally; and this it can never be claimed that the examination on the left side does. That the adoption of this method of examination on the back has led to enormously increased accuracy and minuteness of diagnosis must be apparent to anyone who has followed the course of modern gynaecology both at home and abroad. Thus the determination of the normal position of the uterus, the palpation of the ovaries and their ligaments, as also of the posterior uterine ligaments and the normal Fallopian tubes, have, in my opinion, by this method been rendered possible. That such accuracy of diagnosis is, however, still very rare in this country, may be gathered from a perusal of the ordinary periodical gynaecological literature, in which such a diagnosis as the exact size, shape, consistence, tenderness, position, and mobility of the normal ovaries is rarely ventured on, though such expressions as "ovaries normal," or "ovaries tender," are not uncommon. Indeed, except in such an assemblage of specialists as the present, the statement that one was able to palpate the normal posterior ligaments of the uterus, and trace the normal Fallopian tubes and round ligaments outwards for a considerable distance from each cornu of the uterus, and in cases of pregnancy trace the course of the ureters passing along the side of the crevix, to be lost above in the broad ligament, would be received with a smile of complacent incredulity. There is one point that I would like to emphasise, and that is that it is the position on the back that renders some of the most improved modern treatments, such as the washing out the uterus in cases of endometritis, and the use of constant antiseptic irrigation in all operations on the cervix, vagina, and perineum possible.

Here let me express my conviction, founded now on a considerable experience, that the enormous difficulties inseparable both to the teacher of imparting, and to the student of acquiring, an accurate knowledge of the diseases peculiar to women are materially lessened by the bimanual examination being made while the patient is lying on the back and the practitioner standing in front of her.

In conclusion, allow me again to invite any member of the Association who may desire it to visit the Rotunda Hospital during his stay in Dublin, and to assure him of a hearty welcome from myself and my assistants.

CONTAGIUM OF SCARLET FEVER: A CRITICAL REVIEW.

Read in the Section of Pathology at the Annual Meeting of the British Medical Association held at Dublin, August, 1887.

By GEORGE THIN, M.D., LONDON.

WHEN I consented a few weeks ago, in answer to a request from your Secretary, to venture to take up some of the time of the Section with a critical review on the nature of contagium in the exanthemata, I was quite aware that it would only be possible for me to occupy a very small part of the field suggested by the title of the paper. Indeed, it was the consciousness of the brief and imperfect nature of my communication that induced me to adopt the comprehensive title which may, perhaps, have led you to expect a paper of wider scope than any I can offer you.

My intention was, after taking a survey of the general questions involved in considering contagia, to select certain points that might seem to me specially suited to illustrate the difficulties that present themselves when we endeavour to reach sure ground in these important and attractive investigations. The wideness of the field and the multiplied investigations of recent years soon brought me to see that it would be more profitable for you and for me if I limited my remarks to a consideration of variola, vaccinia, varicella, and scarlatina, as being types of the exanthemata. With this object in view, I prepared a paper for your consideration. But after I had finished writing it I found that recent investigations relating to the nature of the scarlatinal poison had led me to treat this disease at such a disproportionate length, that my paper exceeded the limits which a due regard to your time imposes. I therefore consider it best to bring before you only that portion of it which deals with scarlatina.

The question of scarlatina may be correctly described as being in this particular field the question of the day. It is one to which I regret I can myself add nothing that is new. Five years ago I devoted some time to this investigation, but I did not obtain any results that I considered sufficiently important to justify me in publishing. In several sections of the skin of patients who had died of scarlatina I found blood-vessels blocked with micrococci, but I had no means of deciding whether these cocci were related to the disease or whether they were due to invasion of the circulation by organisms after the patient had become enfeebled by the disease, and at that point I abandoned the investigation.

The part of a mere critic, which I assume in the paper I am now going to read to you, is not a congenial one to me. But criticism in certain circumstances is not only a duty, but is indispensable to investigators, as indicating to them the points on which, in order to produce general conviction, their investigations must be multiplied and controlled; and, although in response to the invitation of your secretary, I have not been able to present to you any new facts, if I succeed, even to a small degree, in arresting the attention of other workers on points regarding which further research may be usefully applied, I shall have done something in furthering the objects of the inquiries.

The contagium of scarlet fever has been quite recently brought before the profession in England in a very prominent way by careful, prolonged, and minute investigations and observations made by Mr. Power, Dr. Klein, Dr. Allan Jamieson, and Mr. Edington, and I purpose to devote the remainder of my paper to explaining to you how the evidence adduced by these observers presents itself to my mind.

On December 14th, 1885, Mr. Wynter Blyth, medical officer of health for the parish of St. Marylebone, London, received a communication from Dr. Hickman, to the effect that there were several cases of scarlet fever in Dorset Square. He at once made investigations, which showed him that the only connecting link between the various households affected was a common milk supply. The milk came from Mr. Panter's farm, near Hendon, to which attention was immediately directed by Mr. Blyth, Dr. Cameron, medical officer of health for Hendon, and Mr. Power. This was the beginning of an investigation which promises to have some historical importance. Facts connected with the outbreak have formed the subject of reports by Dr. Cameron and Mr. Power, and their substance has been so recently published in the medical journals, that it is unnecessary for me to repeat the information they contain. Suffice it to say that it is established beyond doubt that numerous cases of scarlet fever were caused by the scarlatina poison being conveyed in the milk from Panter's farm. It is also beyond dispute that at the same time that scarlet fever was being propagated by the milk, cows from which the milk was obtained were suffering from an eruption on the teats and udders. It is also certain that, up to the present time, it has not been shown that the milk was contaminated by the scarlatina poison being derived from any known ordinary human source. Mr. Power concluded, partly from observations made regarding the connection of the infective power of the milk with certain sheds amongst which the cows were distributed, that the poison was conveyed from a disease of the udders of the cow to the milk, and the assumption was made that the disease in the cow communicated scarlatina to the human subject. The hypothesis was a bold and important one.

However startling it might be to assume that scarlatina, which seems to have been recognised by the Greeks in the time of Hippocrates, was in reality a disease common to man and the cow, yet that was no sufficient reason for rejecting the hypothesis. There is nothing contradictory in the idea that the poison might produce scarlatina in the human subject and an eruptive disease on the udder in the cow. The question is not as to its plausibility, but as to the fact. Let us see how far the fact is proved. To begin with, it is not enough that we have no evidence to show the contamination of the Hendon milk from any human source. It is quite conceivable that it may have been contaminated without any trace of contamination being found; but that does not materially affect the argument. The point to be ascertained is, does this disease of the cow produce scarlatina in man? Not whether in any particular outbreak of scarlatina in milk we are able to trace the source of contamination.

Professor Axe, of the Royal Veterinary College, has already published certain statements calculated to throw grave doubt on the accuracy of the hypothesis put forth in the Hendon case, and as it was in my power to do a little in following out his line of investigation, I have availed myself of the opportunity, and now put before you the information which I have obtained, and which I believe to be

correct. Professor Axe having been kind enough to grant me an interview, and to put me in communication with the purchasers of other cows similarly affected, I find the facts to be as follows. A dealer in cows bought infected stock in Derbyshire. Three of the animals were sold to Mr. Panter. Others were sold to a large farmer in the south-west of London, referred to in Professor Axe's report as "Mr. A." This gentleman resold several cows to another large holder of dairy stock, whom I shall call V. Amongst the stock of both these gentlemen, as well as on Mr. Panter's farm, the disease spread to other animals. About fifty of Mr. A.'s cows became affected, and from twenty to thirty cows had the disease on Mr. V.'s farm. Mr. A., when he heard of the Hendon outbreak and of the disease amongst the cows at Panter's farm, visited the farm, inspected the cows, and satisfied himself that the disease was the same as that from which his own cows were suffering. Mr. V., a man whose evidence is, as I shall show, of unusual value, although he did not visit Panter's farm, has no hesitation in accepting the description of the disease as it appeared there, as identical with that which was communicated to his stock by the cows bought from Mr. A. As regards the capacity of Mr. A. to form an opinion on the subject of the identity of the disease, I may say that I found him a man of intelligence and capacity, who has been in the dairy business for eighteen years, during which time he had had two outbreaks of the same disease amongst his stock previous to this one. He describes it as a localised affection with three stages. The first is an erythematous stage; secondly, there is a vesicular stage, the vesicles rapidly bursting and leaving, thirdly, a scab which gradually falls off and the part heals.

Both on the present occasion and on previous occasions, the men engaged in milking the cows on Mr. A.'s farm had their hands affected by the disease. This capacity for producing local infection is one of its characters. In the present case two of his men were affected by it. Mr. Bate, a medical man, practising at Merton, attended these men, and he informs me that one man acquired a sore on one of the fingers of his right hand. The sore lasted for a week or ten days, the redness and pain extending up the arm. Another man, also engaged in milking the affected cows, scratched a pimple on his left eyebrow. The pimple inflamed, and the redness round it developed into a fairly severe attack of erysipelas of the head and face, which lasted ten or twelve days. Mr. Bate informs me that he had no doubt whatever at the time that the inflamed finger in the one case and erysipelas in the other were caused by infection from the sores on the udders, experience having taught him that men who milk cows, if the skin of the fingers is abraded, frequently acquire sores of this kind when the udders of the cows are affected as Mr. A.'s cows were. He further assured me that the symptoms are always local, and that no case of scarlatina, to his knowledge, ever resulted. He states further that, for the above reasons, a man with a sore on his finger is usually prohibited from milking. By the dairymen, he told me the affection is known as cow-pox.¹

I have stated that the disease was conveyed from Mr. A.'s farm to the farm of Mr. V. Mr. V. is a medical man who has exchanged practice for farming, and whose knowledge of medicine and of comparative and practical pathology is extensive. He has devoted much attention to the maladies of cows, and from having made many *post-mortems* is very familiar with the morbid appearances found in the bodies of these animals. His experience has not only been extensive amongst his own cows, but it began in his youth before he studied medicine, his father having been a large holder of stock. He bought eight cows of Mr. A., some of which had this disease of the udder, and the malady spread until he had twenty to thirty cows affected, mostly young ones. His description of the disease is as follows: First, a red spot appears on the teat or udder. This spot is rose-coloured, very circumscribed, and increases until a ring is formed. There is a little, but not much, induration. After a few days a vesicle appears. The vesicle lasts a few days, one to two on an average; it then bursts, and there is a sore left. Compare this with Dr. Klein's description. The first cow de-

scribed by Dr. Klein had on the teats and udder several flat, irregular ulcers covered with a brownish scab which, when scraped away, left a granulating, slightly indurated base. The margin of the ulcer was not raised, nor was there any perceptible redness of the skin around it. He found afterwards that in the earlier stages a small vesicle made its appearance on a slightly swollen and red teat, in the course of a couple of days assuming the character of the above ulcers.

The similarity between Mr. V.'s description and Dr. Klein's leaves little doubt in my mind that they both refer to the same condition.

Mr. V. has read the various reports which have been published on the Hendon outbreak, taking, naturally, a lively interest in the whole matter, and has not the slightest doubt that the cows at Hendon, at Mr. A.'s farm, and at his own, were suffering from the same malady. We know that the disease at all the three farms was propagated by infection from the same source. It is a fact that at all of them the affection was one of the teats and udders, that superficial ulcers and scabs formed on an inflamed base, and that the disease was communicated from the same stock, namely, the Derbyshire cows. To my mind the circumstantial evidence that the disease was the same in all the three farms is complete. Mr. V. further informed me that he has kept cows for fifteen years, and has had outbreaks amongst his stock some seven or eight times. He is familiarly acquainted with the symptoms, as are his men, by whom it is called "cow-pox," and he states that it is frequently communicated to men who chance to have abraded fingers. In the present instance two of his men suffered, the affection being in both cases quite local, nothing like scarlatina following the infection.

Mr. V. informs me that, as a result of thermometrical observations, he has found that cows are very susceptible animals, a slight cause producing a rise in temperature, and a very slight rise in temperature diminishing the quantity of milk. The affection in question he states is for the most part a local disease, sometimes causing considerable irritation from the pain it produces. His foreman said that in some cases the quantity of milk is diminished for about a week. In reference to the fall of hair in the disease, a matter of importance, in so far as it was observed and noted by Dr. Klein, Mr. V. states that cows lose their hair twice a year, and at other times lose hair from a very slight cause, as removal from a colder atmosphere to a warm shed, and also that change of diet frequently causes loss of hair.

Now, whilst the customers of the Hendon dairy suffered from scarlet fever, what happened to the customers of those two other large dairies in which the cows were suffering from the Hendon malady? Of Mr. A.'s stock, about fifty cows had the disease. They were regularly milked; all the milk was sold and consumed, 400 customers receiving it, probably equal to about 1,000 persons; yet not one of these people contracted scarlet fever. Mr. V.'s cows supplied seventy to eighty families, with children, and none had scarlet fever. A row of villa houses, mostly containing families with children, near his farm received the milk from him direct, and none of them suffered from scarlet fever. If, then, the disease of the cows on Mr. A.'s farm and Mr. V.'s farm was the same disease that prevailed at Mr. Panter's farm, it is quite clear that the infection of the milk at Hendon was not derived from this disease of the udders of the cows.

There is no doubt that a most important experiment was unknowingly carried out at both Mr. A.'s and Mr. V.'s farms. In both instances discharge from the affected udders was inoculated on the skin of milkers whose hands happened to be abraded. Now, what was the disease which was conveyed by this inoculation? Not scarlatina, but in three cases a local inflammation, giving rise to a slight ulceration, and inflammation of a somewhat specific and painful kind, which ran a certain course and then terminated.

At Mr. V.'s farm, one of the two affected men continued his milking, whilst the other man was obliged to give it up for two days. I saw one of these men, the foreman among the milkers, and was informed by him that he is not only familiar with the eruption on the cow, but that it is well within his knowledge that men who have abrasions on their hands and handle the teats and udders of the affected cows get sores which vary considerably in degree. Amongst the men these sores are recognised, and their source is undoubted. He himself has several times suffered from them. Mr. V. is under the impression that successive inoculations are attended with less and less virulence. But sufficient data were not given me to enable me to judge for myself on this point. I satisfied myself, however, that the same man may suffer repeatedly from this accidental poisoning of the skin, a fact of some importance when we consider that farmers and milkers are in the habit of considering this disease amongst the cows to be cow-pox, and the sores which the men contract to be the results of inoculation with cow-pox virus. These men, farmers

¹ I find, from a work entitled *Ueber Kuhpocken an Kühen*, "Nach den, in den Acten des Königl. Würtemb. Medicinal-collegiums enthaltenen, und eigenen Beobachtungen, von E. Hering. Stuttgart, Verlag von Ebner und Seubert, 1839," that there is more than one variety of cow-pox. There is the true cow-pox, which is chiefly distinguished by its inoculability on the human subject, and there are several varieties of what the author calls "false cow-pox," more or less difficult to distinguish from the true cow-pox. Of this false cow-pox, he distinguishes the following varieties: (a) Eruptions on the udder, which are distinguished by running a more rapid course than true cow-pox (*Spitzpocken, nachpocken, and enterseuche*). (b) Eruptions on the udder which are distinguished from true cow-pox by differences in form and structure (A) hard pock—*verruucose, tuberculose*, (B) bulbous pock—*brillöse, vesiculose*, (C) flat, crater-like eruption on the udder. (c) Several anomalous forms of eruption on the udder. The points of distinction between the true cow-pox and some of the forms of false cow-pox seem to be in many cases so slight that the only criterion available is the non-inoculability at all stages of the false pox.

and workmen, know no other form of cow-pox than this disease. Whether it is cow-pox or not, it is certain that it is capable of producing a considerable amount of local inflammation in the skin of a man; and, assuming that it is cow-pox, and given that an individual man has been previously inoculated and is not susceptible to the virus, it by no means follows that the discharge from a cow-pox ulcer is not capable of conveying other septic and irritating poisons, besides cow-pox proper.

As regards the disease amongst cows, Mr. V. is clear on the point that it is mostly young cows that are attacked, and that these attacks act as a prophylactic to a considerable extent against successive infections. In regard to this point, I think it well to emphasise the fact that this is the opinion of a medical man who has had long experience in studying the diseases of the cow, and whose interests and tastes have led him to observe them closely, both in their clinical and pathological aspects.

To discuss a possible source of infection of the Hendon milk other than that of the disease of the cows is not strictly necessary. If it had been proven that the cow disease produced scarlatina through the milk, speculation as to other sources of infection, however probable these sources might have been, would have been useless. Such other probable sources of infection can only have an existence for those, like myself, who find the evidence as regards the cows not only faulty, but disproven; faulty, in the first instance, as not being sufficient on its own merits; and disproven, in the second instance, by the fact that the same disease prevailed in other herds by which no infection was conveyed. Belief or disbelief in the cow theory ought not really, I imagine, to depend on whether it is possible to account for the poison of the Hendon milk by any human sources, but, nevertheless, that part of the question is undoubtedly of very great interest, and deserves the most careful study and investigation. This investigation, I understand, it is now having at the hands of Professor Axe.

From visits to Hendon and Child's Hill, and by conferences with medical men at both places, I learned that at the latter place a district called "the Mead" consists very largely of laundries, great quantities of linen from the northern and western districts of London being constantly brought there. "The Mead" is a colony of laundries, such as can only exist in the neighbourhood of a large city like London. From these laundries there is little doubt, I am assured, that contagious diseases arise and spread, that in lighter cases medical men are not called in, and that there is a desire amongst the laundry people to conceal the existence of infectious diseases on their premises.

I find in Dr. Cameron's sanitary report to the Hendon Local Board for the year 1885 that on September 4th a woman residing at the village of Child's Hill was attacked by scarlet fever, and that on October 10th two children living near her were infected. In the last week of November Dr. Cameron states that two mild cases of scarlet fever came to his knowledge in "the Mead" at Child's Hill. As the district is full of laundries he considers that it is possible the disease was introduced from London. There was no other evident source for it. The fever here, he remarks, did not spread beyond either of these houses. We have, therefore, on the authority of Dr. Cameron, scarlet fever at Child's Hill in September, October, and the last week of November.

Two men, I am assured, who were engaged as milkers at Panter's farm, lived in "the Mead," walking to and fro to their work, a distance not over half a mile. There is not the slightest proof that these men conveyed the scarlatinal infection from "the Mead" to Panter's farm, but it is quite conceivable that they may have done so; the very fact that "the Mead" contains so many laundries, that scarlet fever existed at Child's Hill, and that there was daily communication between "the Mead" and the milking sheds, justifies a suspicion, or at all events affords a possible explanation, of how the milk became infected.

It seems that dairymen, even when they do not dilute their milk with water, are in the habit of adding something to it which they call "colour," and this "colour" is mixed by the dairyman plunging his naked hand into the milking-can, and stirring round the colour in the milk. My authority for this statement is Mr. A.

These outbreaks of scarlatina in connection with milk require to be sifted in the most thorough way, and the country is under a debt of gratitude to Mr. Power for having to a large extent initiated the searching inquiry which was needed alike in the interests of the public, the dairy farmer, the dairyman, and science.

It is well known to readers of the medical journals that Mr. Power's theory received apparently great support from a series of interesting experiments conducted by Dr. Klein. Dr. Klein obtained from the

ulcers of one of the cows streptococci, which, when inoculated on calves, produced a disease similar to that from which the cows suffered, this micrococcus being not only found in the tissues surrounding the ulcers, but in the organs of a calf which died of the results of inoculation with subcultures of the organism, and of another which was killed whilst suffering from the effects of inoculation.

In a lecture delivered at the Royal Institution on May 27th, Dr. Klein states that the evidence previously obtained had been completed. He states that it has been shown that in the blood and tissues of persons affected with scarlet fever there occurs the same micrococcus as was present in the cow, the organism in both cases being identical in microscopical and in cultural characters; that the action of this microbe in animals is the same as that of the micrococcus found in the Hendon cows; and further, that calves or mice fed or inoculated with cultivations of the coccus became affected with cutaneous and visceral disease similar to human scarlet fever, and that from the blood and tissues of animals infected by these cultivations the same micrococcus was recovered. As supplementary evidence, Dr. Klein states that a monkey died of what he took to be scarlet fever, and that from the blood of this monkey the same coccus was obtained. There can be no doubt as to the interest that attaches to the history of this micrococcus, but let us see how far its causal relation to scarlet fever is proved. That Dr. Klein has isolated from the blood and tissues of these animals and from the blood in scarlatina a pathogenic streptococcus is evident, but it is not evident, to me at least, that this coccus is the cause of scarlatina. First of all, there is no proof that the coccus has produced the disease in man which we know as scarlatina; and secondly, there is no proof that the disease produced in animals by inoculation with this coccus is scarlatina, in any form, modified or not.

As regards the coccus, I shall not stop to inquire whether it is quite certain that the coccus described by Dr. Klein is a new one; but, in illustration of the refinement necessary in discriminating between different cocci and the possibility of confounding them, I will bring together Dr. Klein's description of his coccus and Flügge's description of streptococcus pyogenes. Dr. Klein states that the mode of growth of his coccus was extremely characteristic. In neutral gelatine, at the line of inoculation, it appears in the form of small points or granules, whitish in colour and tolerably closely placed. At the end of a fortnight the line of inoculation was seen as a streak of whitish granules. On the surface of the gelatine the growth, which is like a film of granules, spreads slowly in breadth, but even after months remains small. When inoculated into the depth of the gelatine, the channel of inoculation becomes visible as a whitish streak, made up of smaller and larger droplets. The gelatine does not liquefy with this growth.

Compare this with Flügge's description of streptococcus pyogenes. "In gelatine plate cultivations the streptococcus grows in very small dot-like colonies, which on the surface extend as minute, not prominent, transparent droplets. Even after several days they have not spread more widely, and no liquefaction of the gelatine takes place. When inoculated in gelatine there forms in the track of the needle a delicate deposit, which either entirely or partly consists of small isolated colonies. These appear faintly whitish, almost transparent, very small, only a few growing to the size of a pinhead."

In both cocci the growth on agar and solid blood serum is the same as on ordinary nutritive gelatine. Streptococcus pyogenes (I quote from Flügge), when injected subcutaneously in mice in small quantity, usually produced no reaction. Sometimes there is slight suppurative at the points of inoculation; sometimes the animals die. If it is inoculated into the ear of a rabbit, on the following day there is vivid redness and swelling, which disappears on the second or third day. Healthy rabbits tolerate this coccus; but, if the animals are weakened by the injection of toxic substances, death takes place by the abundant growth of the cocci.

In connection with the immunity of rabbits as regards streptococcus pyogenes, it may be noted that Dr. Klein's streptococcus, which had such a decided effect on the cow, produced no effect on guinea-pigs. In how far these resemblances justify the belief that Dr. Klein's streptococcus and streptococcus pyogenes of other authors resemble each other in their mode of growth to a noteworthy extent, it is not my object to inquire; but if it were only to illustrate the nature of the points which arise in investigations of this kind, it was worth while to place these descriptions side by side. By doing so, readers comparatively new to the subject will understand what difficulties there are in the way of mastering a new technique, and in bringing into harmony the descriptions and statements of isolated workers.

I will, for the purposes of argument, assume that Dr. Klein's coccus is a new one, one not described, hitherto, by bacteriologists. To my mind there would be nothing very extraordinary in the fact that in

scarlatinal blood and in the ulcers on a cow's skin, and in certain given forms of septic inflammation, a new coccus had been discovered. It must be remembered that we are yet scarcely on the threshold of investigation regarding the number and varieties of pathogenic organisms; and we may expect that, in a very short time, investigators like Dr. Klein will add many more to the comparatively few organisms that have been isolated, studied, and classified. But a long series of investigations has yet to be made before we can arrive at the conclusion that Dr. Klein's streptococcus is confined to the blood and tissues of scarlet fever, and to certain ulcers in the cow.

The study of the organisms that are associated with scarlet fever is by no means a new one. I learn from an article by Escherich, in the *Centralbl. f. Bacter. u. Parasit.*, for 1887, that Hallier examined the blood of three children who had scarlet fever. In all three he found great masses of micrococci (*tillotia scarlatinosa*), which he figures. Klotzsch cultivated the blood of a scarlatina patient on dough, extract of meat, and slices of apple, but found nothing. Hoffman found numerous micrococci in the sweat. Coze and Felze found bacteria in the blood, mm. 0.0006 in size. Rabbits injected with blood died in from eighteen hours to fourteen days afterwards, and the blood contained the same organism. Klebs cultivated a *monas scarlatinosum* from the inguinal gland of a scarlatina patient. He found balls of micrococci which developed into rods and back again into cocci. Riess, in one fatal case, found the serum filled with moving points, which did not cultivate, and were not found in other cases. Pohl Pinkus found exceedingly small cocci in the scales of desquamation, and in the mouth. Klamann found the same. Crooke found micrococci in the organs in some uncomplicated fatal cases.

Loeffler, in five cases of diphtheria, in which the throat affection was complicated by scarlet fever, found cocci which penetrated the tissues and vessels. They resembled Fehleisen's erysipelas-cocci. These cocci injected into the blood-vessels of rabbits caused purulent effusion into the joints, in which masses of streptococci were found. In synovitis scarlatinosa, in a boy, aged 14, Heubner and Bahrdt found the same.

Litten and Bokai-Babes had previously found rod-shaped bacteria and cocci in pus of scarlet fever inflamed joints.

Loeffler's streptococcus, Escherich remarks, would seem in the light of the latest investigations to be identical with streptococcus pyogenes.

Crooke found in sections of tonsils, and in the mucous membranes of the throat, epiglottis, and larynx, with or without diphtheritic inflammation, infiltration with cocci and breaking down of the tissues. In rare cases they were also present in spleen and kidney. They were in the form of large mono- or diplococci, and smaller cocci in chains and thick zoogloa. In two fatal cases with appearances of pyæmia the source of the joint-affection was in the ulcers, tonsils, and embolic infarcts in both lungs. The capillaries of the alveoli and interlobular blood-vessels were in many cases blocked with cocci.

Fränkel and Freudenburg found chains of cocci in three fatal cases in the submaxillary lymphatic glands, kidney, and liver. They cultivated them and identified them with Rosenbach's streptococcus pyogenes. It is, however, clear that in a great number of scarlet fever cases this coccus is present in the necrosed parts of the throat organs. It finds its way into the general circulation, and there causes severe local and general disease more dangerous than the original disease.

In 1884 Crooke found in the nose, mucous membrane, and infiltrated tissues of the neck, short bacilli, similar to the bacilli of malignant cedema, but smaller, and arranged in chains of two to six members.

Escherich found the same in the case of a boy, who died on the fourth day of the disease, by cultivating numerous colonies of a motile rod, which quickly liquefied the gelatine.

In regard to this question it must never be lost sight of that the diseased condition of the blood produced by the scarlatinal poison may, to an extent that we cannot estimate, render it a fit soil for the existence and multiplication of organisms, pathogenic or otherwise, which cannot live in it in a state of health, and that to find in the blood in scarlatina a coccus which, when inoculated in animals, produces a septic inflammation of more or less severity, by no means shows that in this coccus we have got the scarlatinal poison itself: it only shows that in scarlatinal blood there are present pathogenic organisms.

The crucial proof that the organisms are the cause of a disease is that this disease is produced by subcultures of the organisms; and it has been laid down that without such proof we are not justified in considering the organisms to be the cause and not the accompaniment of the disease. For my own part, I am not disposed to be so strict. I consider the evidence that the bacillus lepræ is the active cause of

leprosy to be sufficient. It convinces me, although it has never been shown experimentally, that leprosy can be produced by cultivations of the bacillus, which indeed has never yet been cultivated artificially. Those who are disposed to hold fast by this absolute criterion may find food for reflection in the fact that for many years trichophyton tonsurans was universally received as the cause of ringworm, although it had neither been cultivated artificially nor inoculated. Indeed, I am not aware that, up to the present time, ringworm has been produced by subcultures of trichophyton. I am not, therefore, prepared to say that we ought to demand the proof that scarlatina can be produced in the human subject by subcultures of the organism isolated by Dr. Klein. If it could be shown that that organism was always present in scarlatinal blood and in scarlatinal tissues, and nowhere else, in proportion as the latter fact became more and more apparent, so much more and more probable it would appear to me that the coccus was the cause of scarlet fever. But we are an almost immeasurable distance yet from this point. First of all the characters of this coccus must be so defined and capable of recognition that any trained observer would recognise it when he found it, and be able to distinguish it from every other known coccus. Next, what an immense number of tissues, physiological and pathological, and other objects must be examined before we conclude that this coccus is not present in them.

But it is said that inoculations with this coccus produce in animals a disease which is very like scarlatina in man. Assuming that this was so, it would undoubtedly be a very strong argument. If the coccus obtained either from scarlatinal blood, or from the tissues or ulcers of a cow, when injected into an animal's tissues, produced in that animal a disease which could be distinguished from septicæmic or pyogenic inflammation, or blood poisoning in the ordinary sense, and which could be identified as having the same distinctive characters as those found in scarlatina in the human subject, a very important link in the chain of evidence would be formed. But has that link been forged?

Let us consider in what scarlatina consists. The essential features of scarlatina it will, I presume, be granted, are the characters of the exanthem on the skin, and the condition of the throat and tongue. As regards the skin, the essential characters are the nature and duration of an eruption and the desquamation. I do not think it will be maintained for a moment that anything approaching the rash of scarlatina and the subsequent desquamation has occurred in the cows affected with the Hendon disease, or has been produced by inoculation with the cocci. Certain scabs and ulcerations in the cows, and a localized marginated eruption about the mouth in the calves are described, but the description alone negatives the idea that this can be in any sense identified with the scarlatina rash. Nor is there anything approaching the desquamation that occurs in the human subject. The partial loss of hair described as having occurred in some of these cows is in no sense parallel to the desquamation produced by scarlet fever. Partial loss of hair in cows, Mr. V. assured me, occurs from very slight causes, and indeed may be seen after any febrile attack.

But what is to be said of the alleged identity of the changes found in the tissues of these animals with the changes that are found in the tissues of scarlatina patients? Are the changes found in the skin and organs of diseased and inoculated animals really, as Dr. Klein believes, similar to those found in human scarlatina?

Dr. Klein, after describing the mode of growth of his streptococcus, goes on to say: "This streptococcus, when inoculated in the groin of two calves, produced the following effect:—After twenty-seven days one calf was found dead. It was then found that the subcutaneous tissue at and for some distance around the seat of inoculation showed much effusion, and the inguinal glands were swollen and red. There was peritonitis, with sanguineous exudation, congestion, and hæmorrhagic spots in the omentum, and in the serous coat of the stomach. The spleen appeared small and its capsule thickened. The liver was greatly congested. Kidneys were large and much congested. The ileum was much congested in its mucous membrane, and the epithelium detached in flakes. The mesenteric glands belonging to the ileum were greatly enlarged and hyperæmic. Both lungs were congested; the superficial lobules showed so much congestion that they looked almost solid and of a deep red colour. There were a few petechiæ under the pleura. The bronchial glands were enlarged and congested. There was pericarditis, and the heart was distended by and filled with coagulated blood. The organs of the throat were found much congested." The other calf was killed after thirty-five days, and on a *post-mortem* examination the following appearances were noted: "Congestion of some of the peripheral lobules in both lungs; the pleura pulmonalis slightly opaque, numerous soft lymph adhesions between it and the costal pleura; in the spleen several hæmorrhagic patches

under the capsule in the shape of bullæ filled with semi-congealed blood; spleen pulp softened and very congested; organs of throat congested."

These appearances convey to my mind the impression of a septic inflammation.

In speaking of septic and pyogenic processes, Klebs remarks that in all diffused septic inflammation of the lungs the micrococci which circulate in the blood fix themselves on the endothelia of the blood-vessels. They accumulate until thrombi are formed and the smaller vessels may be completely blocked up by masses of micrococci. These masses of micrococci sometimes rupture the capillary network, and then there is found between the epithelial cells (which are often degenerated), leucocytes, and red-blood corpuscles as well as the balls of micrococci. In the kidney masses of cocci lead to the blocking up of vessels in the glomerulus, or the process may simulate the appearance of pyelo-nephritis. In the capillaries of the liver micrococci develop, and these channels become enormously dilated, and lead to atrophy and compression of the cells.

Ziegler remarks that metastatic inflammation with fever is probably produced by more than one form of bacteric infection, and that the manifestations of septicæmia are not always produced from the same poisons.

It is quite clear that the organism experimented with by Dr. Klein is capable of producing metastatic inflammation in the organs and symptoms of general blood-poisoning. But these results are not peculiar to scarlet fever, although they may be found in the bodies of persons who have died of it. They are the general symptoms of blood-poisoning, and modern research shows that bacterial poisons generally underlie them.

But special weight has been laid on the changes found in the skin and kidney of these animals as being identical with those found in scarlatina.

In one of the calves infected by inoculation of subcultures it is stated that around the nostrils and lips of the mouth, and on the hard palate and gums there were numerous irregularly outlined patches not raised above the level of the skin. These patches had a discoloured, brownish, very slightly raised margin and a paler centre. They were round or irregular, some as small as one-eighth of an inch, others were four to six times larger.

As regards the affected skin, Dr. Klein states that: "The tissue of the papillæ and of the superficial corium is infiltrated with round cells, and the blood-vessels of the papillæ are distended and filled with blood. In their peripheral portions, their most superficial parts, the papillæ are very much distended by extravasated blood and round cells, in fact, the first rudiments of cavities are forming in them. The same condition, but more pronounced, obtains in the cuticle, where between its layers there are present small cavities filled with blood and round cells, or only fluid and a few round cells. There is, in addition to this, a general infiltration with round cells of the layers of the cuticle. The brownish-reddish colour of the marginal parts is due to this condition. In the central part the cuticle is loosened by the formation of such cavities containing fluid and a few round cells; by this its layers were separately and ultimately detached. In the cavities of the cuticle occur very fine diplococci and chains. So also in the infiltrated and enlarged papillæ, and in the deeper layers of the epithelium in the whole extent of the diseased skin, diplococci and short chains are present.

In neither of these cases of subcutaneous inoculation was there found any rent or breakage of the stratum malpighii, that is, no real ulcer. The anatomical features here described in many respects resemble the lesion of the skin in human scarlatina."

I cannot recognise in this description conditions peculiar either to scarlatina, or to this affection in animals. All congestive and inflammatory conditions in the skin are accompanied by certain well-known changes. The tissues of the papillæ and corium are always found infiltrated by round cells, and the blood vessels are always found congested. If the inflammation has advanced to a certain stage, the epithelial cells of the cuticle are always more or less dissociated, and they are found in the small cavities in the rete mucosum, which are sometimes formed. In these small cavities, when they are present, white blood cells are found, or both white and red cells; and these changes are not necessarily found with an abraded cuticle, or a condition of ulceration. They are really dependent upon lesions of the blood vessels, which lead to the escape of white and red blood corpuscles, and of serum. The exudation of a certain amount of serum from the vessels of the papillæ leads to infiltration of the epidermis, and infiltration of the epidermis leads to more or less breaking down of cells in the rete. If the cause of this inflammation is the presence of cocci, these cocci will, if appropriate methods are

used, be found. What I infer from Dr. Klein's reports is that a certain inflammatory condition of the skin was produced by the presence of cocci, but there is nothing in this condition, as described, which suggests to me necessarily the presence of the scarlatinal poison. Unfortunately, the scarlatinal poison has no monopoly in producing changes of this kind in the superficial tissues of the skin.

But the changes in the kidney are relied upon as affording special evidence of the alleged identity. As regards this organ in the animals experimented on by Dr. Klein, he states:—

"The Kidney.—The changes in this organ are highly interesting, since they completely coincide with those in acute scarlatinal nephritis in man; great congestion of the cortex, leading in some parts to hæmorrhage into the parenchyma; glomerulo-nephritis, with exudation of albuminous fluid and blood into the cavities of the malpighian corpuscles; granular or opaque swelling of the epithelium of the uriniferous (convoluted) tubules, with degeneration into granular debris of many of the epithelial cells; miliary foci of aggregations of round cells around small blood vessels; congestion of the medulla."

It is of course notorious that in scarlatina the kidney becomes affected, but affection of the kidney is not peculiar to the scarlatinal poison. Cornil and Ranvier state: "Acute, diffused nephritis occurs in the course of variola, measles, erysipelas, typhoid fever, recurrent fever, malarial fever, yellow fever, septicæmia, puerperal fever, scarlatina, pneumonia, etc." They give that of variola as a type. The kidney is congested on its surface and its substance; the cortical substance is thicker and very congested. The medullary substance is of an intense red, the cells of the convoluted tubules are swollen, and contain several nuclei and several proteid granulations. The epithelium becomes degenerated. As regards the glomerulus, the vessels are filled with blood, and there exists effusion of blood or an exudation containing white blood-corpuscles in Bowman's capsule. They describe the scarlatinal nephritis as being a temporary nephritis, analogous to the condition in variola, but more intense.

The poison of scarlatina produces inflammation in certain elements of the kidney. The micrococci injected by Dr. Klein into animals also produced inflammation in the kidney; but there is nothing specific in either of these inflammations. Nor does this inflammation of the kidney in animals identify the disease from which they suffer with scarlatina any more than it does with variola, septicæmia, and other diseases. The kidney is an organ which is peculiarly liable to suffer from infection in all forms of blood-poisoning. In Dr. Klein's experiments and in scarlatina there is no exception to this general rule.

The newest text-books on general pathology—that by Klebs, for example—describe in detail how pyogenic micrococci, when once they have found their way into the general circulation, lead to inflammation of the kidney, liver, and other organs. That cocci cultivated from scarlatinal blood or from ulcers on a cow's udder should cause symptoms of general blood-poisoning, and, amongst these, inflammation of the kidney, is a fact of a certain interest, but it does not identify the human disease scarlatina with the disease which finds its chief local manifestations on the udder of the cow.

In the JOURNAL for June 11th, 1887, there is a paper by Dr. Edington and Dr. Jamieson, of Edinburgh, on the prophylaxis and the contagium of scarlet fever. Dr. Jamieson having shown by clinical observations what was before fairly well accepted, that the poison of scarlet fever is present in the scales at the desquamating stage, Dr. Edington undertook a bacteriological investigation, with special reference to these clinically observed facts. The most important point in Dr. Edington's report is that a certain organism, which he calls *bacillus scarlatinae*, is present in the blood in the early stages of the disease, and that the same organism is present in the desquamation of the later stages, but that it is not present in the desquamating cuticle before the end of the third week. I shall say nothing regarding the other organisms described by Dr. Edington. The presence of similar if not identical organisms in the blood of scarlatina is already known, and they are not supposed to be the cause of the disease, but it is a striking fact, which we are bound to accept on Dr. Edington's authority, that the same bacillus that is present in the blood in the early stages only of the disease should be present only in the later stages of the desquamating cuticle. What is important to my mind in the matter is the absence of this bacillus from the blood in the later stages of the disease, and its absence from the cuticle in the early stages of desquamation. There is no doubt that the state of our knowledge regarding the organisms present on the human skin is very defective. Although certain investigations have been made by several observers regarding the organisms on the free surface of the skin, these observations have been too limited in number, and have not been sufficiently controlled. Further, there are discrepancies in the statements

made. Such being the case, it is open to the critic to object to Dr. Edington's *bacillus scarlatinae* that this bacillus is a bacillus that grows on the skin under certain conditions, when there is no scarlet fever present. But the force of this objection is much weakened by the fact that there are stages in the desquamation in which the organism is not present at all. It would seem, therefore, that Edington's *bacillus scarlatinae* is by no means a constant parasite of the epidermis.

It is easy to object to Dr. Edington that he has not made sufficient control experiments regarding the bacilli of the skin in health and in diseases other than scarlatina. Had he done so his communication would not yet have seen the light. There is a limit to the power of one worker, and it seems to me better that he should have published his results, although they have not been controlled by other experiments, because their publication will, it is to be hoped, bring a phalanx of workers into the same field by whom his experiments can be controlled.

Similarly, the presence of this bacillus in the blood in the early stages of the disease derives much of its importance from the fact that this bacillus is identical with that found in the cuticle. The mere fact that an organism is found in the blood of scarlatina at a given stage by no means shows that that organism is the cause of the disease. So far as I am aware, the organisms previously described as being present in scarlet fever are different from Edington's *bacillus scarlatinae*, but that by no means shows that in this bacillus we have at last found the contagium. There is no more reason why this bacillus should not get into the blood from the throat or intestinal canal, when the mucous membrane has been damaged by the disease, than there is to doubt that the cocci which have been described in scarlatina get into the blood by this means. Heubner and Bahrdt, for example, found in a fatal case of scarlatina, with pus in the joints, and with streptococci in the pus, that they could prove that these cocci found their way into the jugular vein, and thence into the blood. What was possible in this case as regards the streptococci is possible in Edington's case as regards his bacillus. The want of sufficient control experiments makes itself felt here, and it is much to be desired that Dr. Edington himself, or other competent observers, should institute a series of examinations of the blood by his methods, in healthy persons, but more especially in other febrile diseases. If it is found that this bacillus is always present in the blood in the early stages of scarlet fever, and is never present in the blood in any other disease, or in health, and if it is further found that it is always present in the later stages of the desquamating cuticle of scarlatina, and is never found on the skin in health, or in any other diseases, the probability of the bacillus having an intimate relation with the disease will become very much stronger, and the more abundant negative results become in other diseases, the stronger will the force of the positive results in scarlet fever become.

It is clear, then, how far we yet are from anything like certainty in this case, so far as the mere presence or absence of the bacillus is concerned. Before anything like conviction can be produced, what an immense number of investigations and experiments must be made! How otherwise can we exclude the presence of this bacillus in other conditions? Not only must the presence or absence of this bacillus be established, but even before that can be done, Dr. Edington has much to do still in defining the characteristic behaviour under cultivation of his bacillus, and other qualities that will enable it to be identified under all circumstances.

What points are open to the critic regarding the effect of this bacillus on animals? When inoculated on rabbits it produced slight but marked erythema if they were young, but if older the erythema was better developed at the point of inoculation, the cuticle afterwards desquamated, and the animals had fever. The bacillus could be re-obtained from the animal's blood. The same thing held good for guinea-pigs. Inoculation was fatal to a calf, in which it rapidly produced sickness and fever. The description of the viscera in this calf (JOURNAL, vol. i, 1887, p. 1266) proves to me nothing more than that the animal died of blood-poisoning. The bacillus was re-obtained from the tissues of this animal. The prominence of the fungi form papillae in this calf, as suggestive of scarlet fever, does not carry with it, to my mind, the same force as it does to Dr. Edington's.

In another calf, which after being ill recovered, it is stated that the skin covering the thorax, upper part of the abdomen, and inner side of the forearm, presented a general redness; that the rash was very vivid, particularly in the throat. Blood from a case of scarlet fever, after being diluted with Koch's jelly, produced when injected into guinea-pigs erythema, with succeeding desquamation. The same diluted blood, when cultivated, was shown to contain the bacillus as well as a streptococcus.

There can be no doubt that Dr. Edington has isolated from the blood of scarlatina a bacillus which, when injected into animals, makes them ill, and may kill them, that some of the symptoms in these animals are erythema and desquamation of the skin, and that when the disease is fatal the viscera show a general state of blood-poisoning. But it by no means follows because an animal when feverish has more or less erythema of the skin, with subsequent desquamation, that, therefore, it is suffering from scarlet fever.

One of the arguments in support of the contention that cocci and bacilli respectively represent the scarlatinal poison is, as has been seen, that, injected into animals, they produce a disease similar in its manifestations to scarlet fever in man. Now it is well that the ground should be thoroughly cleared, so far as this argument is concerned, both as regards past experiments and future investigations. What is scarlatina? So far as we yet know the disease, it is the manifestation of a form of blood-poisoning, in which, in addition to the ordinary symptoms of fever, there are combined more conspicuously certain manifestations in the throat, tongue, and skin. But it must be remembered that even in man redness of the skin, tongue, and throat may and do occur without scarlatina. All redness of the skin is not scarlatina. It is unnecessary to state that in measles, erythema, roseola, and in the early stages of septicæmia and small-pox, the skin is subject to papillary congestion, producing more or less change of colour; and from this we distinguish the rash of scarlatina by certain characters of flatness, colour, distribution, and grouping. In the early stages of nearly all forms of blood-poisoning there is a preliminary roseola, generally overlooked, due evidently to the paralysing effect of the poison on the small arterioles of the skin. That an animal which has received into its circulation a pathogenic organism should, in addition to the usual symptoms of fever, present more or less determination of blood to the skin, is a fact of interest, and one that should arrest the attention of observers. We require more definite information regarding the degree of congestion, its duration and mode of onset, and regarding the differences between the local congestion which surrounds the point of inoculation and any general congestion that may be present in other parts. But more or less erythema of the skin in rabbits, guinea-pigs, or calves is not a proof that the human disease scarlatina is running its course in these animals. As regards desquamation of the cuticle, it is the usual consequence, in a greater or less degree, of all erythematous conditions which have lasted a certain time or have existed in a certain degree of intensity.

It by no means follows that animals, even if they were capable of becoming infected by scarlet fever, should necessarily have an exanthem or a desquamation similar in degree to that exhibited by the human subject; but if the exanthem and desquamation of animals is to be relied on as evidence that they are suffering from scarlet fever, then we must ask that the rash and the desquamation should, as regards time, extent, and distribution, coincide somewhat closely with its manifestations in the human subject. This has not been the case in the animals experimented upon by Dr. Klein and Dr. Edington. These animals suffered from fever, erythema, and partial desquamation; but these symptoms, neither singly nor in combination, were, so far as I can make out from the descriptions, pathognomonic of scarlatina.

Of course there is nothing in the account of these experiments to negative the possibility that the symptoms in these animals were due to scarlatinal poison. In my view there is not sufficient proof that they were so, but there is no objection to the hypothesis being made, and taken as a fair working hypothesis by which future investigations and experiments may be inspired.

Before it can be accepted that Dr. Klein's or Dr. Edington's organisms are the cause of scarlatina, there are sufficiently important lacunæ to be filled up. It must be shown first that the isolated organisms are capable of producing scarlet fever in man. That would, of course, be the most convincing and direct experiment if it were possible or permissible. Seeing that this experiment cannot be intentionally made, the experiments on animals must show that the latter are capable of developing scarlet fever. This would be done if a disease were produced in them which bore so striking a resemblance to human scarlatina as to satisfy the demands of clinical observers; or the same object would be attained if it were shown that in animals suffering from the effects of the injection of these organisms a disease was produced which communicated scarlatina to human beings who came in contact with the animals. The object would also be attained if sick animals communicated scarlatina to human beings, and if in these animals and in the human beings a pathogenic organism were found which in its characters could be distinguished from all other organisms. None of these criteria are, so far as I can see, satisfied.

To satisfy them more fully must be the laudable object of future investigations, and these investigations, it seems to me, premise an amount of experiment and work that will demand the energies and time of a great number of workers. I rejoice, therefore, that Dr. Klein and Dr. Edington have seen their way to publish the results they have obtained at their present stage, and although I am unable to take the sanguine view of these investigators as regards the point at which they have arrived, I still consider that their work is of the greatest value. They have added to our knowledge of septic organisms, and they have in the most forcible way called the attention of the profession to problems of surpassing interest that loudly demand solution. Setting aside the scientific question, we have the national question before us of the enormous annual loss of life caused by this poison; and it seems to me that it has become the duty of every member of the profession to lend what help he can towards throwing light on these difficult questions, even although his light may assume the form of the fitful cross-light of criticism. It is this humble task I have tried to fulfil in the paper I have read to you.

But a higher duty falls to our medical corporations, and might not inappropriately be assumed by the powerful Association which you represent. Undoubtedly it is in the power of the British Medical Association to contribute valuable assistance in the prosecution of these investigations. Even if the whole question were not entered into, there are certain points in the investigations which the Association might most usefully examine, and which would be capable of elucidation. I would suggest that a committee of workers should take up the question of the organisms present in the blood of scarlatina patients from the first manifestations of the disease onwards, and that each of these organisms should be subjected to careful examination and study. I would further suggest that the question as to whether animals do or can suffer from scarlatina should be exhaustively dealt with, and that an attempt should be made to enlist into co-operation the authorities of a veterinary school. In the metropolis at least, workers, cases of scarlatina, and a veterinary institution directed by scientific men, are always to be found. To utilise and combine these opportunities is a task which the Association can well fulfil, and the suggestion that this task should be taken up is my poor contribution so far to the solution of the problem.

ON THE ORGANISATION OF THE THROMBUS FORMED IN AN ARTERY AFTER LIGATURE.

Read in the Section of Pathology at the Annual Meeting of the British Medical Association held in Dublin, August, 1887.

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THIS study is based on the macroscopical and microscopical examinations of a series of sections of arteries prepared by the author for Mr. C. T. Dent, F.R.C.S., Assistant Surgeon to St. George's Hospital. These arteries had been tied in Australia (on account of prohibitive laws) by Mr. E. C. Stirling. Although Mr. Dent has not published the results of his observations on the properties of ligatures used in these cases, he has very kindly allowed the publication of some of the observations which have been made by the author on the organisation of the thrombus. The animals used for these experiments were adult sheep, and the artery tied in all cases was the femoral.

The effects of age, sex, state of the individual, or the influence of the species or of disease are therefore not considered.

The following views are supported or advanced in the communication, and are demonstrated by means of a number of microscopical sections of arteries removed from the body, 5, 9, 13, 17, 20, and 23 days after ligature:—

1. The coagulation, although nearly always present, apparently is not a necessary phenomenon. The presence of a ligature and the obliteration of the vessel are not in themselves sufficient to cause thrombosis, for, if the artery be tied immediately below a collateral branch sufficiently large, the clot may be almost or even entirely absent. The size of the coagulum depends on the distance existing between the ligature and the first collateral branch above. Coagulation may occasionally occur in the portion of the artery which is beyond the ligature (in relation to the heart).

2. The clot which is observed in an artery a few days after ligature is not simple; it is composed of a variable number of smaller clots, more or less recent. The oldest are those nearest to the ligature and

most central; the most recent are, on the contrary, those which are most proximal. In addition, as after coagulation has taken place the clots contract, new coagula become deposited in the spaces formed between the original coagula and the walls of the artery. As these clots contract they carry away with them some of the cells of the intima which are attached to their surface. They may even by their contraction cause a separation between the superficial and deep layers of the intima, causing thus the formation of more or less oblique fissures into which the blood, coming from the still patent portions of the vessel, may rush.

3. The cells of the tunica intima are the chief factors in the so-called organisation of the thrombus, and this accords with the views supported by Cornil and Ranvier, but the most active parts are not, as they say, in the immediate neighbourhood of the ligature. The proliferation of the cells of the intima is most marked at the level of the proximal convex surface of the clot, that is, at a distance from the ligature equal to the length of the thrombus. It is at that level that the new connective tissue, formed at the expense of the intima, penetrates most deeply into the substance of the clot.

4. The leucocytes, or small round cells which are found in the clot, either because they were in the blood before coagulation or have penetrated from outside the vessel into the coagulum by diapedesis through the arterial walls, do not seem to play an active part in the organisation of the coagulum. They have a tendency to accumulate near the surface of the clot.

5. The so-called vascularization of the thrombus corresponds to three processes which follow each other, but are based on different properties.

The first of these processes does not give rise to a true vascularisation, whilst the second produces only a preliminary arrangement during which there is no true circulation.

(a.) The first, or false vascularisation, is simply due to contraction of the clot; it is a kind of mechanical vacuolation. It is the only kind of canalisation that exists during the first decade, and probably it can still produce some effects after that time.

(b.) The second or potential vascularisation, is due to the arrangement of cells of the tunica intima which form the connective tissue invading the clot. This arrangement of cells gives under the microscope the appearance of a vascular network, but there is as yet no true circulation. This state may exist up to the twentieth day, or even later.

(c.) The third or true and effective vascularisation, begins when the embryonic vessels, which have just been mentioned, become hollow, and circulation becomes at last possible through the plug of young connective tissue which has taken the place of the clot.

The embryonic vessels at this stage pass through the tunica media (which has degenerated through disuse) and anastomose with the vessels of the adventitia, of which many are of new formation, in the neighbourhood of the ligature. Blood can therefore now pass from the patent part of the artery into the surrounding tissues through these small channels. Judging by our specimens this does not take place before the twenty-third day, but it is possible that in other cases this may take place either sooner or later.

6. *Conclusions.*—The essential factor in the organisation (or rather the replacement) of the clot is therefore the tunica intima. The clot itself is nothing more than a complication which probably is useful, but which finally entirely disappears, being replaced by the connective tissue resulting from the proliferation of the cellular elements of the tunica intima.

The internal coat is always altered whether there be thrombosis or not, but when there is a coagulum the proliferation is most marked in the region of the proximal surface of that coagulum. The presence of the clot seems to give a greater intensity to these phenomena, as can be seen by comparing the walls of the vessel on the proximal and distal side of the artery and in the cases where thrombosis is apparently absent and those where it is evidently present.

The channels which are found in the clot during the first two weeks are not true vessels, but simply fissures—vacuoles—due to contraction of the coagulum. There does not seem to exist any true circulation in the tissue taking the place of the clot before the end of the third week, at least as far as one can judge from the small number of cases examined.

These views are all based on direct observation, and partly support the views of several observers, such as Stilling, Cornil and Ranvier, Schultz, Riedel, Durante, Hamilton, Ziegler, Ballance and Edmunds, etc., but a critical examination will easily prove that, taken as a whole, these observations present some novel features. On the other hand, they are antagonistic to the views advanced by a great number of writers. Their publication is therefore justified in the mind of the author.