A Lecture

ON

PERICARDITIS IN CHILDHOOD.

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In this lecture I intend to pay particular attention to the non-rheumatic forms of pericarditis, although rheumatic pericarditis must also be taken into consideration because it is the pivot of so much of our knowledge of pericardial affections in the young; it is the most frequent in its occurrence, and for this reason the most thoroughly investigated. No attempt will be made to give an exhaustive account of the subject of pericarditis, but I will try to give some personal experiences of the difficulties and dangers in which one may become involved.

There can be no doubt that all forms of pericarditis are serious, though we may occasionally meet with a rheumatic case which runs a very favourable course, producing no degree of distress and leaving no appreciable damage. Such cases are rare, for it is unusual for rheumatism to cause pericarditis as a solitary fleeting lesion of the heart.

Suppurative pericarditis is a very fatal disease, and tuberculous pericarditis with its formidable complications has a gloomy outlook. When suppurative pericarditis occurs in association with osteomyelitis it is usually staphylococcal in origin, and it has been my unfortunate experience to find it then but one factor in a general septicaemia for which any local treatment has been futile.

The outlook is more favourable in cases of pneumococcal origin, and we win an occasional triumph with the assistance of skilled surgery and excellent nursing. We may be inclined to wonder why the danger is so great in pneumococcal pericarditis, for empyemata, though serious enough, are repeatedly treated with great success, and we do not as a rule see in pneumococcal pericarditis that great cardiac dilatation we meet with in the severe rheumatic form, and the cardiac valves are usually unaffected. There are, however, some good reasons for this. One is the very early age at which pneumococcal pericarditis most frequently occurs. In an analysis of 100 fatal cases of suppurative pericarditis of all varieties I found that 84 per cent. of the patients were under 4 years of age. Another is the rarity of this form of pericarditis as a solitary event. I found only one such case in this series, and have seen one other; 54 were associated with empyemata and 31 with pleurisy or pneumonia. When treating pneumococcal pericarditis, then, we are almost invariably dealing with it as a complication of already serious disease.

There is still another reason due to the difficulties in the diagnosis which leads to delay or actual oversight of the condition. One great cause of difficulty is the frequent absence of pericardial friction. Thus it was only recorded in two cases in the series I analysed, and though it is more likely to be detected in adults and in the older children, it is in my experience usually, even in the latter, soft and evanescent. It is difficult to realize how much we depend upon pericardial friction in the diagnosis of pericarditis—almost as difficult as to realize how much we rely upon coal until we have none. Then, again, there is always difficulty in making a diagnosis of a new event in an illness where already the first event has been a grave one. An empyema takes up much of our attention, and when progress is arrested we naturally and reasonably expect to find the explanation connected with the original trouble, and look for imperfect drainage or loculation of the abscess, or suspect some tuberculous infection to be complicating the suppurative process.

Again, in a very young child the symptoms of suppurative pericarditis are not distinctive. Sudden sharp rises of temperature, sudden attacks of dyspnoea and cyanosis, and sudden death have been recorded, but many cases have never been even suspected during life. Lastly, these cases are comparatively infrequent, and we have time to forget the lesson we have learnt from a previous failure, by the time the next case presents itself.

Diagnosis.

The diagnosis of suppurative pericarditis is naturally much easier when there is pericardial friction, but it is very possible to miss this evanescent sign or not to appreciate its value. The development of a definite effusion is our great assistance in diagnosis when there has been no friction. In medical textbooks you find the signs of pericardial effusion clearly stated, and here I shall only touch upon certain points which have attracted my attention.

The diagnostic signs to which I attach most importance are the gradual disappearance of the heart sounds step by step with an increase in the area of precordial dullness. Unfortunately we may not see the patient in the early stage or the notes of that stage may be deficient or inaccurate, and if this is the case there may be doubt whether the faintness of the sounds is not the result of severe cardiac dilatation or great thickening of the pericardium. The outline of the precordial dullness requires careful mapping out, and we may be struck by its wooden character if the effusion is considerable. A noticeable feature in pericardial effusion is the upward extension of the dull area, sometimes on both sides, but particularly on the left. This upward extension compresses the upper lobe of the left lung, with the result that you may find impairment of the percussion note over the left clavicle, below this tubular breathing from the pulmonary collapse, and below this again the wooden dullness of the pericardial effusion. Nevertheless, these signs may be puzzling, for we have to remember to take into account the possibility of pneumonia in the left upper lobe, or, again, we may know that there is an empyema on the left side, and this may have already been opened. When this is the case, as you know, the physical signs in the chest, quite apart from any pericardial effusion, are apt to be difficult.

The dull area due to pericardial effusion may extend far beyond the apex beat into the left axilla, and then you find yourself wondering whether this dullness is entirely due to the fluid in the pericardium, or whether there is in addition a left pleural effusion. During the war I had a young soldier under my care with a tuberculous effusion in the left pleura, which I tapped. This was followed by a large pericardial effusion, which in turn was drained, and then for some months, at intervals, I drew off fluid from his chest by paracentesis in the left posterior axillary line. I thought I was emptying a recurrent pleural effusion, but when he eventually succumbed I found his left pleura was firmly adherent, and that I had been in reality tapping the pericardium. I mention this case to remind you how extensive a pericardial effusion may become when it persistently recurs.

On the right side the precordial dullness may reach the nipple line, and, as you are aware, the direction of this right line extends from above downward and outward, forming with the horizontal upper limit of the hepatic dullness an obtuse angle opening outward. On the other hand, when the heart is dilated and there is no effusion, the outline of the dilated right auricle is generally curved, and forms with the hepatic line an acute angle. When there is extreme dilatation, particularly when in addition there is an adherent, thickened pericardium, this distinction unfortunately does not hold.

This precordial dullness reaching to the right of the sternum needs as much consideration as that on the left side. It may be the result not of a pericardial effusion, but of a pleural effusion on the left side displacing the heart, or it may be due to a collection of fluid between the right lung and pericardium, and a recent case will illustrate the kind of problem I am now considering.

A girl of 8 years was admitted with the signs of a large effusion in the left chest and a precordial dullness extending to the right nipple line. This was apparently explained by the collection in the left pleura, which proved to be an empyema. Two pints of pus were evacuated, but the child after a brief interval of improvement began to go downhill, and one morning I heard a suspicion of pericardial friction, and found the precordial dullness once more extending to the right nipple. Seeing how freely the empyema had drained, why was this? I was forced to conclude that it was the result of a pericardial effusion, and Mr. Addison explored the pericardium for me and discovered a haemorrhagic exudation. This was, however, unfortunately not the whole explanation, for there was also an overlooked empyema at the root of the right lung.

You will be expecting the mention of radiographic

investigation. It is of great value in these cases, but I have not had a good reason for hurrying to it. Every year the opportunities for radiography are growing, but it is quite possible you may not be within reach of a radiographer, for these cases are very acutely ill. Even if he is at hand I am sure that the use of the rays ought never to replace minute clinical examination, for you want in these difficult cases every atom of evidence you can collect. Without any intention of laying down the law, I would venture to say that the use of this method tends to make us neglectful of minute clinical examination, a danger also illustrated in the diagnosis of thoracic aneurysm. I would remind you that the difficulties in the interpretation of x-ray shadows may be as great as those of the clinician, and carry with them this additional danger, that they are apt to resolve themselves into a dogmatic "yes" or "no" when it is really impossible to make so definite a decision. You must not expect the radiographer to be intimately acquainted with all the intricacies that surround the diagnosis of a pericardial effusion, and he must, however skilled, always be giving you an opinion upon shadows. I doubt, indeed, if it is possible to distinguish by radiography between a pericardial effusion and a dilated heart with a greatly thickened and adherent pericardium; personally I cannot do so, though I realize that the indications for treatment are very different in those two conditions. If you can distinguish the darker shadow of the heart's outline surrounded by a somewhat lighter zone bounded by the pericardium you are a distinct step forward.

There are some very interesting physical signs at the back of the chest in some cases of pericardial effusion—signs which are also met with when there is great cardiac dilatation, and, particularly obvious when, as in acute rheumatic pericarditis, both factors are present. In children these signs are very striking. A patch of intense tubular breathing appears to the left of the spine about the level of the inferior angle of the scapula—below it the breath sounds, though diminished, may be natural and above it they are unaltered. Later the note becomes dull on percussion even to the base, and the area of tubular breathing expands downward, but over this area there may be no adventitious sounds. As the pericardial effusion subsides and the heart becomes less dilated the note improves, the breath sounds become first puerile and finally vesicular again, but the area of intense tubular breathing in the region of the angle of the scapula is the last to disappear.

Two mistakes may be made if you are not acquainted with this phenomenon, of which I have seen most striking examples: you may diagnose pneumonia or a pleural effusion. The condition is, however, one of pulmonary collapse, and is due to the cardiac lesion and not to a secondary pulmonary or pleural infection. Nevertheless, these are such involved cases that I advise you to weigh the evidence for each patient, as it is quite possible that there may be a concurrent pneumonia or pleurisy in any particular case. The area of intense tubular breathing at the level of the angle of the scapula is a very suggestive sign of the cardiac origin of the pulmonary signs when combined with a faint vesicular murmur below this level and the absence of any moist sounds.

Obliteration of the left intercostal spaces in the left precordial region and a wavy impulse over several spaces and absence of diaphragmatic movement may each have their value in the diagnosis. You will notice the rapid short respiration and abrupt cough and pay great attention to the pulse. A small, almost imperceptible, wave is a warning of an embarrassing effusion.

The diagnosis of pericardial effusion once made, the next step is to decide upon the cause. This is often obvious but sometimes difficult. In exceptional cases of pneumococcal origin with loud friction rheumatism may be diagnosed, but it is tuberculous pericarditis, on account of its rarity, that is most likely to deceive us. A blood-stained effusion in a child is not usually tuberculous or malignant in nature, for the most frequent cause is acute rheumatism.

Tuberculous pericardial affections are most interesting and perplexing. There may be friction and no effusion. There may be extensive and recurrent effusions without friction, and there may be recurrent forms with recurrent friction, ending in that rare but definite disease called multiple serositis. The course of multiple serositis in a child

is this: you first meet with the case as one of pleurisy and pericarditis, and may believe it to be rheumatic, although you are surprised by the absence of other rheumatic symptoms or of a previous history of rheumatism or of any valvular lesion, although this latter may be present in tuberculous heart disease. The case drags on month after month, and I have watched one for three and another for two years, the children coming under notice at one time for a fresh attack of pleurisy, at another for fresh pericarditis. Gradually you find the liver enlarging, the spleen becoming palpable, and ascites developing. The heart sounds are now muffled and the precordial dullness is wooden, and there may be clear signs of pericardial adhesion. The ascites may be tapped time after time, but invariably recurs, and the child gradually loses ground. Finally there are convulsions, or ocular palsies, with a rise of temperature and death in coma. The necropsy shows adherent pleurae, an adherent greatly thickened pericardium strangling the heart, an enormous nutmeg liver, ascites, and tuberculous meningitis.

Treatment.

The treatment of pericarditis with effusion is always difficult. The first question is, Ought we to use surgical measures? The second, What surgical measures should we use? The third, How should we apply them?

In the pneumococcal cases we feel sure we ought to liberate the pus. Ought we to drain the rheumatic cases, which are also infective, early in their development?

The answer seems to me to be involved in these considerations. The rheumatic infection is apparently destroyed by the tissues more effectually than the pus-forming organisms. There seems to me also to be this difference in their toxins. The pus-forming infections destroy the cells and survive in the fluid; but the rheumatic organism, though it may often lie dormant in necrotic tissue, is less destructive, and is difficult to find in any numbers in a fluid containing phagocytic cells which, though damaged, are many of them not destroyed. The poisons are of a different nature, and not, in my opinion, merely attenuated suppurative infections.

Thus it is we find that in the rheumatic pericarditis the process generally subsides, leaving, however, behind it traces of its destructive nature. The pneumococcal and other suppurative infections may also quiet down in very exceptional cases of slight severity, but far more frequently they tend to remain active, sometimes acutely so and sometimes with diminished intensity. We must remember, also, that the infection commences within the pericardial tissues, and that drainage of the sac can only remove the bacteria and toxins present in its cavity.

I have seen several rheumatic cases opened in the early stage of pericarditis and a certain amount of fluid removed, but the course of the case has not, as a result, been perceptibly altered for the better, and there is a distinct risk involved in such an operation. Our need in rheumatic heart disease is clear enough: we want a serum which would give that assistance to Nature which would enable the tissues to overcome the infection more rapidly and more completely than at present—a service that salicylate of soda, in my opinion, has failed to give us.

Moreover, we can never afford to lose sight of the cardiac dilatation which occurs in rheumatic pericarditis. I never study such a case without attributing the great enlargement of the precordial dullness first to dilatation. When I am convinced that this explanation is not sufficient I still keep before me the element of dilatation, and when the history points to previous heart infection, recall the fact that a dilated heart with an added pericardial effusion and a dilated heart with a much thickened pericardium are almost indistinguishable.

Yet in spite of this caution, the result of repeated observation, I am guilty of being the inciter of an exploration in which the heart was pierced in three different places! When I tell you that I have seen dilated rheumatic hearts with small aneurysmal projections in the right ventricle due to the visceral pericardium being the only barrier between the blood in its cavity and the pericardial sac, you may well ask me what was the result of this adventure. As so often happens to the wicked in this world, the result was astonishingly successful, for this almost moribund child from that moment commenced to mend, and left the hospital in fair case. I have, however, no intention of

repeating that mistake, and this I can tell you with absolute confidence, that paracentesis of the pericardium in rheumatic pericarditis under 12 years of age is rarely called for. I would venture to impress this general rule upon you as the result of experience—move slowly to paracentesis in rheumatic pericarditis.

The next question, having decided that an effusion should be surgically treated, is, What method should we employ? We have two alternatives. We can explore with a trocar and cannula, or we can open the pericardium. For a decision on this question we need all our judgement, which will be based upon a complete review of the case. A rheumatic effusion is often sero-fibrinous and difficult to drain through a cannula. A purulent effusion requires ample drainage, but a serous tuberculous effusion flows easily through a cannula. Another point for consideration is that of anaesthesia. Upon this I can say from my experience that though these children are desperately ill, I have been much encouraged by the ease with which a skilled anaesthetist has managed them. There must be a risk, but I have never yet seen any mishap even in the worst cases.

As a general rule, I prefer to use drainage of the pericardium rather than to trust to paracentesis, and aim at making the diagnosis sufficiently sure to justify immediate recourse to opening the pericardium. Individual cases in which there is good reason to believe the fluid is serous, or in which immediate relief by the simplest method is urgent, will be excepted from such a general rule.

Lastly, there is the method of exploration of the pericardium. There are various routes, and all things being equal, that by which the most effective drainage can be obtained is the best. The one I prefer, and the one my colleague Mr. Addison has chosen, is the abdominal route—in French literature often termed Marfan's route. In paracentesis the procedure is to define the tip of the ensiform cartilage, and introduce the needle immediately below the tip for some three-quarters of an inch, then to direct it upward, grazing the under surface, and lastly slightly backward, entering the pericardium through the base. When opening the pericardium the ensiform is removed and the pericardium incised from below. This route is not indicated when there is deformity of the thorax or considerable abdominal distension, but I have not met as yet with these contingencies. In such a case the incision to the left of the sternum, avoiding the internal mammary artery and resecting costal cartilages, is the alternative.

I can give precise information as to the result of drainage by the abdominal route, for in a recent case, after the left pleura and pericardium had been drained, death resulted from an overlooked right empyema that lay deep near the root of the lung. The necropsy showed that the pericardium was perfectly drained and rapidly becoming adherent.

There may be some after-difficulty with the drainage, but in my own cases this has generally been easily overcome. The great dangers are the high degree of toxæmia due to the disease, with the consequent tax on the child's vitality, and the liability in these cases for other suppurative lesions to be present or to develop later; for example, the overlooked right empyema in the case I have just mentioned, or a suppurative meningitis, which may be very deceitful in its latency, but which is invariably fatal in such a condition; or, again, a suppurative peritonitis.

The use of an autogenous vaccine is clearly indicated where progress is slow but drainage satisfactory.

Reverting now to rheumatic pericarditis, I would direct attention to a peculiarly malignant type which I have seen on more than one occasion in young children since the war. These are cases with a very gradual onset and with little or no fever, in which the heart has stealthily developed extreme disease. Endocarditis appears first, with dilatation, and then, sometimes after weeks, pericarditis, which may be hæmorrhagic, is detected. Usually small subcutaneous nodules appear, and throughout the child has no pain, but lies quiet and taciturn, reacting to no remedies. I cannot help feeling that it is some result of the poor food during war-time which has weakened the tissue resistance, and, rightly or wrongly, I associate this feebleness with the prevalence of grave anaemias in childhood, of which I have seen of late frequent and most distressing examples.

I also wish to direct attention in rheumatic pericarditis to signs of pleuro-pericarditis and to very superficial crepitations immediately under the sternum and in its neighbourhood, the result of a concurrent mediastinitis. These are indications which will lead you to expect the formation of extensive external pericardial adhesions, which, as you know, are the great factors in the development of serious trouble from an adherent pericardium. The heart, dilated and weakened by the rheumatic poisons, is tethered to the surrounding structures by these adhesions. Compensation, then, is never effectual, and a prolonged history of gradual failure will be the outcome.

If a child previous to an attack of pericarditis has already an aortic lesion you may find that signs of angina develop, and the outlook then is very grave. In a few exceptional cases thrombosis of the large veins in the neck may occur, and you must suspect this complication when when one or other arm suddenly becomes oedematous. I have seen the superior vena cava with all its great branches obliterated by such a thrombosis and death occur from pulmonary infarction.

I have already mentioned several times great thickening of the pericardium, and I would compare the process to that which occurs in mitral stenosis. You suspect it when the pericarditis is subacute, but continually recurring at intervals which may extend over many weeks. Nodules may form in the pericardial tissues, and the heart becomes greatly dilated. You can readily understand that paracentesis or exploration must be a failure and a danger, and unless you have actually seen such a case explored you can hardly realize the difficulty the surgeon will have in locating his path. It is quite easy to burrow into the mediastinal tissues by the thoracic route and never to enter the parietal pericardium at all, and even if you do with a trocar you will very easily find yourself in the cavity of the right ventricle. It was for an adherent pericardium due to multiple serositis that Mr. Trotter did for me the first published case of Brauer's operation in this country, although Mr. Thorburn had previously undertaken a like operation. This operation consists in stripping an area of the chest wall off the adherent pericardium, and is an alarming undertaking. The indications that the cardiac failure is due to the adhesions must be very clear to justify it; in my case three years of comfortable life resulted. Previous to the operation the boy could not walk down the ward and rapidly developed oedema in the erect position.

In this case, when the ribs were freed from the apical region, it was remarkable to see the heart jump back as if it had been held by a spring. There was no valvular disease, and the tough adhesions were chiefly located to this apical region. It was, as you can understand, a very favourable and very unusual case, and the patient would have done very well indeed had it not been tuberculous in origin, and that later tuberculous pleurisy developed and recurred. This embarrassed his respiratory system, and eventually caused heart failure. For two years this boy, who had been unable to walk down the ward, was able to act as cricket scorer to his club. I have never had a rheumatic case in which I could find the courage to advise this operation, though others have had successful ones. The presence of valvular disease, and the possible disaster that might occur if the diagnosis was incorrect, are formidable deterrents.

In one case of rheumatic serositis I have seen the Talma-Morrison operation done for the recurrent ascites, but it was a failure.

The medical treatment of rheumatic pericarditis has not altered in recent years; there are still some who believe that sodium salicylate is a specific, and others who do not. Which side be right, I cannot say that I am much impressed by the efficacy of our treatment. We are waiting for further researches to discover some specific serum or other biochemical therapy. You must all have been struck from time to time with the remarkable recoveries that result occasionally from serum and vaccine therapy in acute streptococcal infections; we wait in hope for such a result with the rheumatic. In the meantime, Sir William Gull's warning remains as true to day as when he gave it: not to persecute the child with over-treatment.

The indications and the remedies in vogue are plainly stated in handbooks on diseases of childhood, and I need not detain you with a recapitulation of them. It is essential to remember that it is not sufficient for the

symptoms to subside, we have to wait also for the recovery of the damaged cardiac muscle and adaptation of the heart to the valvular lesions which are almost invariable in the rheumatic form of pericarditis. Six months spent in nursing the heart back to efficiency is a very small part of a lifetime, and you cannot go far wrong if you make each forward step a test, guided by the pulse, the apex beat, the cardiac outline, the temperature, and, above all, the general condition of the child.

In conclusion, though I realize you already know much that I have commented upon, this lecture may help to recall to you that in the treatment of pericarditis in childhood we must be prepared to display all our clinical knowledge and that balance of judgement which it is so difficult to keep when pressed by urgent illness, complicated conditions, anxious parents, and possibly divergent opinions

A Study

OF

SOME FACTORS CONTROLLING THE NORMAL SUGAR CONTENT OF THE BLOOD.

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ACCURATE knowledge of the mechanism by which the sugar content of the blood is normally maintained and controlled is obviously an indispensable preliminary for a correct interpretation of the means by which hyperglycaemia and glycosuria may be produced. When, therefore, we found it impossible to explain satisfactorily on current theories many of the phenomena we observed in the course of an experimental investigation of diabetes mellitus to which we had been led by previous work upon the changes in carbohydrate content of the blood associated with pancreatic disease, it became necessary to study the subject afresh. The experimental part of the work was commenced in 1919, and reference has been made to some of the results in a previous paper,¹ but we now propose to discuss the subject in greater detail.

Before doing so it will be advisable to deal briefly with the methods of analysis adopted, for the discrepancies between the figures quoted by different observers are no doubt to be explained to some extent by the various processes for estimating the carbohydrate content of the blood employed. Many of the older findings were obtained with methods which do not completely remove all traces of protein, and are therefore of little value, but even in some of the more modern processes, such as Benedict's picric acid method, where this is successfully accomplished reducing substances other than sugar are included in the determination. After much preliminary experiment to discover a method of analysis which would give a reliable estimate of the reducing sugar, and that alone, we adopted in the first place a modification of the process described by one of us in 1917.²

In this the proteins are removed by filtration after they have been precipitated by heating with sodium chloride and dilute acetic acid. The reducing power of an aliquot part of the filtrate is then determined by boiling with a solution containing copper sulphate, sodium carbonate, and potassium citrate, converting the cuprous oxide formed into cuprous chloride by adding hydrochloric acid and then estimating the cuprous chloride with standard iodine and sodium thiosulphate solutions, using starch as the indicator.

Later, we more frequently employed a modification of the process described by Folin and Wu,³ as a considerable saving of time is effected when a large number of estimations have to be made, as was often necessary.

In the Folin and Wu method the proteins are precipitated with a solution of sodium tungstate and dilute sulphuric acid; an aliquot part of the filtrate is heated with an alkaline copper solution and the reduced copper dissolved in an acid mixture containing sodium molybdate and sodium tungstate. This solution is then made alkaline with sodium carbonate, diluted to a fixed volume, and the depth of the resulting blue colour compared in a colorimeter with that given by a standard solution of pure dextrose treated in the same way.

Although these methods differ in principle, numerous control experiments with sugars, and many simultaneous estimations of the sugar content of normal and pathological bloods, have shown that they give results which correspond within the limits of experimental error, the variation being not more than 0.002 per cent. either way in experienced hands. It is therefore probable that they give as accurate a determination as is possible of the proportion of reducing carbohydrate. Since our investigations of the blood were carried out at hourly, or in some instances at half-hourly, intervals for several hours, and sometimes throughout the whole day, it was necessary that we should work with as small an amount of material as possible and obtain it with a minimum of discomfort, to avoid the effects of nervous disturbance and fatigue; we therefore employed as a rule 0.3 c.cm., taken from the root of the nail in the human subject and from the marginal vein of the ear in animals. This amount was drawn into an accurately calibrated narrow pipette, direct from the puncture made by a sharp needle, without the use of oxalates or other anti-coagulating substances.

It is now recognized that the percentage of sugar present in the blood is not a fixed quantity, even in health, but varies within limits which are, however, confined to a comparatively narrow range. As the most important factor influencing the proportion of sugar in the blood at any particular time is the ingestion of food, it follows that, to obtain comparable results, the blood must be taken after a fast of sufficient duration to eliminate the direct action of food, or that the effects of test diets of known composition should be studied.

To consider first the figures obtained after fasting. We have found that in fifty human beings from whom samples of blood were taken in the morning, twelve to sixteen hours after the last meal, the sugar content of the blood averaged 0.085 per cent., with extremes of 0.070 per cent. and 0.102 per cent., but that nearly half (41 per cent.) gave a fasting level of 0.080 per cent. or 0.082 per cent. This agrees with the results obtained by Rona and Döblin,⁴ who found an average of 0.080 per cent. in ten individuals, with extremes of 0.048 per cent. and 0.128 per cent. by the polariscopic method. In the carnivorous dog our average fasting level for eight animals was 0.083 per cent., with extremes of 0.074 per cent. and 0.090 per cent., which corresponds closely to Oppler and Rona's polariscopic average of 0.085 per cent. for four animals, their extremes being 0.073 per cent. and 0.102 per cent. The average fasting value for twenty-five rabbits, which we took as examples of herbivorous animals, worked out at 0.083 per cent., the extremes being 0.080 per cent. and 0.096 per cent. These figures are lower than were obtained by Oppler and Rona and most other observers, but agree with the more recent values quoted by Jones, working with MacLean's micro-method,⁵ who found an average of 0.085 per cent. in sixteen rabbits, the highest being 0.116 per cent. and the lowest 0.068 per cent. The great difference in the blood sugar values found in rabbits by many experimenters is probably due to the fact that they are peculiarly liable to emotional disturbances which raise the percentage of sugar in the blood. The fasting value for cats is usually stated to be very high. Lyttgens and Sandgren⁶ give 0.291 per cent., and Oppler and Rona an average of 0.280 per cent. for four estimations, with extremes of 0.154 per cent. and 0.354 per cent., but a sample of blood we obtained from a small accidental cut on the paw of a fasting cat showed a blood sugar content of 0.094 per cent., a figure which corresponds more nearly to the average values for other mammals, and agrees fairly closely with the value of 0.088 per cent. quoted by Pavy⁷ as given by the heart blood of a cat killed by pithing. The higher figures for cats, like those quoted for rabbits, are probably to be attributed to emotional excitement.

Although we have found that the same person, or animal, does not invariably give exactly the same fasting value, the length of the fast does not appear to exert any material influence on the proportion of sugar in the peripheral blood, judging from our experience with rabbits which we have examined after twelve to seventy-two hours' abstinence from food. Allen⁸ has come to the same conclusion, and states that "approximately the normal percentage is stubbornly maintained through prolonged starvation, almost up to death." It would therefore seem that, when the digestive apparatus is functionally inactive, the sugar content of the blood is kept at an almost constant level for the same individual, and only varies within very narrow limits for different mammals, irrespective of their usual diet.

Turning now to the effects of food on the sugar content of the blood, we find that the rise in the percentage of sugar associated with functional activity of the digestive apparatus follows a curve which ranges within well-defined limits that appear to be practically identical for all