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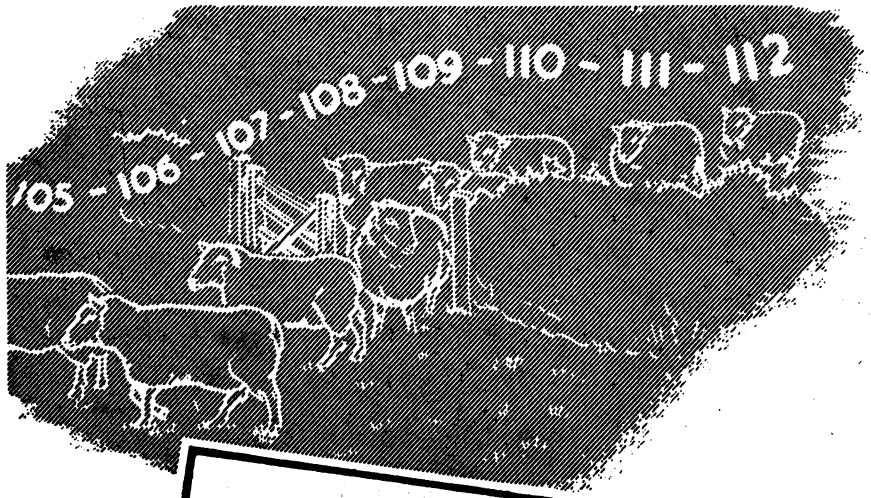

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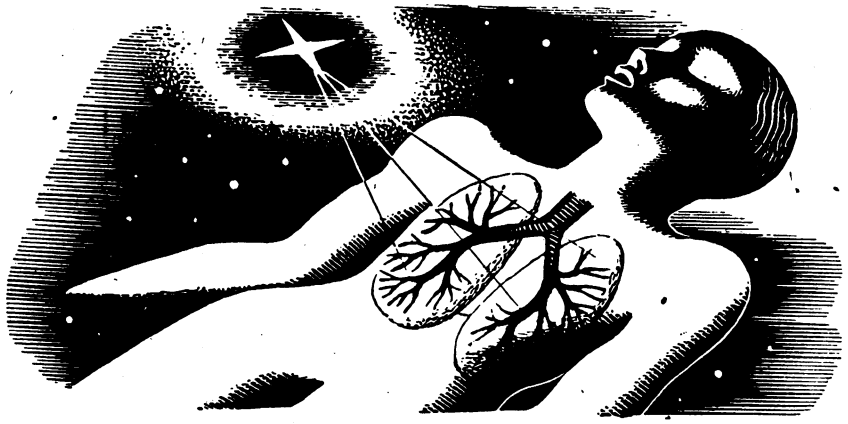

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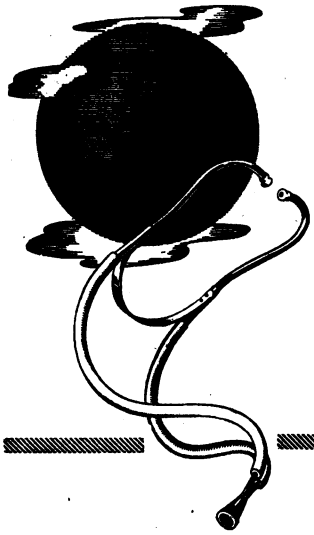

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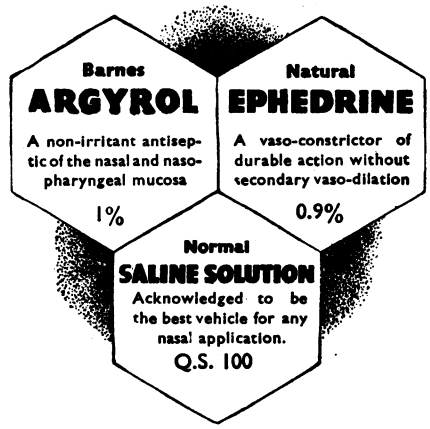

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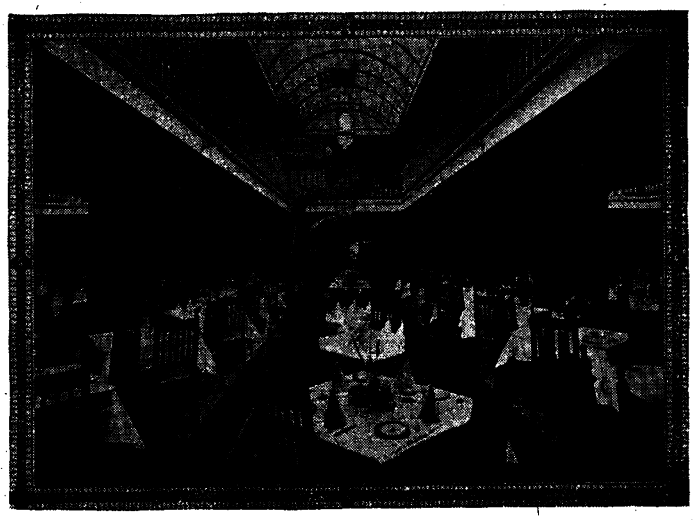

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Yours faithfully,

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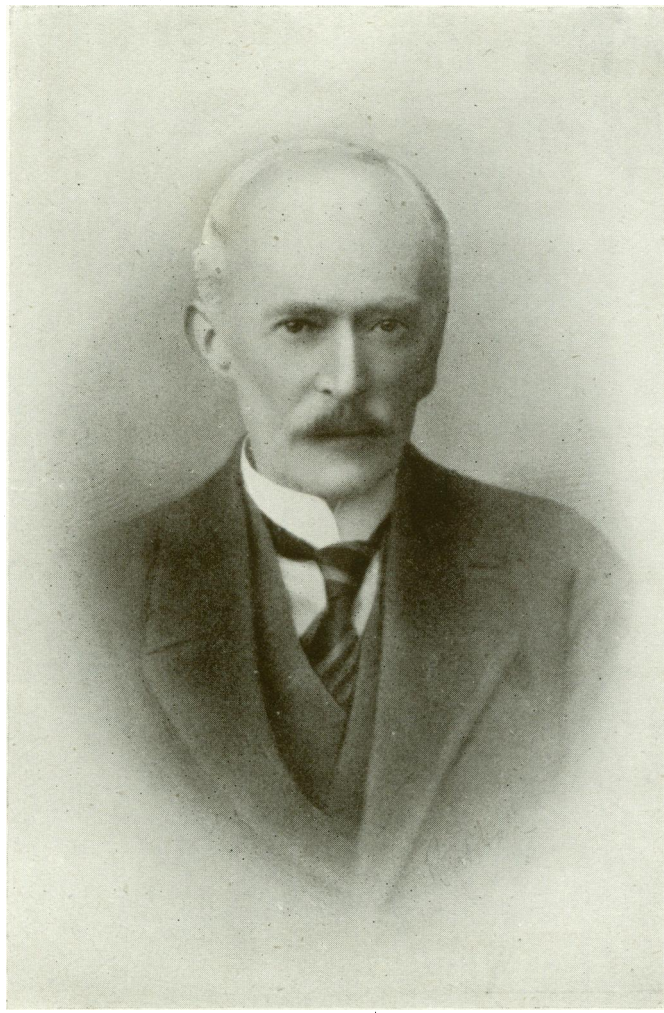

ROBERT HALL
1861—1941

Senior Physician, Belfast Infirmary, 1891-1941
President of the Ulster Medical Society, 1921-2

THE
ULSTER MEDICAL JOURNAL

:: PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY ::

Vol. XIII 1st NOVEMBER, 1944 No. 2

Soil and Nutrition

By W. A. ANDERSON, D.L., M.A., M.D.

Presidential Address, Ulster Medical Society, 19th October, 1944

THE subject I have chosen for my address is one of such magnitude that I cannot hope to do more this evening than scratch the surface of it.

It is, however, of supreme importance to all, and to none more so than to the medical profession, for not only does each member of the profession owe to it his own life, but also he must know something of the nature of its products, so that he may be able to advise his patients in the matter of diet.

Twice within the last quarter of a century we have been, in these islands, on the verge of starvation, and only by the superhuman efforts of the farmer has this been averted. This is a state of affairs that can be prevented, and therefore should never be allowed to recur.

The very fact that we have been so hard put to it has stimulated many to seek again, in the cultivation of the soil, some of the joys that enriched the life of these islands, and laid the foundation of our present greatness.

When we speak of soil, I think that we ought to keep clearly in our minds two things—first, the soil as such, and secondly, the many additional constituents that go to make up what I might describe as real soil.

Some years ago I paid a visit to the North Cape and, despite the beautiful picture of the midnight sun, the utter desolation of that scene still lingers with me.

As I wander across some of our fertile fields here at home, it is hard to believe that, if one could go back far enough in time, one might see here just a similar picture of desolation as exists to-day on the North Cape.

This wonderful change has been brought about by the weathering of the rocks with the formation of soil, and its deposition here and there by the movement of ice, water, and wind.

But just as the rocks from which it springs are composed of different substances, so also the soil varies between sand at one extreme to clay at the other.

These two substances, sand and clay, are, as we all know, very dissimilar in

their properties, but I should like to comment very briefly on some of these points.

First of all there seems to be something permanent about sand; the winds and the tides beat upon it, but, apart from moving it from one place to another, no other change takes place.

If a particle of sand could be kept under observation from one age to another, no change would appear to have taken place in its shape, and it is this power of the particle to maintain its consistency that makes the mass porous, and this allows of rapid drying.

Growth in sand is practically impossible, but how different it is with clay. This is a substance made up of minute particles, which can be packed so closely together that the air space between them is limited exceedingly. It is described as a "colloid" and therefore is "like glue." So strong is this quality that only a very little is required to be used to give this characteristic to other soils. It is interesting to point out that the sum of the pores is as great, and indeed may be greater, than an equal bulk of sand. The pores are, however, so fine that movement of water is difficult, and one may have the unusual experience of seeing a plant withering because it cannot extract the water from the very small pores. When water-logged soil, deeply impregnated with clay, dries in the summer-time, it shrinks, and thus the cracks in the soil, familiar to us all, are produced. Clay therefore tends to dry in lumps, and this renders cultivation difficult and exacting, and demands knowledge and patience on the part of the farmer as to how best to deal with it.

I assume that at first this soil is incapable of supporting life, but later this quality is obtained by absorbing into it many forms of organic life. Thus we have our soil, but experience teaches us that something more than mere soil is essential to produce the maximum of food, and when we examine this something we find that it is sub-divided into certain factors, and that these, because they exert a limit on production, are known as limiting factors.

Six of these factors are recognised :—

1. Plant food.
2. Water.
3. Air.
4. Temperature.
5. Root room.
6. Freedon from harmful substances, e.g., pests.

None of these factors can replace another; all must be present; absence of any of them restricts growth.

Let us look at each of these in turn—and first, PLANT FOOD :—

In the "London Chronicle" dated Saturday, September the 2nd, 1786, there appeared the following :—

"A gentleman at Hendon who farms largely has just erected a mill, which is worked by the Brent brook, for grinding bones into a coarse powder for manuring land. According to experiments made in some parts of the county, the ground dressed with this kind of manure is rendered surprisingly prolific, and it is

supposed that the energising quality will not be exhausted in less than twenty years."

Historically it might be of interest to follow up this experiment, but our time is too limited.

Chemistry as early as 1755 had commenced on the "Principles of Agriculture," but was itself not sufficiently advanced to accomplish much. Changes in this branch of science were already under way, and with the new methods Theodore de Saussure of Geneva was able to prove that plants derive their carbon and oxygen from the air, and their nitrogen and mineral matter from the soil.

This work was confirmed by a Frenchman, J. B. Baussingault, who, working from the farmer's angle, measuring and weighing the manures applied and the crops obtained, was able to show how far other sources, e.g., air, rain, and soil, had been drawn upon.

The next step in the advance was made by the German Liebig, who suggested that farmers could increase their crops by adding more of the necessary mineral matter to the soil in the form of definite salts.

Looking back from our present standpoint it seems a simple observation, but at the time it was fraught with great possibilities, and showed wonderful forethought.

The next event was staged in England—John Bennett Lawes commenced to make a number of experiments to test the manurial value of various substances. The chemists had provided him already with the information that bones contained calcium and phosphorus in the combination known as phosphate. Further, they had discovered three other phosphates of calcium—one of which was soluble in water, i.e., superphosphate of lime, and the other two insoluble. The soluble one could be prepared from the insoluble by the addition of sulphuric or hydrochloric acid. Geologists were keeping well in step, for they had discovered large deposits of mineral calcium phosphate, and Lawes recognised the importance of this mineral, and showed that by treating it with sulphuric acid the same soluble phosphate as bones could be produced.

In addition, Lawes also demonstrated by experiment that sulphate of ammonia increased plant growth. He went even further and showed that it was the nitrogen element in the ammonia that was the active agent. He carried out field experiments with these two artificial fertilisers, and showed that the yield of wheat could be increased from twenty to thirty bushels per acre.

These advances made in 1842 were received, as one can well understand, with a good deal of scepticism and foreboding by the men of the time, and yet by 1855, and presumably by the use of fertilisers, the farming industry had entered on a period of prosperity hitherto unknown.

Liebig had emphasized in 1840 the importance of potassium salts as plant nutrients, and Lawes and his co-worker Gilbert had added potassium sulphate to their "mineral manure" without carrying out any experiment to prove or disprove its worth.

About the year 1861 the Stassfurt mines were opened, and some three years

later these were visited by one Agustus Voelcker, and he ordered a quantity of the crude potash salt and carried out experiments in England, but these were inconclusive. Later, with the improved cultivation of the potato, the advantages of this salt became apparent.

Of the next four limiting factors—water, air, temperature, and root-room—all might be described under the word cultivation.

In the lapse of time since Adam was expelled from the Garden of Eden, and was told—"In the sweat of thy face shalt thou eat bread," one might be justified in concluding that a definite plan could have been formulated, and that cultivation could have become an exact science, but this is not so, and the very first act of all cultivation is still a matter of controversy.

H. L. Gee makes one of his characters say :—Plough shallow, and you'll get a worthless crop. Plough deep, and you'll get a good harvest, most years."

I have watched ploughmen of the old school lay the furrow well over, for, as they say, it makes a good seed bed. But perhaps, in the very next field, another ploughman will be setting the furrows on their sides so as to give plenty of depth for good root formation.

The point is debatable, but for myself I agree with Gee's ploughman, and I do so for the following reason amongst others :—As the sole of the plough passes over the ground it tends to consolidate it and, when this is done repeatedly and to the same depth, a "sole or pan" is formed through which penetration, for either roots or water, is difficult, and the crop suffers. Therefore, by going as deep as possible there is ample room above the pan for root-room and water.

But ploughing is the first step in what should be a very extensive process. To obtain a good tilth is the object and aim of all good farmers, and all labour spent on this work is well spent and returns a good dividend.

Temperature plays an important part. A severe frost on the newly ploughed land is worth many discings, and will often turn a sticky clay into a friable crumb; and here let me turn aside for a moment, and remark that frost is of benefit also because it locks up the moisture, and so limits the loss of nitrogen in the form of nitrates. This is the origin of the old proverbs :—

"Under water, famine; under snow, bread."

and

"A snow year is a rich year."

But a knowledge of what the weather is going to do for the next twenty-four hours is of great importance, and will often save days of labour if interpreted correctly. Hence the importance of more correct weather forecasts in the future.

"Speak to the earth and it shall teach thee," said Job, and I have no doubt of the truth of this remark. Haphazard sowing of crops on ground ill prepared is worse than useless, and produces its own penalty.

Having discussed cultivation, I think it would not be out of place if I made a few remarks, at this point, on seed and sowing.

It may not be understood generally that for the small cost of a few pence the

Ministry of Agriculture will supply you with a report on a specimen of the seed it is proposed to sow.

This report deals first with germination and, as a rule, the quality of seed, but it also deals with purity, and gives an idea of the number of weed seeds per bushel. I do not think that it is a good policy to dogmatize from a few facts, but it is my experience that seed is being used at present without being adequately cleaned. In other words, there are far too many weed seeds present, and of course these, when sown, naturally reproduce themselves, with the result that the land becomes more and more polluted by their presence. But there is another point of importance; the seed itself may be diseased and the resulting crop also infected. Much has been done to overcome this by the use of certain dressings. These dressings are composed, for the most part, of a mercurial preparation, and can be used as a dusting powder and applied to the seed immediately before sowing. I do not know if the addition of even a small quantity of mercury to the soil is likely, in the long run, to have a detrimental effect, nor do I know whether the diseased condition of the crop is likely to have any injurious effect on the human consumer, but these are points which for the present I should like to leave to those with more adequate knowledge.

Now, as regards sowing, the picture of the sower going forth to sow and treading lustily across the plough is almost a thing of the past. It may be seen occasionally however, but if so it is usually the farmer-owner, and he is almost certain to be an old man, for few of the present-day farm labourers are sufficiently skilled in this art.

There is, however, in the mechanical seeder a first-class substitute. This has two great attributes: first, the rate of sowing can be controlled to a nicety, and secondly, the seed is sown to an even depth, and is covered immediately. It is easy to obtain the rate of sowing by referring to a book, but on referring to the practical farmer a very considerable difference may be disclosed. On inquiring, it will be pointed out that by sowing rather more than is thought necessary, and thus by crowding the breird, a finer straw is produced, which is more palatable and nutritious to cattle.

I regard this as a very debatable point, and from my own experience I believe that by sowing as lightly as justifiable, a straw is produced quite as good from a feeding point of view, although it may be a little coarser; but what is of far greater importance—the yield of grain is better.

We now come to the last of our limiting factors, viz., pests. What a wealth of expression there is in that work. How exceedingly annoying to see the result of your labours turned to naught by some insignificant looking animal, but even worse still by something invisible to the human eye, and for whose presence we have to accept the word of the bacteriologist.

To enter into a diatribe against any or all of these evils would serve no useful purpose, but it is important to note that there is a school of thought advancing the teaching that if crops are nourished properly in what they describe as nature's way then all insecticides and sprays become unnecessary.

Having dealt briefly with these preliminary steps, I propose to discuss some of them in more detail.

It might be supposed that with nitrogen playing such an important part in the production of the plant protein, the addition of nitrogen to the soil in the form, say, of sulphate of ammonia would increase this very important food, but in practice this is not found to be so. When nitrogen is added to the soil, the response is different according to the amount added. First, with small amounts little, if any, change takes place. Second, with larger amounts, changes in the leaf become apparent; the size increases, and the colour becomes a darker green. The increase, however, in the size of the leaf is not accompanied by increased efficiency, and this is capable of proof.

Finally, with still larger amounts a baneful effect may be produced; this is caused by an alteration in the amounts of the protein and carbohydrates present, with the result that a plant is produced which is more susceptible to diseased conditions due to fungi and other pests.

I think it is this latter effect that has brought this artificial fertiliser into a certain amount of disrepute with some farmers. If you discuss this point with them, they will say that such plants as turnips and mangolds winter badly and decay more easily, and from what I have said it may be obvious that such is the case.

Many farmers will condemn whole-heartedly the application of sulphate of ammonia to potatoes for the same reason, and they claim that much of the flavour is lost, and the potato has the same well-known "soapy" appearance.

Tests have been carried out on this point by competent cooks, and marks assigned, and the result shows that nitrogenous manuring has reduced the quality. Against this, however, it can be shown that for every hundredweight of sulphate of ammonia used there are certain definite increases,

e.g., Wheat 2.5 cwt.
Barley 3 cwt.
Potatoes 20 cwt., etc

Reducing these figures to terms of food value, we find that

2½ cwt. of wheat per acre = 27 lb. protein and 212 lb. starch equivalent.
3 cwt. of barley per acre = 23 lb. protein and 258 lb. starch equivalent.
20 cwt. of potatoes per acre = 13 lb. protein and 403 lb. starch equivalent.

As so many other factors modify the action of nitrogen, these figures must only be regarded as approximate. The composition of the grain is also affected, but varies according to the different grain. In wheat, high protein content determines baking quality, but the physical qualities of the protein are equally important.

Much work has been done on the composition of barley as affected by varying amounts of artificial manure such as sulphate of ammonia, and so far as malting barley is concerned, it has been shown that a low nitrogen content is desirable.

These two facts alone demonstrate that considerable thought is necessary when it is proposed to use a nitrogenous fertiliser. But there are other points, and amongst these I would place weather conditions first. As I have pointed out

already, a severe winter is good, because it locks up the moisture and so prevents loss of nitrogen. Heavy rain throughout the autumn and winter months removes an appreciable amount of nitrogen and thus, theoretically at least, the farmer has to weigh up mentally the amount of nitrogen lost before adding more. As the amount varies with the nature of the soil, an additional difficulty arises.

If the amount of nitrogen lost by drainage were known, it might be supposed that to replace this an equal amount would only be required. But this is not so, as the amount of sulphate of ammonia necessary is greatly in excess of that which has been washed out.

One inch of rain above the normal during the winter months requires about 40 lb. of sulphate of ammonia per acre to replace what has been lost. If too much sulphate has been used, harmful effects may be produced, and of these I would mention :—

1. Acidity.
2. Lodging of corn.
3. Bad keeping qualities of roots.
4. Increased susceptibility to invasion by fungi, pests, etc.

Now a few words about phosphorus. I have dealt already with the history of phosphorus as a plant food, but there are many points of considerable importance, a few of which I should like to mention.

Dealing with it first in the simplest possible way—the addition of phosphorus in the form of phosphates to the soil :—

1. Improves root formation.
2. Promotes tillering.
3. Hastens maturity.

These are three very important practical points, any one of which in my estimation is sufficient to warrant the use of phosphates. But these points constitute only a beginning.

In Northern Ireland we have been credited with a marked phosphate deficiency in our soils. Therefore, if phosphates hasten maturity, the absence of phosphate would tend to cause delay. If we add to this the vagaries of our weather, which may be the cause of an early or late harvest, it will be obvious that anything tending to stabilise the time will be of benefit.

Phosphate starvation is not detected easily, in fact the first indication may be a complete failure of the crop. The cause is not quite clear, but there seem some grounds for stating that, where farmyard manure is given, starvation does not exist. Phosphate is different from nitrogen in that it does not leach out, and therefore no matter how wet the season it remains in the ground.

Plants respond differently—potatoes taking pride of place, then come swedes and turnips. One of the most marked effects is the production of wild white clover.

I have noticed that where sulphate of ammonia has been used on grass land to produce an early bite, there is almost a complete disappearance of clover, but if phosphate has been used, abundance of clover is produced.

It used to be thought that phosphates, like ammonia, by uniting with the lime tended to produce acid soil, but this is incorrect.

It might be asked, Does the addition of phosphate increase the phosphorus in the plant? But unfortunately the answer is not quite definite; the composition of hay, and therefore the feeding value, is known to be improved; but apparently, if the soil has been well cared for, the addition of phosphate has little, if any, effect in the composition of cereals or roots; but where there is known to be a deficiency, as in much of our grazing land, the additional phosphate increases the phosphorus in the grass to the distinct benefit of man and beast.

As much of our phosphate comes from North Africa, and that for Australia and New Zealand from Nauru, sources have been denied us by the War, and an opportunity may have been afforded to our scientists for a future study of the effect of the absence of this important plant food.

Just a word about potassium, the third of the plant nutrients. In a certain sense it is the direct counterpart of nitrogen, as it increases the efficiency of the leaf, but not its size. In addition, it performs some function called translocation, i.e., it favours the removal of carbohydrate from the leaf to its place of storage.

As time goes, potassium might be described as a modern fertiliser, for although it has been in use for at least one hundred years, it was not until about fifty years ago that it became so popular. This could be accounted for by the fact that a change has taken place in farming rotation, and that mangolds, swedes, and potatoes are in greater demand. A yield of five to six tons of potatoes about eighty years ago was considered quite good enough, and there was sufficient farmyard manure to produce this quantity; but with the decrease in available farmyard manure, and the increased demand for potatoes, potash came into its own. Its chief use is in association with nitrogen, e.g., used with a barley crop and in combination with nitrogen, it produces a barley low in nitrogen content so favoured by the distillers, but in addition it tends to reduce the susceptibility of wheat, flax, mangolds, etc., to infection by pests or fungi. It also tends to prolong vegetation, which in certain crops may be desirable, but generally speaking I regard this as an unfavourable point. It does not seem to have any appreciable action on the composition of, for example, potatoes, although tests have been carried out by competent chefs, and first place has been given to those that have had a dressing of potash.

The feeding value of hay is reduced, and if the potash is withheld over a number of years the quality of hay is also reduced, and there is a tendency to weed formation.

Lime.

I must say something now about lime. In the first place, from my point of view, I consider the term lime to be unfortunate; it suggests to me something in the soil, and in the soil only; something, that is to say, that has nothing to do with plant life, but rather is concerned with the p.H. of the soil, and certain other vague and ill-defined functions, which attain to different degrees of importance according to the views of the various authors writing on the subject. But calcium

—that is a different word altogether : it calls up to my mind a sticky, unworkable clay made nice and friable and easily worked; it suggests a nice clean soil, free from those acid-loving weeds, and it reveals a beautifully tapered root to all my cabbage plants, instead of that twisted, knarled, and distorted monstrosity known as club-root. It encourages activity by the worms, and thus prevents that mat-like formation that is so detrimental to our grass lands. Bacteria seem to thrive, and altogether there is a sense of certainty that all is well.

To speak of the available lime or of the lime in excess does not sound quite the same as available calcium or calcium in excess. You see, the word brings home to us the very close connection between what we are applying to the soil and something of extreme importance in our own composition.

I have written at some appreciable length on these four major elements, but there are others, and although for the present they might be described as minor, yet who can say but that one day some, or indeed each of them, might occupy a very prominent position amongst the plant foods.

Dr. Katherine Warington as recently as 1923 showed, and showed for the first time, the importance of a minute quantity of boron. Copper, cobalt, manganese, and zinc all play an important part; indeed it would seem that as yet we have touched only the fringe of the possibilities of these elements. So far as is known at present, copper and zinc exert their influences by their curative properties, but boron, manganese, and iron are essential to the proper growth of plants, and their absence reveals itself by certain diseases. Amongst these may be mentioned heart-rot in sugar-beet and swedes. This, which before Dr. Warington's work was regarded as incurable, now yields to a small quantity of borax. Potatoes also may suffer from this deficiency and so also may carrots.

Manganese deficiency seems to be known on the Continent and in United States of America, but so far it seems more of a name here than an actual disease, although marsh-spot in peas has been credited to it. Apparently it plays an important part in the oxidation processes of plants, and from this it seems probable that a similar process of oxidation may take place in animals.

May I pause here to remark upon the prevalence, at present, of staphylococcal infections, such as boils, styes, and furuncles, involving all classes of society, and all ages from a few months old up to "old age," and to state that in my practical experience deep injections of collosol manganese are almost a certain cure. When this fact of the curative value of manganese is considered alongside the fact that we are all at present, theoretically at least, partaking of the same diet, then it would seem that some of us are unable to make use of the manganese available, or, per contra, fail to obtain an adequate amount.

It is a remarkable thing how that so many great discoveries have been made simply by the ability of someone to observe accurately. I need not quote examples in proof of this statement, but it is not without interest to relate that "fruit and nut trees in parts of the United States suffer from various physiological diseases." Ferrous sulphate was tried as a remedy, but only certain samples were found to be beneficial—and these, on closer examination, were discovered to be in galvanised

iron containers. Zinc sulphate was therefore tried, and it was found to cure the disease.

No discussion of plant nutrients would be complete without considering farmyard manure. One does not go far through the country before hearing adverse criticisms upon the use of artificial fertilisers, but, judging from my experience, one would be surprised to hear anything unfavourable about farmyard manure. Nor can this be put down to prejudice, for I have listened to discussions on this point, and the opinions expressed always seemed to me to be well founded. It forms the basis of all good farming, and the only complaint I can make about it is its scarcity.

Straw manure is best, although peat manure is not to be despised. It contains all three elements, but it requires a minimum of ten tons per acre to effect an adequate manuring.

So far as nitrogen is concerned, it is the urine that counts, and this introduces quite a nice point in efficient management in view of dairy regulations.

The food supply of the animal plays an important part, and one great advantage of the imported cotton cake was its beneficial effect on the manure. When removed from the sheds, every effort should be made to protect the manure from the weather, but I am afraid this is never done in Northern Ireland, and the black liquid seen running away from manure heaps must represent a very severe loss per annum.

Bacteria play an important part, and to aid this action frequent turnings are necessary. Nitrification takes place, and humus is formed, and it is this latter product that places farmyard manure on a plane by itself.

One could imagine that Shakespeare had this in his mind when he wrote:—

". . . The earth's a thief
That feeds and breeds by a composture stolen
From general excrement."

The method of application varies, some preferring to broadcast the manure and then plough it in; and when labour is scarce this is the method adopted; but if the ploughing does not take place immediately, and the manure is left to weather, it may be a very extravagant method, e.g., a delay of three weeks reduced the yield of sugar beet by 14 cwt. per acre as compared with farmyard manure ploughed straight in. The better method of application is to put it in the drills at time of planting, and then it is covered immediately. It tends to retain the moisture in the soil, and in dry seasons or on sandy soils this is a very important point.

It is claimed by some to produce a warmer soil, not by its chemical action, but because it produces a darker soil and absorption of the sun's rays increase. The increase of even so little as one degree by this means might have a very beneficial effect at seed-time.

I have pointed out already the scarcity of this product, and judging from my observations many fields at present under cultivation are being treated inadequately, and for this default a penalty in due time will have to be exacted.

Time does not permit me to speak of compost or town refuse, except to say that these have been tried, and tried with benefit, but so much importance has been and is being attached to the question of farmyard manure that a very brief description of McCarrison's work is not out of place.

A field whose past history was known perfectly was divided into three equal parts. One was dressed with farmyard manure, the second with chemical manure, and the third was left without any. A crop was grown, and the result on the separate portions examined. The farmyard manure portion produced, first, the best crop; secondly, the best growth in animals feeding on it; and thirdly, the best crop when grown again, but McCarrison's own summary of his work is well worth repeating.

1. The manurial treatment of the soil was shown to have influenced the nutritive value of millet and wheat grown upon it.

2. The soil manured with 'natural' or farmyard manure yielded a millet or wheat of higher nutritive value than the same soil when manured with a complete mineral or so-called 'artificial' manure. Soil that has not been manured at all for many years, but which has been continuously under crops, yielded a millet of very low nutritive value which was actually harmful to adult pigeons; on the other hand, the same soil yielded a wheat of relatively high nutritive value. It seems that different grains may be affected in different ways by want of manure.

3. The difference in nutritive value of grains grown on soil treated with cattle manure as compared with grains grown on soil treated with chemical manure amounted in millet to about 15 per cent., and in wheat to between 10 and 17 per cent.

4. This difference appears to be due, in considerable part, to differences in the vitamin-content of the grain; wheat grown on soil treated with cattle manure contained more vitamin A than wheat grown on soil treated with complete chemical manure; millet grown on soil treated with cattle manure contained more vitamin B than millet grown on soil treated with complete chemical manure.

5. The inferiority of 'chemical manure wheat' as compared with 'cattle manure wheat' was evidenced in 41.6 per cent. of young rats. The remaining 58.4 per cent. did as well on the basal diet containing 'chemical manure wheat' as some animals on the basal diet containing 'cattle manure wheat.' Individual idiosyncrasy to the deficiencies of the 'chemical manure wheat' was a notable feature.

6. One gramme of 'cattle manure wheat' when added to the basal diet used in these experiments as the sole additional source of vitamins A and B, gave better growth in rats than when these vitamins were provided by cod-liver oil and marmite; one gramme of 'chemical manure wheat' gave as good growth.

7. Whole wheat was shown to be a rich source of growth-promoting factors.

Vitamins.

About the year 1912 a very important discovery swam into the ken of the scientists; a discovery which has had far-reaching effects on the health of the nation. Hopkins, working at Cambridge, demonstrated that milk contained a

substance of great importance to growth—to this he gave the name of "Accessory Food Factor," a name that, in my judgment, should have been maintained, because it drew attention to the fact that this substance was a food—an agricultural product—something that could be grown on the farm as opposed to a drug, or something made in a factory. But the scientist, again in my opinion leaving the substance for the shadow, proceeded to determine the chemical formula, and succeeded before long in producing a synthetic preparation said to be as beneficial as nature's product.

I regard this as a misfortune, for I contend that the natural source of every vitamin discovered should have been declared, and that by propaganda the benefits derived from the consumption of this accessory food factor should have been brought home to people instead of, as it is, clothing the natural product in a strange guise, and prescribing it in the form of a drug instead of what it really is—a food.

One has perforce these days to prescribe capsules or tablets containing this or that vitamin, but can one be confident that by doing so one is doing the best for one's patient. You will notice that I use quite naturally the word patient, but surely if greater stress had been laid on the natural source of these foods, a person could only have become a patient by neglect or starvation.

The natural source of these vitamins is of extreme importance, particularly as we know that different varieties of the same species contain different amounts, and that different parts of the same species may be better supplied than others. Thus I read that—the vitamin C value of Bramley Seedlings may be ten times that of Cox's Orange Pippins, or again in tomatoes, the vitamin A value of the skin may be about twenty times that of the flesh, and a thousand times that of the juice.

But the farmer has little, if any, control over these substances; the scientist has gone away ahead of him; and there is little he can do about it except in the case of milk.

When one looks at cows grazing in a field, a pretty picture may be formed in the mind of the observer, but like many other things in this world there is more in it than meets the eye.

If we look at the grass with the mental eye of the trained scientist, the grass becomes the storehouse of the substance known as ergosteral, and if we carry the flights of our imagination a little further and imagine that it is summer and that a bright sun is shining out of a clear sky, we have all the ingredients necessary for the manufacturing of vitamin D.

I have stipulated two conditions, a bright sun and a summer's day, because it would appear that by this combination the necessary ultra-violet rays which react with the ergosterol and manufacture vitamin D are alone produced. This is, however, not a complete process, as not all the ergosterol is changed, so our cow gets some vitamin D and also some of the unchanged ergosterol. But the same ultra-violet rays are playing on the cow's skin and act in the same way as they do on the grass, and convert more of the ergosterol into vitamin D. Now, the

cow very obligingly secretes this vitamin in her milk, and thus presents us poor humans with a very important source of this vitamin.

I have stressed this story somewhat in order to emphasize the importance of sunlight, and by contrast the deficiency that is produced by withholding the cow from its influence. Now, as it is the general custom in this country to close the cow in its stall from November till May, it will be seen that our source of 'D' becomes markedly reduced, and when one adds to this the fact that hay, on which the cow depends for its maintenance ration, is a poor source of vitamin D, then the possibility of getting vitamin D in milk (or in butter) in this country in winter is reduced to almost vanishing point.

So far I have been dealing with the nutrition of plants, and now I should like to take the next step and deal with the effect of this on animals and man.

First of all the cow. From a nutritional aspect it is necessary to consider this animal from two points of view.

(a) Milk. (b) Beef.

Now it is obvious that a selection made for one of these qualities may not be suitable for the other, and, therefore, in breeding these points have to be considered.

To assist in this decision it is very important to have milk records, and these should be kept. A cow that gives a poor yield may be guessed at by the farmer, but it is much better to be able to produce figures. If this is done, feeding becomes much more economical, and all poor yielders can be culled.

In the summer, good grass supplies all the necessary ingredients for the maintenance of the cow and the production of milk. For six months of the year these ingredients must be supplied in the form of concentrates, and as these for the most part are imported, considerable difficulties arose at the commencement of the War, and milk was in consequence greatly reduced.

Foods rich in proteins are essential, and amongst home-grown varieties field beans are considered best, but other crops, e.g., kale, also may be used, although the protein supply in it is small.

There is a simple rule, recognised by all, that states—Hay may be used for the maintenance of the cow and the first gallon of milk, but afterwards 3½ lb. of concentrates must be fed for each gallon of milk, and this is known as the production ration. As the production ration is expensive, the importance of knowing the exact yield becomes more apparent.

As regards the quality of milk, some cows are recognised as producing a high butter-fat, whilst others are the reverse, but all efforts should go towards producing a butter-fat of at least 3.5 per cent. together with a clean and safe milk.

The object of all this work on the farm and in the cow-shed is to supply plenty of milk for human consumption, so now let us return to this aspect of the work and examine the recent report by Sir John Orr.

This observer has divided the population into six groups by income. The first and sixth containing ten per cent. of the population, and the others twenty per cent. each. The graph shown in his book, "Food, Health, and Income," dealing with the consumption of milk, is most interesting. It shows that 3.1 pints per head per

week are consumed, but that the graph is well into the fourth group before this amount is reached. In other words, groups 1, 2, and 3 consume far too little milk in the liquid form, and even when the condensed milk, which is used in large amounts by these three lower groups, is added, the consumption is still below the required standard for health.

This failure to make adequate use of the milk available has accounted for much ill-health. Experiments on rats have been devised and have been carried out to prove this point, and whilst it must be admitted that such experiments are not a true guide, yet when they are contrasted with the known facts of closely allied tests on school children, and are found to be very similar, there is definite ground for stating that a greater consumption of milk would improve the health of the nation.

As milk supplies calcium and phosphorus in the most assimilable form, no one need be surprised when the graphs already referred to show that the adequate calcium requirement is reached only by those in group 6.

It is now many years since I pointed out that such conditions as neurosis and catarrh were associated with a high degree of translucency of the facial bones, to which my house-surgeon of that time, Dr. Bob Smith, gave the very descriptive title of "Tissue-Paper Face." But these defects are, I am sure, within the experience of you all, and it scarcely requires me to add that more attention to this point is of vital importance, and to quote that "the extent of calcium deficiency in this country is very widespread, and if the larger numbers of children in the lower group be taken into account, the degree of deficiency in these groups is even worse than here portrayed."

I come now to the question of beef, and here let me start off by remarking that this is a product of the farm and not, as so many seem to think, of the shop. No greater problem faces the farmer at present than that of grazing. When I say that many people were recently quite content to pay as much as ten pounds an acre for food grazing land in and around Belfast, it shows the importance they attached to it. I have pointed out already how that in the past the grazing lands of Northern Ireland were notoriously deficient in phosphates, so that it becomes a matter of considerable urgency to see that, as a result of the War, this state of affairs is not allowed to recur.

As calcium plays such an important part in the growth of these animals, it must be always present, and so, constant care and attention is required to see that this and all other essential minerals are present, and what is of almost equal importance —a good water supply.

The day is therefore past when a few head of cattle were bought in the spring and put out to graze with, no doubt, a fervent prayer that before the winter set in they would sell at a profit. Every farmer to-day is alive to the importance of this end of the industry, and therefore tries to get as big a turnover as possible in the shortest time.

Let me explain, for the benefit of those who do not understand, that all beef cattle offered for sale are graded, i.e., they are examined by an expert whose

decision is final, and they are given a grade in accordance with their condition, and the price paid varies directly with their grade obtained. It is therefore to the farmer's own interest to produce his cattle in the best condition possible, and to the interest of the State in that more food is supplied to the public per head of cattle. If we turn now to the consumption of beef as shown in Sir John Orr's groups and graphs, we find that when the average is shown as 38.2 ounces per head per week, the graph is well into group 4 before the average is obtained. Whether this deficiency in the consumption of beef is to be regarded as a defect or not, is open apparently to debate, e.g., in 1917-18 the Danes, by reason of blockade and therefore shortage of feeding stuffs, were forced to destroy large numbers of their herds, and they themselves were compelled to live on dairy products; coarse whole-meal bread and potatoes. This diet differed from their pre-war diet in that the animal protein was replaced largely by protein from dairy products. "This change in diet was associated with a drop of 17 per cent. in the mortality of the whole country down to 10.4 per thousand, the lowest ever known in any country."

Apart from this, the cost of meat always seems to me to be out of proportion to the amount of energy obtained, and it is worth recording that the total expenditure on beef reached the colossal figure of 294.5 (million pounds) in the year 1934.

Beef can be regarded therefore as an expensive item, but if even the small average of 38.2 ounces per head per week be regarded as a minimum post-war allowance, then there must be a considerable increase in consumption in the three lower groups, and this would reflect in favour of the producer, i.e., the farmer.

Now that the greatest experiment of all time in nutrition is approaching its termination, it is justifiable to take stock of the situation as it is revealed to each of us.

Whatever our own private feelings may be as regards rationing, each of us must admit that much useful, and possibly revealing, data will have been collected, and will form the basis of future ideas on this subject of nutrition.

So much is hidden from us at present that no one is in a position to criticise. One fact does seem to be obvious however, the beef ration of approximately twelve ounces per head per week has been sufficient to maintain health. When this is compared with the average—as shown in Sir John Orr's groups and graphs —of 38.2 ounces per head per week, it would seem that this average was, if anything, unnecessarily high, and therefore those in groups 1, 2, and 3 were not so badly done for as otherwise it might appear, and that our vital statistics, on the analogy of the Danes in 1917-18, might be expected to show a very excellent result per thousand.

A glance back over the figures for the past hundred years is interesting, because it reveals that—and here I quote :—"The rise in the standard of living of the last hundred years has been accompanied by a decrease in percentage of the income spent on food." Strange to say, sugar is the one article that seems to have shown a marked increase in consumption, and it has increased five times. I am interested in this because most, if not all, of this sugar would have come from abroad, and

it would be a nice calculation to try and determine what the result would have been in additional health if even fifty per cent of the cost of this sugar had been spent on extra green vegetables.

One could continue this line of argument and show that, with the exception of potatoes, bread, and flour, the consumption of other farm products, and especially green vegetables, is much too low, and conclude that as long as it remains so the health of the nation cannot be what it ought to be.

As the Minister of Agriculture has recently said :—"I see no reason why we should not be able to absorb . . . the greater total of food supplies, both home and imported, by raising the level of nutrition of the people."

Commenting on his words, "The Farmers Weekly" adds :—"Backed by the Minister's speech and the outlook that speech represents, we feel that we are at last tackling the future with a proper recognition of values. Food for the people means work for the people, health for the people, and it is not too much to hope that it will also mean peace for the people."

In a letter to "The Field," the secretary of the Economic League wrote as follows :—"At the present time, when the fifth war harvest is being carried in, it seems desirable to stress yet once again the great part that has been played by British agriculture in winning the war on the home front, and its future vital importance in relation to industry and the whole national economy.

"Britain to-day is not only getter better balanced food, but more of home-produced commodities, including milk, potatoes, and vegetables. Great credit for this is due to British farming. Pre-war, the amount of potatoes consumed by the civilian population annually in the United Kingdom was 177 lb. per head. The figure for 1943 was 256 lb. British farmers are producing not only enough potatoes and vegetables for our own population, but also enough to feed the vast American forces over here.

"The pre-war consumption of milk was 38 lb. per head; in 1943 it was 49 lb. Where civilians had 99 lb. of vegetables per head per annum before the war, last year they had 133 lb. Cereal consumption had risen from 211 lb. pre-war to 247 lb. in 1943. As may be expected, there was, due to rationing, a fall in the consumption of poultry, fish, meat, and imported foods.

"It cannot be emphasized too often that the prosperity of agriculture and urban industry are interdependent. The prosperity of any great nation, if it is to be sound and lasting, must include prosperity for agriculture. This will apply in Britain to an even greater degree after the war than it ever did before."

So far I have been speaking of food and health, but it must be quite obvious that a person who was receiving food adequate for health would be under-nourished if his work is taken into account.

I have referred already to the cow's ration as consisting of two portions : (a) maintenance, (b) production, and this division is quite justifiably applicable to man. The point is of some little interest because in the ordinary everyday life few, if any, arrange their diet according to their work.

Many of us on entering a restaurant for a meal are guided in our choice of food

by our inclination or desire. Others, however, less fortunate in this world's goods, are compelled to make their choice a monetary consideration, and often select their food to suit their purse, instead of making a scientific approach, and selecting their food according to its value in calories.

In order to make this possible, the value in calories of the food would have to be shown on the menu, and in point of fact I believe that this is done in Toronto; and although from the point of view of appetite this might be most uninteresting, it is just as practical and as economic as using a high-grade coal to drive an express engine instead of one inferior in quality and cheaper in price.

I do not wish to nauseate you with an overdose of facts and figures, but I should like to point out that there are two problems; one of agriculture and the other of nutrition. Ages ago these two were joined in wedlock, but in more recent years they have been drifting apart until, in the years between the two great wars, they might have been described as "separated." I am, however, one who believes that in this case divorce is impossible. Indeed, on the contrary, I am all in favour of a closer union. All who have followed me so far must admit that there is a scientific side to agriculture that requires an education and an ability of a high standard. Further, there is a dignity about this most ancient of professions that requires no pen to describe, but which is always present and visible to those who have the adequate knowledge and understanding.

"Far back in the ages,
The plough with wreaths was crowned;
The hands of kings and sages
Entwined the chaplet round."

I know of no more glorious venture of faith than that of the man who, despite many set-backs, goes forth as spring revisits the earth and once more demonstrates his abiding trust that what he doeth then shall bring forth fruit abundantly.

I regard it as a call to one's manhood; a call that no one need be ashamed to answer, and yet there is a drift from the land into the towns which already has reached alarming proportions, and reminds one of Goldsmith's famous lines—

"But a bold peasantry, their country's pride,
When once destroyed, can never be supplied."

This year, as indeed every year, but this year especially, the farmer is fighting a strenuous battle; with inadequate and often unsuitable labour he is being asked to gather in one of the largest harvests on record, and this, not in order to make himself rich, but in order to supply additional food, so that all may have enough.

Too often in the past the cry has gone up for cheap food, and the farmer has been exploited to meet this demand. This is not the way to produce a contented peasantry nor, on the other hand, a healthy nation, but this is a point of political importance, and so I must leave it.

Let me hark back for a moment—I said above that nutrition was also a problem, but it is a problem that in one sense is governed by heredity and environment. By nutrition a plant may be forced to produce up to its maximum, but beyond that it is impossible to go, and any additional plant food is uneconomical.

The same is true of man. Heredity sets its stamp on each family, and therefore

any attempt to reach a common standard is bound to fail, but it should be assured to every one that the standard as set has been reached. If this ideal be attained, the circle will be complete; the health of the nation will be improved, and farming will prosper.

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REVIEW

HANDBOOK OF DIAGNOSIS AND TREATMENT OF VENEREAL DISEASES. By A. E. W. McLachlin, M.D., Ch.B.(Edin.), D.P.H., F.R.S. (Ed.) Pp. 364. Illustrated. Edinburgh : E. & S. Livingstone. 1944. 15s.

ONE of the important accompaniments of war is an increase in the incidence of Venereal Diseases, and the present war has been no exception to the general rule. One good thing has resulted from the present state of affairs, and that is an increasing knowledge of the importance of these diseases, both from a medical and social point of view, and pathological conditions which previously took a somewhat back place in the medical curriculum, have now been recognised as being of very great importance, and both students and qualified practitioners alike are now taking an increasingly sane interest in the study of Venereal Diseases. In spite of this fact, it is often difficult to recommend a suitable text-book on Venereal Diseases to an already overtaxed student or a busy medical practitioner.

This little book by Dr. McLachlin has come at an appropriate moment to meet the present demand. It is written in a clear, lucid style. The language, if somewhat pedantic in places, is, on the whole, simple and straightforward. There is a host of excellent reproductions of the various stages and manifestations of both syphilis and gonorrhœa, and the treatment of both diseases is clearly set out in simple style and according to generally accepted British principles. The author's handling of sulphonamide therapy in the treatment of gonorrhœa and its complications is well worthy of study : his dosage has reached the happy medium of being neither too heavy nor too light, though, if there is any criticism to make here, it is perhaps that experience has shown the advantage of administering these drugs four times rather than thrice daily, in order to ensure a more even concentration of the drugs in the blood stream. There is much good advice about the importance of the Wasserman reaction and on the interpretation of results obtained, whilst his warning about the disadvantages of using local antiseptics on suspected genital lesions before diagnosis, is both timely and necessary. The use of instruments and the necessity of tests of cure in gonorrhœa are stressed, and there is a very excellent chapter on the use of the urethroscope.

That there has only been a passing mention of intensive therapy in the treatment of syphilis, and whilst some of the newer sulphonamides and penicillin have not been mentioned at all, is hardly the fault of the author in a subject where so much is happening in such a short time, and more perhaps could have been said with advantage about conditions allied to the Venereal Diseases.

On the whole, however, this is a very excellent little book which can be recommended to medical students with confidence and which the busy practitioner will find of real value for a rapid revision of the study of the diagnosis and treatment of Venereal Diseases. J. S. McC.

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Penicillin

THE ROBERT CAMPBELL ORATION

By Sir Alexander Fleming, F.R.C.S., F.R.C.P., F.R.S.
from the Inoculation Department, St. Mary's Hospital

I have in the last few years received a certain number of honours, but none has touched me more than the invitation to deliver the Robert Campbell Oration for this year in Belfast. I did not know Robert Campbell personally, but I have read much about him and have appreciated my great misfortune in not having come under his personal influence. It has been my pleasure, however, to have known for a considerable time many of his colleagues and pupils in Belfast, and I have the greatest respect for their judgment, so when I have read what they have written about Robert Campbell I know that he was one of the great ones taken away long before he had finished his work. Still his memory remains, and that is perhaps the greatest thing that can happen to any of us. I have chosen as the subject of my address "Penicillin," not only because of its topical interest but because it is a subject which would have been dear to Robert Campbell, a thoughtful and progressive surgeon who loathed sepsis. Before, however, I say anything about penicillin I want to make allusion to some of the work which led up to the possibility of my noticing a certain happening which proved to be the beginning of penicillin.

The first event of importance was the coming of Almroth Wright (a Belfast man) to St. Mary's Hospital when I was a student. He was just beginning vaccine therapy and the opsonic index had appeared shortly before I qualified. As soon as I qualified I went into the laboratory (and incidentally I have stayed there ever since). Then for years I worked chiefly at phagocytosis, so I could never forget the importance of the leucocyte or of the body's natural defences.

Next, Ehrlich introduced Salvarsan, and sent some over to St. Mary's. It was my good fortune to use it, and the extraordinarily dramatic effect it had on syphilitic lesions made an enormous impression on one who for years had been accustomed to the slower and more leisurely effect of vaccine therapy on septic and other conditions. It showed what happened when the right chemical was introduced into the right patient with the right infection.

Then during the last war I went to France with my chief, now Sir Almroth, and we settled down to study septic wounds and the action of antiseptics, in association with my good friend Professor W. W. D. Thomson. Ever since then I have been partial to work on antiseptics, but other things had to be done, and this was merely a side issue.

Then in 1922 I happened on a very interesting and powerful naturally occurring antibacterial ferment which I called lysozyme. This occurred in almost all cells of the body and some of the secretions, especially those of the lachrymal gland and the respiratory tract. There again I was associated with Belfast in the person

of Dr. Allison. Lysozyme had not much effect on therapeutics, as it affected especially those microbes which were non-pathogenic, but it was fortunate that much of the technique used for lysozyme was again employed in investigating penicillin. Throughout my career, then, I have been associated with Belfast men, Wright, Thomson, Allison.

Then Wright devised a technique for investigating the bactericidal power of whole blood—the slide cell technique—and I adapted this to show the effect of chemical antiseptics and, indeed, any chemical on leucocytes and on bacteria. By this method I was able to show that the older antiseptics had a much more destructive effect on leucocytes than they had on bacteria, and that in certain concentrations these antiseptics made blood a much better culture medium than it naturally is.

Let us see what happens with carbolic acid when it is tested in blood infected with staphylococcus. Into each cell some thirty staphylococci had been planted. Where there was no carbolic acid only one staphylococcus colony appeared—the rest of the staphylococci were destroyed by the leucocytes. As the concentration of carbolic acid increases the number of colonies increases until in a concentration of 1 in 640 every staphylococcus develops, because this amount of carbolic acid destroys all the leucocytes and does not affect the growth of the staphylococci. Stronger carbolic acid destroys both leucocytes and staphylococci. We have, then, the picture of a well-known antiseptic inducing, in certain concentrations, a much more copious growth of bacteria in blood. That this effect is due to the leucocytes is shown by testing the action of carbolic on other leucocytic functions—emigration and phagocytosis (see fig. 1). What I have said of carbolic acid applies to almost all the older antiseptics.

Now let us come to the beginning of penicillin. Professor Bigger (another Belfast man) had published an article on the variation of staphylococcus colonies. This interested me, and I was making some observations on how easy it was to breed out staphylococcal variants. This involved planting out staphylococci on agar plates, and examining the colonies at intervals with a dissecting microscope. To do this the covers had to be removed for an appreciable interval, with the attendant risks of contamination. Naturally contaminations occurred, and one of these contaminations was a mould. That was in no way unusual, but what was surprising was that the staphylococcus colonies in the neighbourhood of the mould faded away. They did not completely disappear, but changed from the usual densely opaque appearance of a staphylococcus colony to become pale and transparent (see plate I). It seemed as if something was diffusing from the mould which induced a lytic change in the staphylococcus colonies.

Now, had I been intensely interested in staphylococcal variation and uninterested in antibacterial substances I would have cast out the plate, possibly with suitable language, and carried on my original programme. However, it was the other way about—I was much more interested in antibacterial substances than I was in staphylococcal variation, so I subcultured the mould and the staphylococcus, and proceeded to see why the mould colony should have acted as it did.

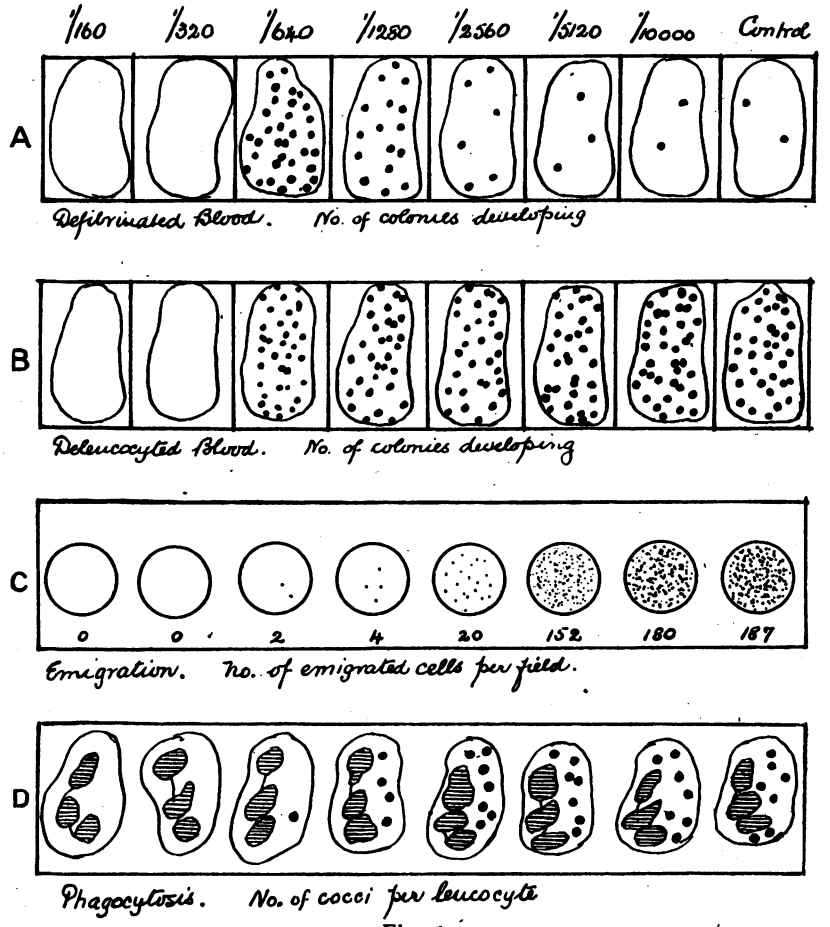

Fig. 1

Action of carbolic acid on bacteria and leucocytes in human blood.

A.—In defibrinated blood with its full complement of leucocytes.

NOTE increased growth in presence of 1/640 and 1/1280 carbolic acid as compared with control.

B.—In deleucocyted blood.

NOTE same growth in control and in all cells containing less than bacterio-inhibitory dose of carbolic acid.

In these cultures the staphylococcus colonies which appear in the blood-carbolic acid mixtures are indicated by black spots.

C.—Number of leucocytes emigrating in the presence of carbolic acid.

The figures indicate the number of emigrated leucocytes per microscope field.

D.—Phagocytosis of staphylococci by leucocytes in the presence of carbolic acid.

The ingested cocci are indicated by black spots.

One of the first things I did was to plant the mould at one side of an agar plate and allow it to grow in a cupboard in the laboratory for four days, after which I streaked a number of different microbes radially from the mould colony to the circumference, and incubated the plate for twenty-four hours. Then there was a very striking result which could not fail to impress. Staphylococci, streptococci, and diphtheroid bacilli would not grow anywhere near the mould colony, but B. coli and typhoid bacilli grew right up to it (see plate II). It was clear then, without at that time any thought of a possible therapeutic action, that this was worth pursuing.

The next thing was to plant out the mould on the surface of a fluid medium, and see whether this antibacterial substance appeared in the fluid. The medium first used was the ordinary broth we used for our bacterial cultures, as this was readily available. Some mould spores were sown on the surface of the broth, which was left in a cupboard for a week. The broth in that time had become bright yellow, and on the surface of the mould there were small droplets of an intense yellow colour. Then the broth was passed through a bacterial filter to rid it of all the mould culture, and it was tested in various ways. But we had to give this antibacterial substance a name. The mould which produced it belonged to the genus Penicillium, so the obvious name was Penicillin.

One of the early methods, and one which gives much information, was to incorporate penicillin in an impregnated strip or gutter in a culture plate of solid medium, and then to streak at right angles to this strip various microbes. The appearance of the original plate showed that whatever was produced by the mould diffused out for a considerable distance into the agar, and this was confirmed in the last experiment cited. Exactly the same thing now happened. The antibacterial substance from the culture filtrate diffused out from the gutter into the medium and inhibited growth of bacteria according to their degree of sensitivity. I show you an illustration from the first paper I wrote on penicillin, which shows some bacteria inhibited and some not (see plate III).

Since that time penicillin has been purified and tested on many organisms, but this illustration is not out of date. It shows the relative sensitivity of a number of common organisms, and what is shown there is true to-day. The most sensitive organism shown is the gonococcus, and there is no infection which is more easily cured than a gonococcal one. The insensitive ones have been shown to be unaffected by penicillin treatment. I am rather proud of this illustration, which not only points out the relative sensitivity of a microbe to penicillin but points out the way to assay penicillin in a simple manner. In this experiment a strip across a culture plate is impregnated with penicillin and the sensitivity of a number of microbes is compared, but if a plate is inoculated with a single sensitive microbe, and then different penicillins are placed in cups made in this plate, the potency of these different penicillins could be compared by the radius of the inhibitory ring around the cup. This is, except for technical details, the method which is very largely used for assaying penicillin at the present time.

Then the culture filtrate was assayed against a number of organisms by the

serial dilution method, and it was found that, using staphylococcus as the test organism, a good culture fluid would completely inhibit growth even when diluted five hundred to a thousand times.

By these methods the following list of microbes were found to be sensitive or insensitive :—

TABLE

SENSITIVITY OF BACTERIA TO PENICILLIN.

SENSITIVE.	INSENSITIVE.
Staphylococcus aureus.	Enterococcus.
,, epidermis.	Non-pathogenic gram-negative cocci found in the mouth.
Streptococcus (hæmolytic).	B. pyocyaneus.
,, (viridans).	B. proteus.
Pneumococcus.	B. friedlander.
Gonococcus.	B. coli.
Meningococcus.	B. typhosus.
M. catarrhalis.	B. paratyphosus.
B. anthracis.	B. dysenteriæ.
Air-borne micrococci.	V. choleræ.
Sarcina.	Pasteurella.
Actinomyces.	*Brucella abortus and melitensis.*
B. welchii.	*B. tuberculosis.*
Vibrion septique.	
B. œdematiens.	
B. tetani.	
Spirochætes.	

Those in *italics* have been added since my original paper in 1929.

Since penicillin has been concentrated, this work has been repeated with the purer material, and my results have been amply confirmed, and the list has been slightly added to.

We have seen already what happens when carbolic acid or other antiseptic is added to infected blood. It kills the leucocytes much more readily than it kills the bacteria. It was another story when I tested penicillin. It had no antileucocytic action, and it was the first antibacterial substance I had ever tested which had this property. It was this, combined with the fact that it was non-toxic when injected into animals, which made me certain that some day it would come into its own for application to, or injection into, septic areas. It has done more.

You may then say : "Why was there a gap of ten years between these findings and the real use of penicillin as a therapeutic agent?" As regards myself the reason was quite simple. I was a bacteriologist working in a laboratory where there was no skilled chemist. We made some amateur efforts at concentrating the penicillin without much success. The crude filtrate was very weak. We made some tentative trials of it as a dressing, chiefly on old sinuses, and the results were good, but not miraculous. When we asked the surgeons if they had any septic cases, they never had any, and then perhaps a septic case would turn up and we had no penicillin, for it was an unstable substance, and if left at room temperature for a week its activity had disappeared. When we had penicillin we could not find suitable cases, and when a suitable case presented itself we had no penicillin.

In this way therapeutic use lapsed, but I continued during these ten years to have a small amount of penicillin in the laboratory for purposes of differential culture, and exceedingly valuable I found it, especially for the isolation of the influenza and whooping-cough bacilli.

In 1930 Raistrick and his collaborators made some important observations. They showed that the mould would make penicillin in a simple synthetic medium, and that it could be extracted with acid ether. Lack of bacteriological co-operation, however, hampered their work, and having obtained certain results they published them, and transferred their attention to other problems.

So the matter rested until in 1938 Chain and Florey at Oxford, having completed their work on lysozyme, took up a study of antibiotics and, having consulted the literature, considered that penicillin offered promise. They used my culture of the mould and Raistrick's synthetic medium, and by rapid extraction with acid ether at a low temperature they were able to concentrate penicillin and to dry the final product so that it remained relatively stable. They then showed that a very small amount of the concentrated penicillin would cure mice of experimental infections of streptococcus, staphylococcus, and vibrion septique.

They continued their work and succeeded in preparing sufficient to treat a certain number of patients. The results were so remarkable that they thought the penicillin they prepared must be approximately pure, but it is now known that it was only about 1 per cent. pure.

Then, as there were some difficulties in getting large-scale manufacture undertaken in England (the Battle of Britain was on), Florey went to America and conveyed to the authorities there the information in his possession. He convinced them that penicillin was worth while and manufacture started there.

In 1942 I had my first real experience of treating a patient with concentrated penicillin. A certain friend of mine came to hospital with an infection which eventually turned out to be a streptococcal meningitis. Sulphonamide and other treatments were useless, and the patient appeared to be dying. I was fortunate enough, however, to obtain some penicillin from Florey, and this was injected intramuscularly and intrathecally, and the man was practically well in a week. This made a great impression on me, and I brought penicillin to the notice of the Minister of Supply, Sir Andrew Duncan, who, with his characteristic energy, called together immediately a meeting of scientists and manufacturers interested, and so started the Penicillin Committee which has been instrumental in stimulating British production.

Penicillin production now has passed far beyond the laboratory, and is a matter for the chemical engineer.

Now we have concentrated penicillin for clinical use. It is not pure; sometimes it is only 10 per cent. pure, sometimes as much as 40 per cent. pure. It is issued as a dry powder in a sealed container, for it is only in this condition that it will remain potent over long periods. When we have an impure substance like this it is absolutely essential that there should be a measure of its potency. There is

as yet no chemical test of potency—it has to be assayed by its power of inhibiting a sensitive microbe, and in most cases it is the staphylococcus which is used. The Oxford workers, as soon as they succeeded in concentrating penicillin, established a unit which has been generally adopted both here and in America. It was an arbitrary unit, but roughly it corresponded to a concentration of penicillin which, when diluted fifty times, would just inhibit the growth of an ordinary staphylococcus. This unit was established in the days when penicillin was in its boyhood, but just two weeks ago we may say that penicillin has come of age, when a conference of representatives of all the countries producing it agreed on an International Standard so that penicillin, wherever made, shall have the same relative potency. This was possible because pure penicillin had been prepared, which would serve as a standard, and it was agreed that this pure penicillin contained a little over 1,600 units per milligram. This leaves the unit as we know it at the same value, but it furnishes a yard-stick by which all penicillin manufactured shall be measured.

At present the dosage of penicillin is measured in units — and I have just mentioned that an international standard unit has been agreed to, but that is only temporary. The time is coming when the dose will be in milligrams of pure penicillin—a much more satisfactory state of affairs.

This International Conference on Standardisation of Penicillin was marked with the great cordiality which has marked all exchanges in penicillin in war-time. The manufacturers here and in the United States and in the Dominions have freely exchanged information, and the delegates from the different governments to the Standardisation Conference were remarkably unanimous in their views.

Pure penicillin is a white crystalline powder, but the impure product which is issued for treatment is a yellow powder. The colour is due to impurities which are difficult to get rid of. The ninety per cent. or less of impurities vary with the different manufacturers, according to the culture medium used, and the method of extraction. Fortunately these impurities are more or less harmless.

Titration of Penicillin.

This is done in two ways, both of them dependent on the bacteriostatic power towards a test organism. The original plate on which penicillin was noticed showed that it was very diffusible in agar, and another illustration in my original paper made it clear that penicillin put in an agar plate diffused out and inhibited organisms for a distance corresponding to their sensitivity. This property of diffusion was used by Heatley to develop a method of standardisation dependent on the diameter of the ring of inhibition, using staphylococcus as the test organism, and this method has been adopted by many manufacturers. The other method used is the obvious one of making serial dilutions and noting which one inhibited the growth of the test organism. Both methods are used, and with extreme care both give very accurate results, so we can rest content that when it is stated on a container that it contains, say, 100,000 units, it does contain this within narrow limits.

Sodium and Calcium Salts.

Penicillin comes to us for use as a powder of the sodium or the calcium salt. What is the difference between these two salts? The chief difference is that the sodium salt is more deliquescent than the calcium salt, and when exposed to the air it rapidly absorbs moisture and when it absorbs moisture it tends to lose its activity. To preserve the sodium salt, therefore, it must be hermetically sealed, but there is a little more latitude with the calcium salt. It was said that the calcium salt was unsuitable for injection, but with the purer preparations now available it can be injected in the same way as the sodium salt without inconvenience to the patient. Because of its non-deliquescence it is more suitable for making into powders or snuff, and it may well be that in the future it will be the way in which penicillin is presented for pharmaceutical purposes.

Both sodium and calcium salts are extremely soluble in water, but after solution they should be used without undue delay. That does not mean that they must be used within a few minutes of solution—or even within a few hours—but it is an indication that as soon as a solution is made such solution should be preserved in such a way as to minimise the loss of potency, and the easiest way is to keep it at a low temperature in the refrigerator.

Therapeutic Use of Penicillin.

For penicillin to affect infecting microbes it must be brought into contact with them. This can be done in two ways; penicillin may be injected into the veins, the muscles, or under the skin, when it is absorbed and reached the microbes through the blood stream wherever they are, or it may be applied to, or injected into, the infected area. We might consider these two methods of treatment separately.

1. *General or systemic treatment.*

This is necessary whenever it is impossible to apply penicillin locally in such a way that it reaches the infecting bacteria. It requires much less skill than local treatment, but it uses up much more penicillin. A solution of the penicillin is made and this is injected intravenously, intramuscularly, or subcutaneously. It may be given by any of these routes by injections at intervals, or by continuous drip, and in different cases different methods may be adopted.

Whichever method is used the penicillin gets into the circulating blood and so reaches the infecting microbes. But it also reaches the kidney, which excretes it with great rapidity. This is a serious disadvantage, as to keep a reasonable concentration in the blood, injections have to be repeated every few hours. Florey has compared it to filling a bath by turning on the water-taps and leaving the plug out.

Before we knew what we were doing we had to estimate the amount of penicillin in the blood after an injection. We have done a good deal of work in this direction and we have, I think, got a sound basis for dosage.

We have used various methods for estimating the penicillin content of the blood.

There is no chemical test, so the titration had to be based on the bacteriostatic power of the serum towards a test microbe.

The methods we have used and the results we have obtained appear in the next number of the "Lancet." There we reproduce charts showing the penicillin blood level after various sized doses, from 15,000 units to 100,000 units, and after continuous intravenous, intramuscular, and subcutaneous drips.

If given by intramuscular injections, the usual method, penicillin can be detected in the blood for the following times :—

	No. of hours penicillin detectable.
15,000 units	2½—3 hours.
20,000 ,,	3 ,,
35,000 ,,	3½—4 ,,
50,000 ,,	4—5 ,,
100,000 ,,	5—6 ,,

We can see from this that if it is intended to keep a constant detectable concentration of penicillin in the blood it is wasteful to give the larger doses. Seven 15,000 unit doses (105,000 units) given three-hourly will keep up the concentration for eighteen hours where a single injection of 100,000 units will only last for, say, six hours. But an intramuscular injection every three hours day and night for a week is a trying ordeal for the patient. If we take a staphylococcal septicæmia, all is well with the three-hourly injections for perhaps two or three days. The patient is too ill to care. But as he recovers he gets more and more restive, and there is a tendency to lengthen the interval. For efficient treatment this can only be done by unduly increasing the dose which, in these times of scarcity, is not justified.*

But there is the alternative method of continuous drip, which is probably the most economical in penicillin, and which ensures a continuous, though low, level of penicillin in the blood. This continuous drip may be intravenous, intramuscular, or subcutaneous, but probably the intramuscular route is the method of choice. With single injections the bacteria have a blitz, and possibly a rest before the next injection. With the continuous drip they have a continuous but weaker attack. Which is the better method we do not yet know—possibly it varies in different conditions, but both are effective.

The systemic use of penicillin is imperative whenever the infecting microbe cannot be reached by local application. It is used in all cases of generalised infection and in spreading local infections. As penicillin becomes more plentiful it will be more and more resorted to even when local treatment is given as well. Acute or generalised streptococcal, pneumococcal, and staphylococcal infections readily respond to penicillin. The first two infections, it is true, have usually responded to sulphonamide treatment, but even with the most effective sulphonamide treatment a case of generalised staphylococcal infection gave great anxiety.

*Recently Romansky and Rittman have showed that penicillin can be dispensed in peanut oil containing 1 to 5 per cent. of beeswax, and if this mixture is injected intramuscularly it is more slowly absorbed, and can be detected in the blood for about six hours after a dose of 15,000 units.

Now with penicillin available a case of staphylococcal septicæmia need not be regarded so gravely, as almost all recover unless complicated with endocarditis. And the cases of carbuncle of the face which were always regarded seriously because of the possibility of a venous thrombosis can now be looked on more lightly if a two-day course of systemic penicillin be given. We have treated now a considerable number of staphylococcal septicæmias at St. Mary's, and we have had no deaths in any patients who were not so far gone that they died within twelve or eighteen hours of the commencement of treatment. If the disease is too far advanced, nothing can save the patient, but even when death appears imminent there are some remarkable recoveries.

One patient we had illustrates this. He was admitted from another hospital with staphylococcal septicæmia and cavernous sinus thrombosis. Normally he would have been considered too ill to be transferred, but we could only treat him if he came to St. Mary's, and so he came by ambulance. X-ray showed that he had multiple abscesses in his lungs large enough to show a fluid level. He appeared to be dying, but after penicillin had been administered for a few days (15,000 units every three hours) the condition changed, and it seemed likely that he would recover. Then we had a setback—one of the lung abscesses burst into the pleura, giving a pyo-pneumothorax. Another setback was an intraorbital abscess which caused marked unilateral proptosis until it was relieved by a small incision. The third setback was when he developed pyo-pneumothorax on the other side. However, in spite of all these he made an excellent recovery with two courses of ten days' treatment with penicillin, and he is now in robust health.

That is just an example of the extraordinary recoveries one sees with penicillin therapy. Staphylococcus infections usually require more prolonged treatment than do those with streptococcus and pneumococcus. For an acute staphylococcal infection treatment for seven to ten days may be necessary, but for pneumococcus or streptococcus three to four days may be enough, although treatment may have to be extended to a week or even more.

The most dramatic results of systemic penicillin treatment are perhaps obtained in gonococcal infections. In the Forces, especially in the American Forces, this disease has been treated extensively, and practically every case has been cured with five doses of 20,000 units at three-hourly intervals, or seven doses of 15,000 units at the same interval. But in all but a few we have found that a single injection of 100,000 units will effect a cure. We are at present using a two-dose method: 100,000 units in the morning and another dose of 50,000 units in the evening as a routine method. So far it appears to be working out successfully, and if it does it is eminently suited to a civilian clinic.

In this infection pus examined, say, two or two and a half hours after the first injection still shows gonococci, but they are very abnormal. They are not the regular kidney-shaped intracellular diplococci, but the individual cocci are swollen and bloated, and obviously the normal method of cell division has been interfered with. Then after three or three and a half hours they completely disappear. The discharge ceases in perhaps twelve hours. In a very few cases there may be a

recurrence, but this can always be cured by a further, and rather more strenuous, course. Gonococcal infection in women disappears just as in men. We had one woman with an infection of several months' standing who cleared up normally after twelve hours' treatment, but who relapsed in a few days, so that positive cultures were obtained from both urethra and cervix. Fortunately we left things as they were, and the gonococci disappeared spontaneously in a week, and they have not returned in a period of six months.

The fact that a gonococcus infection can almost with certainty be cleared up in a few hours may have important results in the control of venereal disease. It was little use making regulations while efficient treatment was lacking, but now that rapid and efficient treatment is available, regulations might be made which in a short time might eradicate this infection.

The early experiments showed that gonococcus was among the most sensitive organisms, but it came rather as a surprise that the group of spirochætes were susceptible. As we all know, the most important spirochætal infection in these countries is syphilis, and results have been obtained which indicate that penicillin is going to be the most efficient treatment of this disease.

If penicillin is administered in an early case the spirochætes disappear in about twelve hours; the lesions heal up and the Wassermann and Kahn reactions disappear in four or five weeks. The optimum dose has yet to be worked out, but it seems as if two and a quarter million units are necessary, given in three-hourly doses over seven days. Of course, we shall have to wait to see whether there are relapses, but it looks as if penicillin would be the most effective drug for syphilis as well as for gonorrhœa.

Other spirochætal diseases have been treated, and it looks as if most of them were susceptible. We have had some experience of Vincent's angina treated locally or systemically with dramatic success with penicillin.

Systemic treatment has now been carried out on a large scale in military surgery. Injections of penicillin were given to the wounded throughout the whole course of transit from the front to the base hospital in which effective surgery could be done. So far no statistical results have appeared, but the surgeons are unanimous that there has been a very great diminution of sepsis and gas gangrene.

Another use of systemic penicillin is to give a large dose just before an operation through infected tissues, so that during the operation and for some time after the blood will be strongly bacteriostatic. This appears to be particularly valuable in war wounds involving the face and limbs, and it enables the surgeon to operate and close wounds which otherwise would remain open and suppurating for a long time. War wounds involving compound comminuted fractures of the femur can often be sewn up, and there may be firm union in about six weeks. What a change from the last war!

This is a very short sketch of the systemic treatment with penicillin. It is impossible to do more in the time.

2. *Combined systemic and local treatment.*

Then there are cases where systemic treatment should be combined with local

penicillin treatment. These are actually very common, and when there is an ample supply of penicillin this method will be largely adopted. I would refer now more especially to extensive or generalised infections which have invaded one of the body cavities and set up a meningitis, empyema, peritonitis, or suppurative arthritis. In such cases the systemic treatment is aimed at the destruction of infecting bacteria outside such infected cavity, but as the penicillin cannot reach the cavity from the blood stream in very high concentration it should be directly introduced into it. When this is done the concentration in the cavity may remain at a high level for forty-eight hours or more. Many cases of meningitis or empyema can be treated by local means alone, it is wise to supplement this by systemic treatment.

In *meningitis* a solution of penicillin containing 1,000 units per c.c. can be injected by the lumbar route, by cisternal puncture, or into the ventricles. Too strong a solution is not desirable, but probably the limit of strength varies with different batches of penicillin, and is dependent on the impurities. There is usually a reasonable concentration of penicillin in the fluid after twenty-four hours, but to be sure of maintaining a sufficiency daily injections should be made. Although there may be a limit to the concentration of the solution injected, the amount may be as much as would almost replace the fluid removed.

One danger in pneumococcal meningitis is the formation on the vertex of an area of fibrino-pus into which the penicillin never penetrates. We have tried to get penicillin all over the surface of the cerebrum by injecting it into the sub-arachnoid space after withdrawing fluid from the ventricles, when the cerebral surface tends to fall away from the skull.

Empyema.—Amounts up to 100,000 units have been injected into empyemas, usually after removing some of the fluid. The injections are repeated every two or three days until the fluid is sterile. In this way, with doses of from 20,000 to 100,000 repeated three or four times, the empyema can be sterilised (assuming that the infection is by a sensitive organism). The treatment after the cavity has been sterilised may be a matter of argument, but by that time penicillin has done its job.

Joints.—Penicillin does not appear to pass readily into joint cavities, but in an acute infection a small amount of a solution of 1,000 units per c.c. or stronger may be injected, and repeated in much the same way as for empyema.

Other local treatment.—So far I have alluded only to local treatment by injection of a penicillin solution into a cavity, but the local injection of penicillin has many more applications. Boils, abscesses, whitlows, and many other local infections can be so treated with advantage, either by injection into the abscess cavity, or the infected tissue around, or both. Because of the inflammatory tension in the tissue the injection of even a small quantity of fluid may be painful, but fortunately penicillin can be mixed with procaine, and it is often desirable to use procaine in these local injections. Incidentally, there have been some batches of penicillin which have caused considerable pain on injection, but this was not due to the

penicillin itself, but to some unfortunate impurities which had not been removed.

When it comes to the application of penicillin to surface infections, burns, and wounds, or to the eye, mouth, throat, or nose, it can be made up in a variety of ways, and we are nowhere near finality in regard to penicillin pharmacy.

A most important point in the dispensing of all penicillin preparations is the maintenance of absolute sterility. We have seen that penicillin has no effect on many bacteria, and there are many which will grow in penicillin solutions. B. pyocyaneus is one of the worst offenders. And it is worse than a simple contamination, for many of these contaminants produce a substance—penicillinase—which breaks up penicillin and renders it inactive. So that we can, if we are careless, have a so-called penicillin preparation contaminated with possibly pathogenic microbes, and containing no penicillin. Such a preparation may be harmful, but is of no use.

At present we have :—

(1) Simple solution.

(2) Cream made up with Lanette wax, or with Lanette wax and vaseline. It may be, however, that much more suitable excipients may be found.

(3) A powder. Penicillin is much too powerful to be used undiluted as dusting powder, so it has to be mixed with some other powder. So far the best diluent for penicillin has been one of the sulphonamides, sulphanilamide or sulphathiazole. These do not injure the penicillin, they are themselves active, and they eventually dissolve in the discharges and disappear.

(4) A snuff. Here again the penicillin powder is diluted with a light powder, and magnesium carbonate seems not unsuitable. A small pinch of snuff can be inhaled frequently for nasal and post-nasal infections.

For the powder and the snuff it is better to use the calcium salt of penicillin, as this does not absorb water from the air nearly so rapidly as the sodium salt, and we have to remember that while penicillin is stable when dry, it tends to deteriorate as soon as water is present.

For this reason these local preparations should be made up only in quantities which are going to be used in a week or so.

(5) Lozenges. Penicillin can be incorporated in flat gelatin lozenges and used for local mouth and throat infections. We recently had some made up, and found that one of these lozenges placed between the upper jaw and the cheek, and just allowed to dissolve without sucking, would last for one and a half to two hours, and that during that time the saliva contained a considerable amount of penicillin. We also found that after one day's treatment with these lozenges (one every two hours) all the penicillin sensitive microbes had disappeared from the surface of the gums, tongue, and tonsils, and that in one or two cases of sore throat and superficial inflammation of the gums there was almost immediate improvement. We have only just started to use penicillin in this way, but it seems to have great possibilities, more especially as we found that when the lozenge contained 10,000 units, penicillin was apparently absorbed from the mouth, and could be found in the blood.

In the local use of penicillin the whole object is to bring the penicillin into contact with the infecting microbes, for although penicillin is very diffusible there are very definite limits to the diffusibility of any chemical in the body. The surgeon must therefore use his wits, and in each case use penicillin in such a way that it does have a chance of reaching the microbes. There is no doubt that efficient local treatment is much more difficult than systemic treatment, and I would hate to say that I had used penicillin treatment on a carbuncle if I had merely spread some cream on the surface. That is using penicillin, but it is not penicillin treatment.

We have now seen how penicillin was born, and how it has grown up. We have seen some of the ways in which it can be used. There is no doubt that in many cases it induces results which may be described as marvellous, but we must never forget that it is not the magic elixir which will cure all ills. I have shown you a list of microbes which are sensitive to penicillin, and patients infected with these can be successfully dealt with. But I have also shown you a long list of microbes which are insensitive, and to treat with penicillin these insensitive infections is simply waste of your time, and the patient's time, and of penicillin.

Penicillin was the first antibacterial substance described which was made by a mould. There are thousands of moulds, and research workers are testing them one after another in an attempt to discover something better than penicillin. This may be difficult when we consider the potency of penicillin, and that when rid of impurities it is about as little toxic as glucose. Then the chemists are busy with the constitution and synthesis of penicillin. The synthesis may well have no immediate effect on the method of production, but it will pave the way to deliberate changes in the molecule—a group substituted here or added there, with the result that new compounds will appear, perhaps more powerful, perhaps more stable, perhaps less easily excreted, or perhaps with a wider range of action. It is then that we shall see the next great advance.

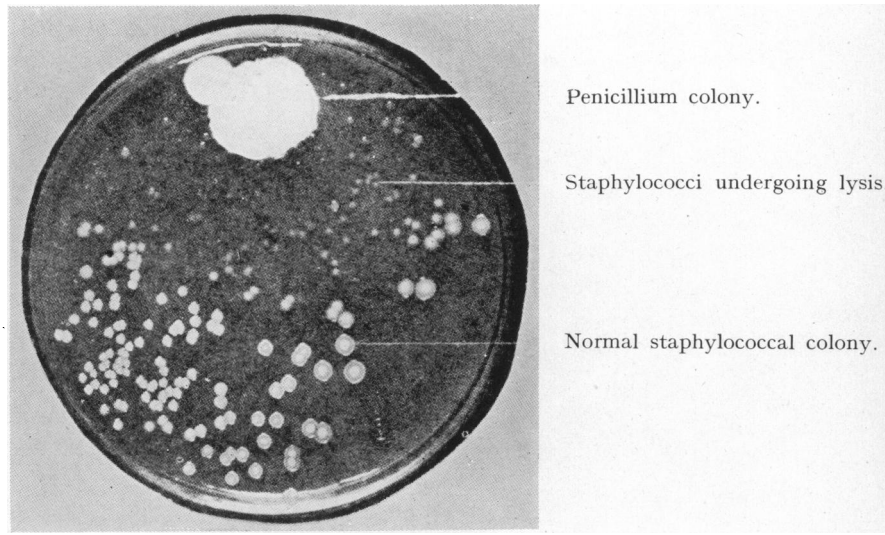

Plate I

Photograph of a culture-plate showing the dissolution of staphylococcal colonies in the neighbourhood of a penicillium colony.

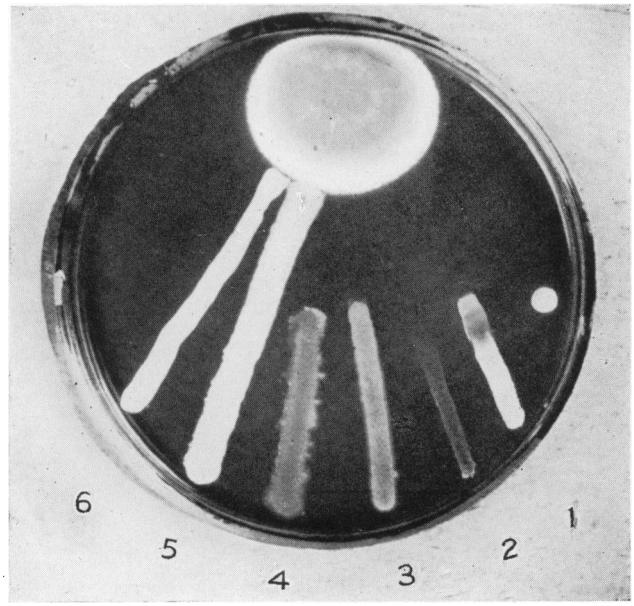

Plate II

Different bacteria streaked radially to a four-day-old colony of P. notatum on agar. The bacteria are:—

1.—Staphylococcus.
2.—Hæmolytic streptococcus.
3.—B. diphtheriæ.
4.—B. anthracis.
5.—B. typhosus.
6.—B. coli.

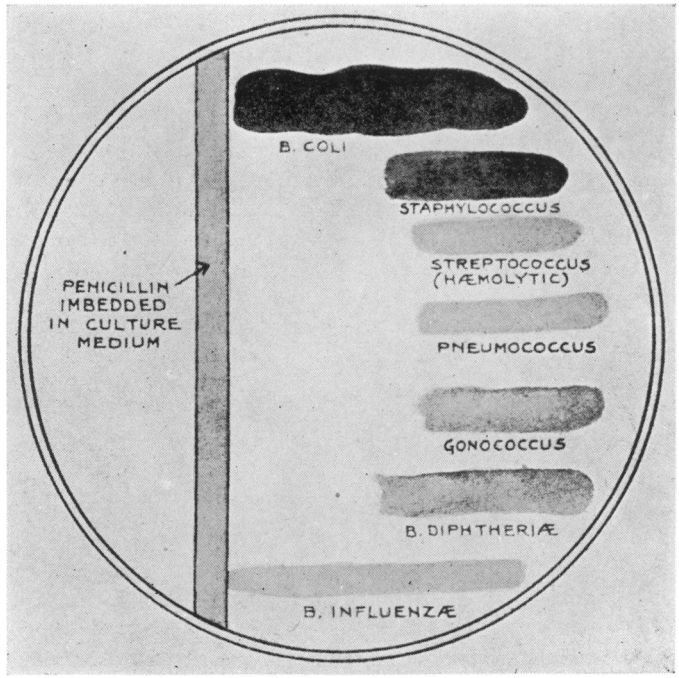
B. COLI
STAPHYLOCOCCUS
STREPTOCOCCUS (HÆMOLYTIC)
PENICILLIN IMBEDDED IN CULTURE MEDIUM
PNEUMOCOCCUS
GONOCOCCUS
B. DIPHTHERIÆ
B. INFLUENZÆ

Plate III

A Synopsis of the History of Dermatology

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Opening Address to Students, Royal Victoria Hospital, Belfast; Winter Session, 1944-45

IT is my pleasant duty, as a member of the honorary medical staff, to extend to the students a very warm welcome at the beginning of this winter session. Some of you are approaching the final medical examination and are in familiar surroundings, while others are in the process of becoming acquainted with the mysteries that encompass us; but many of you, having completed your preliminary training, are about to commence clinical studies. To the latter in particular, therefore, I would offer this advice—observe and learn all you can, making the best of the numerous opportunities which will be set before you. The great reputation of this hospital, built up by the work and studies of a long line of able physicians and surgeons, is known not only in Ulster, but throughout the British Isles, and it will be your honour and duty to impart your knowledge and enhance the reputation of the hospital when later you take up your work in the various branches of our profession.

We are now in the sixth year of the world-wide war, and it is our fervent hope that recent victories will lead to the establishment of an enduring peace in the very near future. Many members of the honorary medical staff are still serving with His Majesty's Forces :—Surgeon-Captain R. S. Allison, Major C. A. Calvert, and Lieut.-Colonel J. T. Lewis, whose safe repatriation from a prisoner-of-war camp has caused much rejoicing among his many friends. Also the following members of the auxiliary staff :—Lieut.-Colonels T. H. Crozier and Ian Fraser, D.S.O.; Surgeon-Commanders H. E. Hall and W. Lennon; Majors D. H. Craig, J. C. Davison, D. J. C. Dawson, J. Houston, E. W. McMechan, and R. W. Strain. We honour them all, and hope the time is not far distant when they will be free once more to return and resume the work which they felt it their duty to lay aside in order to serve their country. Their absence has added a strain to the routine work and the clinical teaching in the hospital, but this has been mitigated by the excellent help so willingly given by the consultant members of the staff. These members :—Mr. J. A. Craig, Dr. V. G. L. Fielden, Mr. H. Hanna, Sir Thomas Houston, Mr. S. T. Irwin, Dr. J. C. Rankin, and Mr. Howard Stevenson—although they have officially retired from active service on the staff, have returned to duty in order to ease the burden. In this respect we welcome the recent return of Surgeon-Commander F. A. MacLaughlin, who has so ably served his country since the beginning of the war.

In delivering the opening address it has been the custom of many members of the staff to choose as their subject the special branch of medicine or surgery in which they were interested, but last year Mr. Woodside carried you forward and gave you an insight into the future of medical affairs in general. To-day, however, I intend to revert to the past, and in so doing introduce to you some celebrated men, and to recall the progress made through the centuries in connection with the particular branch of medicine in which I myself am interested.

From the beginnings of medicine skin diseases loomed large in the earliest literature of Egypt, and continued to be described right through Grecian, Roman, and Arabian medicine. This seems natural, because the earliest and most vigorous of man's medical efforts were made to relieve his itching and to rid himself of the sores, scabs, and parasites which afflicted his skin. This is supported by the emphasis given to skin diseases in ancient records of the seventeenth and sixteenth centuries B.C. For example, much space is devoted to cosmetics and diseases of the skin in the Ebers Papyrus, which was written in the sixteenth century B.C. This is the oldest complete medical book in existence, and is a compilation of medical lore going back to about three thousand years B.C. From this early antiquity to comparatively recent times dermatology was a part of general medicine, and it is only within the past century and a half that its study and literature have been the works of specialists. The history of dermatology, then, can only be divorced from the history of medicine since the end of the eighteenth century.

In ancient times nearly all diseases were thought to be due to the entry of demons into the body, and the humoral theory of pathology postulated by Hippocrates dominated medicine for more than two thousand years. So, we find skin diseases not described as such, but as manifestations of this or that humoral pathology. Nevertheless, certain skin diseases are recognisable in ancient literature on account of their striking characteristics, and are described repeatedly by various writers. Alopecia, leukoderma, cloasma, psora, and lepra; herpes, pruritus, and inflammations of various kinds, including impetigo, erysipelas, scabies, boils, sycosis, elephantiasis, etc. (There was a considerable nomenclature, but the terms were used loosely, and it is not always possible to identify diseases by their names.) Their descriptions were, unfortunately, usually short and inadequate, because the author's interest was centred more in their hypothetical humoral pathology than in the diseases themselves.

Some diseases are alluded to so vaguely that it is almost impossible to identify them with any latter-day equivalents. Modern dermatologists contend, for instance, that most cases of Biblical leprosy (Leviticus 13 : 1-46) were psoriasis, but the leprosy of which Naaman was healed by "dipping himself seven times in Jordan, . . . so that he went out from his presence a leper as white as snow" (II Kings 5 : 1-27), and which he passed on to Gehazi was, in reality, scabies.

Leprosy is frequently mentioned in the Ebers Papyrus, but the famous Egyptologist, Elliot Smith, in his extensive examination of Egyptian mummies, found no evidence of this disease earlier than the Christian era. It may be added incidentally that he did not find any evidence of syphilis until modern times.

This Papyrus devotes a considerable amount of space to cosmetics and the treatment of skin diseases, and numerous remedies were prescribed for the purpose of driving away the demons. Grey hair and baldness appear to have exercised the minds of the ancient Egyptian physicians, and the same frenzied and fruitless efforts seem to have been made to cure them as are carried out at present. One of the oldest remedies for baldness was an invocation to the sun spoken over a bolus of iron, red-lead, onions, alabaster, and honey, which was then to be taken. Thus to-day, in a similar manner we invoke the sun's rays or ultra-violet light to restore the hair in alopecia. A favourite Egyptian pomade for baldness consisted of "equal parts of the fats of the lion, hippopotamus, crocodile, goose, serpent, and ibex." On the contrary, there were remedies recommended for removing the hair, not, however, for beauty's sake, but for revenge; in these cases the instructions for use were :—"To be poured over the head of the hated woman."

Most of the Egyptian remedies were amazing concoctions, many of them containing nauseating and disgusting animal substances, but among the rational remedies used we find antimony, calamine, sulphur, lead, wax, oil, goose-grease, and many others. Bandages were used, and the remedies were incorporated in plasters, poultices, ointments, and lotions. The really useful internal drugs were compounded in various kinds of absurd mixtures, hence treatment was more by magic than by intelligent use of the remedies.

Records of Assyrian and Babylonian medicine show that similar importance was attached to the same skin diseases, the remedies resembling those used in Egypt.

The next advance in medicine occurred in Greece, and, as elsewhere, it began in magic and superstition. Æsculapius, son of the great physician Apollo, became so skilful in healing that he interfered with the population of Hades, was destroyed by a thunderbolt of Zeus, and became the patron of medicine and of physicians. Fortunately, many temples of Æsculapius were founded and maintained by groups of physician-priests called Asclepiades, for the cultivation of medicine and the healing of the sick. These Asclepiades began to study the physical factors of disease and to treat maladies according to their findings, thus sowing the seeds of scientific medicine. The healing art in these temples was, to a great extent, a matter of propitiation of the demons, aided by elaborate deceptions to affect the imagination of the patients, but there are also many records of active treatments. Extracts from records of the temple at Epidauros give accounts of many patients treated there for skin diseases. For example, one record states :—"Pandaros had a mole on his forehead. The gods commanded him to place a cloth over the mole, and remove it when he left the temple. When he removed the cloth the mole was gone. Pandaros' companion, on the other hand, was tricky with the gods about money matters, and instead of removing his mole they gave him another one. A man had the twin afflictions of no hair on his head and too much in his beard; the gods gave him a good balance by the use of a salve which made hair grow on his head. A boy had an ulcer on his ankle which was cured by the temple dog licking it." Licking of wounds by the dogs of the temple was a common method

of treatment in those days. Another man who was afflicted with a great number of lice slept in the temple, and went away clean the next morning.

Hippocrates (460—370 B.C.), the "Father of Medicine," was an Asclepiad of the temple on Cos, an island in the Dodecanese which came into prominence during the fighting there last year. To him medicine owes, among many other things, the art of clinical inspection and observation, accomplishments which I would recommend to you all. There is no other field in medicine, by the way, better adapted to these arts than that of dermatology, because here the disease and its causes lie open in many cases for your observation and deduction.

The Hippocratic Collection, a group of medical books edited at Alexandria about a hundred years after the death of Hippocrates, bulks large in the history of dermatology on account of the great attention given to skin diseases. Of this collection of sixty books, however, only a few are the works of Hippocrates himself. In these we find comments on perspiration and its metabolic function, and on the relation between the glands and the skin in health and disease, showing that some consideration was given to the anatomy and physiology of the skin. Case histories and symptoms of skin diseases were carefully detailed, the important ones emphasised, and an effort made to interpret their significance and to discover their causes. In depicting symptoms and in clinical description the Greeks were unsurpassed; for example, the description by Hippocrates of clubbed fingers and their association with chronic pulmonary and cardiac disease is well known; also that of the Hippocratic facies of impending death. The list of cutaneous afflictions recorded in Hippocrates' works, together with the vocabulary used, does, in fact, constitute a short catalogue of modern skin diseases. In those days skin disease was regarded as a manifestation of general disease, the veracity of which we know in many cases at the present time.

The Greeks devoted great attention to athletics, hygiene, and the care of the human body, all of which, fortunately, lent themselves to the relief of skin diseases. Their emphasis upon baths and cleanliness, their massage and unctions with fresh oil, their application of the therapeutic influences of sunlight, fresh air, and salubrious surroundings were invaluable not only in prophylaxis, but in treatment. Otherwise, their remedies and methods of application were similar to those of the Egyptians, their greatest virtues being, first, to treat patients as sick individuals rather than examples of disease; and second, the realisation of the healing powers of nature and a consequent withholding of heroic methods of treatment. The actual contribution to specific knowledge given to medicine by the Greeks is small, however, compared with the example of originality of mind which they showed in their scientific spirit and method.

In the next four hundred years, between Hippocrates and Galen (A.D. 130—200), power moved from Greece to Alexandria, during which period there was a gradual accumulation of clinical knowledge. This added much to the symptomatology and diagnosis of skin diseases, as is evident in the works of Celsus (30 B.C.—A.D. 50), and many important clinical observations were made during that time. For example, the sixth book of Celsus is devoted chiefly to skin diseases, of which he described

forty, the terminology being the same as that used by Hippocrates. He called attention to the dangers of carbuncle of the face, and was the first to describe kerion ringworm of the scalp in children, now known as Kerion Celsi. He considered a number of eruptions under the heading of "scabies," but gave the first recognisable description of psoriasis. Among many other conditions, he described erythema multiforme and connected it, as we often do to-day, with rheumatism.

Galen, however, developed an ingenious metaphysical theory of disease, which was based on the pathological humours of Hippocrates and combined with the theory of the four elements—earth, air, fire, and water. He thus offered a ready explanation for all pathological processes and supplied a working theory for treatment. So, unfortunately, he substituted a philosophy of medicine for the rational explanation of disease based upon careful clinical observation. Although the sixth book of Celsus was chiefly on skin diseases, Galen was the first to write a book entirely on this subject. He classified skin diseases into "those of the hairy parts of the body and those of the non-hairy parts," a classification which persisted until the eighteenth century. His speculative pathology, however, gave his book a newness and originality, with many theories regarding etiology. Many of his views were speculative and erroneous, but the same can be said of our own to-day; for example, his explanation of baldness as being due to thinning of the scalp is no more fantastic than other theories which are seriously entertained now.

After the fall of the Roman Empire, intellectual activity gradually diminished until about the tenth century, when it was at its lowest. In Europe, Grecian and Roman medicine was preserved only in Arabic versions and copies of early writings. Byzantium, fortunately, preserved the original works of the great masters in its libraries, but contributed practically nothing else to medicine. The Arabs, however, contributed a considerable amount of scientific knowledge, Arabic medicine being really monopolised by the Persians and Jews. They were careful observers, discriminating diagnosticians, and as great alchemists were the true founders of pharmacology. Rhazes, the Persian of Baghdad (860-932), one of the great clinicians of that time, is of interest to dermatologists for his studies of the exanthemata. His classical description of smallpox, which had apparently been recognised by the Byzantines as early as the fourth century and had later been termed Varcola (and Djidri), established it definitely in medical literature. Its contagious nature, however, was not recognised for hundreds of years, and the name of smallpox was only introduced in the sixteenth century, in order to distinguish it from syphilis, the pox. Avicinna (980-1037), also of Baghdad, gave good descriptions of anthrax, carbuncle, and diseases of the head, and was an authority on skin diseases through the middle ages.

Between the years A.D. 500 and 1500 the institution of hospitals and nursing had gradually taken place, and the study of leprosy had aided dermatology. References to leprosy are as old as civilisation itself, and, as I have mentioned previously, many other diseases were included under this heading. It became pandemic in mediæval Europe between the eleventh and fifteenth centuries, and then gradually died away. Its great prevalence during the later Middle Ages was

thought to be due to infected Crusaders returning from the East, and the attention of European medicine was focused upon it. It was recognised as contagious and was treated by segregation, but it is possible that a relative immunity was developed, thus accounting for its decline after 1450. This study of cutaneous leprosy was of great value to dermatology, not only because of the added interest it gave to skin diseases, but it also developed habits of careful observation and recording symptoms.

In the sixteenth century began the most intellectual period in history. The study of skin diseases was more than ever a subject of major interest in medicine on account of the cutaneous manifestations of syphilis, a disease which had made its sudden appearance at the beginning of this period. The first reference to the supposed West Indian origin of this disease is contained in a work by Diaz de Isla, written about 1510, in which it is described as an absolutely new and unheard-of affection in Barcelona, brought from Hayti by Columbus' sailors in April, 1493. Syphilis is supposed to have first appeared in epidemic form at the seige of Naples in 1495, and to have been communicated to the French invaders by the occupants, who had contracted it also from Columbus' sailors. In favour of its West Indian origin, Hutchinson contended that, if transmissible syphilis existed in Europe before 1492, it would have been mentioned by Chaucer and Boccaccio, while it was found in Hayti and San Domingo after Columbus' second voyage. That sporadic syphilis existed in antiquity, and even in prehistoric times, is quite within the range of probability. Virchow, however, maintained that the "caries sicca" of prehistoric and pre-Columbian skulls was not true syphilis, but either arthritis deformans or caused by plants or insects, a theory which would eliminate the question of prehistoric syphilis in Europe. It was not until four centuries later (in May, 1905) that the organism which causes this disease was discovered by Schaudin and Hoffman.

The history of dermatology during the period between 1500 and 1750 is that of rapid increase in knowledge through the investigations of great men like Paracelsus, Fernel, Falloppio, Ambroise Paré, and others. Many monographs were written on skin diseases, some of them important, but all significant of the intense interest taken in dermatology. Various efforts were made to classify skin diseases and to study cutaneous anatomy, considerable knowledge being gained in therapeutics. It was in the seventeenth century that the microscope came into use, hence the minute anatomy of the skin became a subject of intensive study by men such as Malpighi, Vater, Pacini, and others. Perhaps the greatest worker in this field was Jean Astruc (1684-1766), who differentiated mucous membrane, epidermis, corium, sebaceous glands, hair follicles, and nerve papillæ; not only did he make a modern effort to relate cutaneous lesions to the anatomical structures involved, but also indicated the pathology of certain affections in the light of that knowledge.

About the same time Daniel Turner (1667-1740) of the College of Physicians, London, wrote two books, one on skin diseases and the other on syphilis. These were the first comprehensive publications on these subjects in English, and gave a good summary of the knowledge of that period. Turner should be regarded, in

a minor way, as the founder of British dermatology, although Willan, who followed at the end of the eighteenth century, is the accepted holder of this title.

The first work relating to industrial and occupational dermatitis was published in 1700 by Bernardino Ramazzini (1633-1714), an outstanding physician of his time in Italy. He investigated every occupation with which he could come into contact, and described accurately most of the skin diseases which we find to-day in industrial workers. His interest in industrial diseases was not accidental, but was due to his recognition of their importance. From Hippocrates' time occasional notice had been taken of occupational affections, but Ramazzini was the first systematic student of this interesting subject, which is one of the foremost problems in the minds of dermatologists and many employers of labour at the present time. Since then frequent references to occupational dermatoses have been made; for example, Percival Potts' celebrated observation of cancer of the scrotum in chimney-sweeps, Rayer's description of anthrax in hair workers and nail changes in leather and acid workers. Many others have made observations on this subject, but it was Hebra who finally made dermatologists really conscious of its importance, and Prosser-White's recent monumental work on industrial dermatoses is the most modern treatise on this subject.

During these two hundred and fifty years dermatology had, therefore, gained momentum, and considerable knowledge was gleaned in pathology, etiology, and treatment. The great Robert Willan (1757-1812), the accepted founder of British dermatology, now comes into prominence. His studies led to a clearer conception of most dermatoses which, until then, had been rather vague and indefinite, his greatest achievement being the new classification of skin diseases which he presented before the Medical Society of London in 1785. Not only this, but he was a clinician of outstanding ability, few of the masters having given us more original observations in dermatology than he. His grouping of various forms of dermatitis under the term Eczema, gave us our modern conception of this disease, and it was largely due to Willan's teaching that skin diseases began rapidly to be described and named in the terms which we now employ.

On the basis of his new classification, Willan undertook the production of a treatise "On Cutaneous Diseases," the first volume of which appeared in 1808. His untimely death, however, prevented his issuing the second volume, but, fortunately, his famous pupil, Thomas Bateman (1778-1821), continued and elaborated the teaching of his master. This one work of Willan's exerted an enormous influence in dermatology, and was translated into most European languages, one of the chief reasons for its success being the fact that Willan introduced for the first time many coloured plates, a feature which was adopted by the majority of his successors.

The first part of the nineteenth century was the threshold of modern medicine, but it was not until the middle of the century that Hebra was able to make his celebrated classification of skin diseases on a pathological basis, and thus inaugurate the modern period of dermatology. This was partly due to the fact that about this time marked improvements were made in the microscope which

overcame many defects and transformed it into an instrument of precision. Discoveries, inventions, and advances in science, together with numerous investigations, now paved the way for greater development. The French Revolution, in spite of atrocities, such as the murder of Lavoisier, was, in reality, favourable to the cultivation of science, and during the following years France became a theatre of scientific activity. Pre-eminence in dermatology also went to France; this may have been in part due to the old St. Louis Hospital in Paris becoming a dermatological hospital, thus furnishing a centre for the study of skin diseases which French medicine was at that time in the right spirit to utilise. From this centre emerged a group of masters such as Alibert, Biett, Rayer, Cazenave, Gibert, Devergie, and Bazin, who followed the road indicated by Willan, and achieved outstanding fame. Baron J. L. Alibert (1768-1837), one of the brilliant physicians of his time, was the founder of dermatology in France, and so occupied the same position there which Willan enjoyed in Britain. It was he who was chiefly responsible for the establishment of the St. Louis Hospital as a dermatological centre, and one of the wards in the hospital bears his name. One of the curiosities of medical history in his "Dermatological Tree," which grew out of his passion for the classification of skin diseases. In Ernest Bazin (1807-1878), however, French dermatology reached its zenith. He, with Gibert, recognised the important rôle played by parasites, and by his revolutionary work in the treatment of scabies and fungus infections established himself chief of the St. Louis school.

In Germany Willan's work was spread and patterned by many celebrated men, their studies and efforts tending mainly towards classifications. Since the days of Morgagni and Malpighi knowledge had been gained in anatomy and pathology, but with better technical facilities at the beginning of the nineteenth century, a more rapid development took place. An advance in etiology was the discovery by J. L. Schönlein (1790-1864), in 1839, that favus was caused by a fungus. It had been known for centuries that scabies was caused by the acarus, and that pediculi and other vermin caused skin diseases, but a fact difficult at that time to appreciate was that diseases could be produced by fungous parasites which were almost structureless. Schönlein's discovery, therefore, was revolutionary, and led to investigations which revealed many other pathological fungi. Pioneer investigators in this field were Remak, Bassi in Italy, Audouini, and Gruby (1810-1898). The brilliant work of the latter, which was carried out in Paris under the ordeal of poverty and religious prejudice, was practically forgotten until Sabouraud called attention to it half a century later.

The Allgemeines Krankenhaus, the general hospital of Vienna, is a good illustration of the important part played by great institutions in fostering medicine. It was the home of a group of masters, such as Skoda and Rokitansky, which made Vienna famous as a centre of medical teaching, and from this group emerged Ferdinand von Hebra (1816-1880), the most brilliant dermatologist of his time. Hebra's reputation was made not only in pathology, but also in clinical dermatology, to which he contributed many monographs and an atlas of skin diseases. He gave the first descriptions of several skin diseases, and his classical exposition

of the essential nature and treatment of eczema was masterly. Hebra's ability as a teacher must have been unique, his clinic being famous and his course of lectures the most popular of the time in Vienna, probably on account of his genial off-hand style of lecturing and his keen, often sarcastic, humour. Proof of this was the fact that his disciples became the next group of leaders in dermatology throughout the world.

In Vienna, the Hebra dynasty was continued by Kaposi, Auspitz, Neumann, and their successors. Moritz Kaposi (1837-1902) directly succeeded Hebra's chair of dermatology, and continued to spread the traditions and teachings of his father-in-law. His book on "Diseases of the Skin" was translated into French and English, and his atlas is one of the recognised collections of illustrations in dermatology.

Under the influence of these leaders, numerous other centres of dermatology developed in Berlin, Budapest, Breslau, etc., but mention must be made of Scandinavia, where, from the days of Carl W. Boeck (1808-1875) and D. C. Danielssen (1815-1894), centres of much importance have been established, especially for the study of tuberculosis and leprosy, which at that time were both common and severe. The work carried out by these two men on leprosy and parasitic diseases of the skin and their classical description of "Norwegian scabies" ranks high in the progress of dermatology. The most spectacular contribution, however, was the discovery of the bacillus of leprosy by G. A. Hansen (1841-1912) in 1871, eleven years before Koch discovered the tubercle bacillus. Hansen's discovery, therefore, was one of the earliest observations of pathogenic bacteria.

In order to bring my remarks up to date, I must return to France, where the traditions of Bazin and Hardy had been upheld by a succession of able dermatologists such as Vidal, Besnier, Hallopeau, and Leloir. Of these, E. Besnier (1831-1909) appears to have been the most celebrated, and was considered to be one of the greatest leaders of dermatology in the world. His reputation was gained by his teachings and contributions during twenty-five years connection with the St. Louis Hospital, where he succeeded Bazin in 1872. An inspiring teacher and prolific writer, his papers were models in substance and form, and his translation of Kaposi's book is a classic of dermatological literature.

During the nineteenth century the French school gained distinction by the progress it made in the knowledge of syphilis, this knowledge being acquired, as far as was possible, before the discovery of the spirochæte. Foremost in this was P. Ricord (1800-1889) of Paris; but others outside France contributed to this, as for example, William Wallace of Dublin, who established the contagious nature of secondary syphilis in 1835. It was Wallace also who, in 1834, made the important contribution of the use of potassium iodide in its treatment; and Virchow, who, in mapping out the course of syphilis and establishing its distribution through the blood, gave us the first clear interpretation of its stages of activity and inactivity.

My remarks concerning the second half of the nineteenth century have so far been chiefly concerned with events in continental Europe, and I now turn to British

dermatology during this period. This was ushered in by the advent of Sir Erasmus Wilson (1809-1884), who, having first distinguished himself in anatomy, and on being elected a member of the Royal College of Surgeons decided to devote himself to dermatology, in spite of the prejudice against specialism in England at that time. By his writings on the care of the skin for laymen, he is credited with having made the bath more popular in England, and he established the first British dermatological journal in 1867 ("Journal of Cutaneous Diseases"). Through his comprehensive knowledge he attained a commanding position, became president of the Royal College of Surgeons, and early in his career was elected a member of the Royal Society. Through his practice and investments he amassed a large fortune, which provided him with the funds to carry out many benefactions. He made a gift of £5,000 to the College of Surgeons to establish a chair of dermatology, and founded a chair of pathology in Aberdeen University. His philanthropy extended to other cultural subjects; being an extensive traveller and Egyptologist, he brought back from Egypt the monument known as Cleopatra's Needle, and set it up on the Thames Embankment at an expense of £10,000. Altogether, his contributions to the arts and sciences must have reached £300,000—a truly unique accomplishment among medical men.

The next able dermatologist was Tilbury Fox (1836-1879), who clearly established impetigo contagiosa as a definite clinical entity. He also established, by experimental inoculation, the contagious nature of this disease, which from the earliest time had wandered through dermatology without definite recognition.

Sir Jonathan Hutchinson (1828-1913), primarily a surgeon, was famous both in dermatology and syphilology. In his study of clinical syphilis he called attention to a combination of three conditions known as Hutchinson's triad, which are pathognomonic of hereditary syphilis; i.e., peg-shaped notched teeth, chronic keratitis, and the deafness produced by syphilitic middle-ear disease. He described innumerable dermatoses, this being due to the fact that he gave a name to any dermatosis he saw which was unknown to him; indeed, he sometimes used the patient's name to designate the disease, such as Mortimer's Malady. For many years he was the leader of medicine in London, and in his later years his weekly clinical demonstrations were thronged with medical men.

During this period there were so many men, not only in Britain but on the Continent and in America, who studied dermatology and advanced its knowledge that it would be impossible here to mention them all. There are a few, however, whose work and investigations are important, and to whom reference must be made. Huxley in 1845, when a medical student and only twenty years of age, described the layer of the root-sheath of the hair which bears his name. Addison, in 1855, described the syndrome which is now known by his name, and in 1869 described scleroderma. In 1874 Sir James Paget described a "disease of the mammary areola preceding cancer of the mammary gland," now known as Paget's disease of the nipple. In 1876 Squire introduced chrysarobin for the treatment of psoriasis, a treatment upon which we still rely. "The British Journal of Dermatology" was established in 1888, and Radcliffe Crocker's book on skin diseases,

which went through several editions, was considered the best of its day. (Many authors produced useful monographs and books which contributed to the progress of our knowledge. The best-known of these are works by William Frazer and Austin Meldon of Dublin; John L. Milton, Thomas Hillier, and Robert Liveing. Also T. McCall Anderson of Glasgow, W. Allan Jamison of Edinburgh, Henry Radcliffe Crocker—the successor of Tilbury Fox at University College, London, Sir Malcolm Morris at St. Mary's Hospital, and J. N. Neligan of Dublin. Then came Colcott Fox and J. J. Pringle of London, and H. G. Brooke of Manchester; these, together with Radcliffe Crocker, Sir Malcolm Morris, and Sir Norman Walker, were the immediate predecessors of the present generation of British dermatologists.)

In Belfast there is no record of dermatology until 1865, when Henry S. Purdon started a dispensary for skin diseases at a house in Academy Street, and as the work increased, a small hospital with six beds was opened in Regent Street in 1869. Later, through the generosity of Edward Benn, Esq., a hospital for diseases of the skin was erected in 1875 in Glenravel Street, a street which owes its name to Glenravel House, the home of J. F. Hodges, Esq., M.D., J.P., who was the first president of the hospital. The cost of the building was nearly £4,000, and, as Purdon stated in the preface to one of his books ("Cutaneous Medicine and Diseases of the Skin," 1875), it "contained thirty beds and a suite of baths of every description." Purdon was not only interested in dermatology, but was one of the physicians to the original Forster Green Hospital for Chest Diseases, which commenced its career at the corner of Great Victoria Street and Fisherwick Place (where the Ritz Cinema now stands). Amid a busy practice he continued active work at Glenravel Street Hospital until about 1900; his assistants were his son, Elias B. Purdon, and S. W. Allworthy, both of whom were appointed in 1893. The half-century of excellent work carried out at the Skin Hospital by these two physicians is well known, and only ceased there when the hospital was destroyed by an air-raid in May, 1941. It is surely fitting that Henry S. Purdon, together with his son and S. W. Allworthy, should be recognised as the pioneers of dermatology in Northern Ireland. This short reference to Belfast would be incomplete without mentioning William Calwell, who instituted a weekly skin clinic at the "Royal" about 1910.

In the United States dermatology was, until late in the nineteenth century, simply a reflection of European observations on this subject. Two events, however, should be mentioned: firstly, the establishment in 1837 by H. D. Bulkley (1804-72) and John Watson of the first skin department in New York City; and secondly, the publication of the first complete book on skin diseases in America by N. Worcester in 1845. (Bulkley and Worcester were ahead of the times, and the real development of American dermatology belongs to the ten-year period between 1866 and 1876, during which the influences of Hebra and the Viennese school were transplanted from Europe.) In 1869 the New York Dermatological Society was founded, and is now the oldest dermatological society in the world.

There were many outstanding men in the United States. James C. White

(1833-1916) was the strongest force in shaping the early course of American dermatology, and was influential in starting and advancing medical education at Harvard. Louis A. Duhring (1845-1913) was a student of Hebra, but his methods of approach to skin diseases suggest more the attitude of the French schools. His book ("Diseases of the Skin"), together with his firm establishment (in 1884) of a group of obscure itching eruptions under the name dermatitis herpetiformis, often called Duhring's disease, made him America's most famous dermatologist. He acquired a large fortune, and was second only to Erasmus Wilson in his benefactions.

In speaking of Duhring's disease, I am reminded of the Emperor Napoleon's supposed affliction with scabies. Reuben Friedman of Philadelphia, after careful consideration of the literature, comes to the conclusion that Napoleon's ill-health and cachectic appearance were, in fact, due to the association of active tuberculosis and uncured malaria, rather than to scabies. He states that Napoleon's skin disease was neither cured by sulphur treatment nor transmitted to the Empress Josephine, but maintains that this chronic itchy condition was dermatitis herpetiformis, a condition not recognised in Napoleon's time. He also regards the Emperor's characteristic pose of his right hand inserted into his waistcoat as merely a mannerism, and not placed in that position for the purpose of scratching.

Since 1880 our knowledge of the etiology of skin diseases has been enlarged by improvements in the technique of histopathology and bacteriology. During this period the revolutionary discoveries which have also been made in physics and chemistry, as well as in the biological sciences, have led to important advances in therapeutics. The leaders in these advances were Albert Neisser (1854-1916) of Breslau and Paul Gerson Unna (1850-1929) of Hamburg. Neisser's wide knowledge and comprehensive ability, together with his physical qualities, combined to make him a striking personality, and at the age of twenty-five he discovered the gonococcus and firmly established its pathogenicity. He set up a laboratory in Java, where, from 1904 until 1907, he carried out experiments on syphilis in apes; in his later life his contributions to the study of this disease were so important that his name is linked with that of Wassermann in the original designation of the Wassermann reaction.

Unna was no less distinguished. His original and ingenious investigations in histology and pathology were so startling that they were slow of acceptance, but were provocative of study and research. His book ("Histopathology of the Diseases of the Skin"), which embodied his investigations and views, was a landmark in dermatological history. This monumental work of twelve hundred pages was translated into English in 1896 by Sir Norman Walker, the celebrated Edinburgh dermatologist. It is an interesting and remarkable fact that Unna's career was worked out with his own independent resources, unaided by university or other support. Early in his career he established a private clinic near Hamburg, which grew into a large institution, and which for a generation was the centre for students of every nationality.

In bacteriology, during the period between 1880 and 1910, the important rôle

played by fungi had been demonstrated, and the investigations of Raimond Sabouraud (1864-1938) of Paris revived discoveries which had been made by Gruby half a century before. Since then much important work has established these organisms in the etiology of familiar eruptions, the prevalence of these diseases, and new methods for their treatment. Again, through the studies of Theobald Smith, Albert Neisser, Von Pirquet, and others, came our knowledge of anaphylaxis and allergy, which has thrown a new light on the pathology of many toxic dermatoses.

The application of the knowledge of physics to dermatology has also had far-reaching results, especially in therapy. Although from ancient times the invigorating effects of sunlight have been recognised, it was not until between 1894 and 1897 that Niels R. Finsen (1860-1904) of Copenhagen, through his researches on tuberculosis placed ultra-violet light treatment upon a scientific basis. He devised efficient apparatus for the production and application of this light, and in giving us the first satisfactory treatment of lupus vulgaris, opened up a new field in therapy. It is interesting to note the first Finsen lamp in Great Britain was acquired by the London Hospital through the interest shown in him by his countrywoman, Queen Alexandra.

About the same time Röntgen discovered X-rays (1895), and it was soon found, through unfortunate experience, that as well as their penetrating powers these rays had actinic properties on living tissues. The inevitable therapeutic trial of X-rays was carried out by Freund in Vienna (1897); not only did he design the apparatus and offer a careful technique for its safe employment, but also, on the basis of the action of X-rays upon the skin, established therapeutic indications for its use.

In 1898 Madame Curie discovered radium, her experiments and disappointments being well known. Three years later Becquerel, through carrying a forgotten tube of radium in his waistcoat pocket for two weeks, developed an area of severe dermatitis on his abdomen. Besnier promptly suggested its therapeutic use, and it was found to have effects similar to those of X-rays. The earliest experiments with radium were carried out in Paris at the same time as Freund was developing his X-ray therapy in Vienna.

The therapeutic effects of excessive heat and intense cold have also been utilised in dermatology during the past forty years. The actual cautery has been used for many years for the purpose of destroying various skin lesions, but more recently this form of treatment has been replaced by the high-frequency electric current in the form of diathermy. Intense cold was first applied as liquid air in 1899, but being inconvenient and not readily obtainable, it was superseded by solid carbon dioxide in 1907.

With the discovery of Penicillin by Fleming in 1928 and its therapeutic elaboration by Florey ten years later, a new era in bacteriology is being established. The sodium and calcium salts of this mould have already been used with success in the treatment of several types of skin disease, so that when it becomes generally

available, Penicillin will provide a valuable addition to our improving methods of treatment.

Since 1900 a rapidly increasing number of able physicians, whose names and researches it would be almost impossible to enumerate, have interested themselves in the many problems of this branch of medicine, with the result that a vast literature has accumulated and our knowledge has steadily increased. There is still, however, as in all other branches of medicine, a multitude of unsolved problems, and it will be the duty of ourselves and future generations to endeavour to unravel these mysteries.

For the student I would emphasise the unique opportunity which skin disease offers, in the fact that normal and pathological conditions may be studied on and in the skin without difficulty. Indeed, the whole course of a skin disease can be seen either with the naked eye or under the low power of the microscope. Experience will probably show in the future, as it has done in the past, that the living skin is the best field for the study of many important problems in medicine. From this point of view, therefore, dermatology is immensely instructive, in that it teaches the student to observe for himself and form his conclusions from his own discoveries.

We are living in an age of great progress, drawing plans and laying foundations for a future we can but try to envisage, and although the cloud of war may appear to shorten our vision, many brilliant discoveries are being made in the fields of science and medicine which will come to light when the cloud has passed, and which will make our task less difficult.

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The Renal Heart

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For several centuries physiologists have concentrated their researches on the production of urine by the kidney. Many theories have been formulated, and it now seems to be established that this is a process of filtration and selective reabsorption. The problem cannot yet be said to have been completely elucidated.

Perhaps partly because of the exhausting nature of their researches, and the lack of finality achieved, they have devoted little attention to the next stage—the conveyance of the urine to the bladder.

This dynamic function begins when the urine leaves the apices of the pyramids by the openings of the collecting tubules, to enter the pelvis of the ureter.

The ureter achieves its union with the kidney by expanding into a triangular chamber, from which bud forth two limbs, which we call the major calyces, and from these again spring other limbs, three to four from each calyx. These end in little cups, each embracing one or more pyramids of the renal medulla. The collecting tubules open into these cups, and so they receive the finished product of the kidney. By a little tedious dissection, the pelvis of the ureter can be coaxed from its embrace of the inner surface of the kidney proper; leaving behind the hollow space properly called the renal sinus. I emphasise this distinction between the renal sinus and pelvis because the latter is essentially part of the ureter, and should be called pelvis of ureter, not of kidney, as so often happens.

This collecting chamber of bizarre shape is, of course, the dynamic mechanism by which the urine is propelled down ureter to bladder. Its walls, and those of the ureter, have their smooth muscle of muscularis mucosa type, and there is a peristaltic rhythm, probably in normal circumstances at a rate of about four contractions per minute. It was not until I began to study the effects of hydronephrosis, that it became impressed upon me that some sort of ordered peristalsis must be operative. The physiologists have been handicapped by lack of abnormal material, which in this case gives the first clue to normal function. It is, of course, well known that any hindrance to the flow of urine into the bladder, acting over any length of time, will cause dilatation of the ureter and its pelvis. In most of the cases I encountered, this dilatation was confined to the pelvis of the ureter, and the site of obstruction was at the junction of ureter proper and pelvis. Many explanations of why it should occur at this point have been postulated, the favourite one, perhaps, being a stricture in this region, the consequence of some chronic infection. In fact, however, in almost every case the ureteral catheter passes easily into the pelvis, and a history of infection, or evidence of it at the time, is very

rare. Of course, a developed hydronephrosis may become infected, but this is irrelevant. Further, in my experience, very few subjects who have suffered from pyelitis get hydronephrosis.

Kinks and bends in the ureter have also been blamed, but they are a feature of many normal ureters, and, in any case, almost always are incapable of causing obstruction, as it has been shown by animal experiment that only a complete ligature of a knuckle of ureter can bring this about, and even this often fails. Aberrant renal arteries have been incriminated, and it is a fact that they are present in a high proportion of these cases, but the effect is certainly not a mechanical obstruction, and they do not cross the ureter at the pelvi-ureteral junction unless fortuitously.

Gradually, recognition of the fact that there was a sphincter mechanism at this junction, and that this, like the œsophago-cardiac one, can be the victim of achalasia (i.e., failure to relax), became appreciated. I think this is now generally accepted.

Radiologists, in their reports on pyelograms of hydronephrosis, laid great stress on clubbing of the ends of the minor calyces, i.e., those cups called infundibula, realising that when they lost their cup shape, serious kidney damage was beginning. I found, in looking over pyelograms, that even with relatively advanced dilatation of the pelvis, clubbing was often absent. If the pelvis and its adnexa were a simple chamber, surely pressure must be equally distributed throughout, and its effects, i.e., stretching of all parts of it, must be coincident; but it is not so. Sometimes the triangular part is bloated, and all its calyces as sylph-like as ever. Sometimes the major calyces share in the distention, but the minor remain slender, and their infundibula cupped. This was even more noticeable when the latter were sessile on the major calyces, as happens not infrequently as an anatomical variation.

Pursuing the matter further, when the obstruction is lower in the ureter, producing a hydro-ureter above it, as happens when a stone impacts, the pelvis seems to escape the effects for a time, so that there is a bulged ureter, but a pelvis still not corpulent. This gave rise to the thought, that the pelvi-ureteral sphincter is not always a malefactor; it can protect also. From this arose the idea, "maybe there are other sphincters in this queer amœboid chamber, and they too may prove guardians against the evil of back pressure lower down. This would account for the non-stretching of these appendages." This led to the question, "If such sphincters exist where major calyces sprout forth, and the minor in their turn, and probably where these last expand to their cups, could these sphincters ever be themselves the site of an achalasia?" So I searched, and encountered cases where dilatation was confined to major calyces, and in others to the infundibula alone. The chain of evidence was growing, and histological proof was sought. Professor Walmsley's help was enlisted, and indisputable evidence was obtained that, at any rate, where major calyx joined a triangular pelvis, there is a demonstrable muscle thickening.

If all this is true, then physiological function becomes clear, or more accurately, a workable theory can be propounded.

The infundibula fill until a pressure is reached at which the sphincters between cup and stem yield. Then the major calyces fill, and a similar process is repeated. In turn they fill and contract, and their sphincters relax so that the pelvis proper receives their contents. Finally, this chamber repeats the same rhythmic sequence and the ureter receives the yield. Contraction of proximal sphincters, of course, must occur during the contraction of each chamber and coincident relaxation of distal sphincters, to make the system mechanically efficient. Thus there is a series of chambers, probably equivalent in capacity, filling and emptying into the next series, and so qualifying the pelvis of the ureter for the title of my address, "The Renal Heart." Legueu claims that serial radiography shows that emptying and filling of this kind takes place. All this, however, would be merely academic if it led to no practical solution in the treatment of hydronephrosis.

From time to time, individuals are attacked, and their sphincter mechanism in this heart fails to yield to physiological pressures, presumably because the sympathetic nervous system takes control and overwhelms the opposition of the parasympathetic, which is weak in the kidney. By analogy with the cardiac sphincter, relief might be obtained by stretching, as is done with the mercury bougie, but in the nature of things, this would be an ordeal beyond human endurance, involving, as it would, cystoscopy and ureteral catheterisation several days a week. I do not know even then if it would succeed. What is the alternative? The primary factor, pain, which leads to discovery of these cases, is a variable phenomenon, sometimes causing little and transient inconvenience, but all the evidence is that inexorably back pressure increases, leading to kidney destruction; this, because in advancing cases the pressure is transmitted to the renal substance, affecting chiefly the vascular flow, and ending in fibro fatty change.

There is, however, a relevant and fortunate factor, namely, that all the renal nerve supply must reach the kidney via the vessels, and it is mainly sympathetic so far as we know. Even if some nerve fibrils entered via the capsule, any exposure and isolation of the kidney would inevitably sever them; so denudation of the pedicle must cut off the organ from its systemic nervous connections. If the hypothesis be true, that sympathetic predominance or imbalance of control be the cause of these achalasias, we have to hand a remedy unique and complete, in comparison with other regions. For example, the nerve supply of the œsophageal sphincter is a relative will-of-the-wisp, many paths being available, and in the lower limbs, interruption is only possible by removing the lumbar sympathetic chain by abdominal section.

In the kidney, if denervation of the renal pedicle be complete, the object is achieved. I can make little attempt to assess etiology. In nearly all these imbalance syndromes, between sympathetic and parasympathetic, psychological factors play their part, hidden from even the prying eyes of physicians or surgeons. In the words of the Russian parable, "The heart of another is a dark forest." Locally, the existence of an aberrant vessel crossing the ureter, when present, is said by Quinby of America to act as a stimulant by its everlasting throb in proximity to or near the sphincter. Lane of Dublin has shown most conclusively that rest and

posture reduce the dilatation of the pelvis in such cases, but it recurs, when the patient goes about again—no doubt because close contact between vessel and ureter is broken during recumbency. The findings at operation under anæsthesia are often strangely negative, in so far as is found a flattened pelvis, enlarged, but not distended, so that all my hopes of presenting a series of cases with measured pressures, fell to the ground. On rare occasions, a bulged pelvis is seen, but this is unusual.

I must conclude that anæsthesia has a temporary sedative effect on the aggressive sympathetic.

So far as I can trace, the first sympathectomy for renal pain was performed by Papin in Paris in 1931. Professor Fullerton, ever in the vanguard when new methods were on trial, preformed the operation once in the Royal Victoria Hospital in 1933, shortly before he retired.

Consequently, when I first began in 1935 to try this measure, in the hope of saving kidneys hitherto condemned to removal, I had no experience to guide me. Little had then been published of indications and results. It was essentially a path of adventure; I was hopeful, and, no doubt, inspired by wishful thinking.

Experience has ever a sobering effect. Technically, the difficulties and dangers are not inconsiderable, and I have had my vicissitudes. I knew that denervation must be extensive and complete to be effective, but at first I was much handicapped by the inadequate exposure afforded by the usual nephrectomy incision. For a time I tried excision of the eleventh rib, as advised by Bernard Fey; it gave excellent access, but pneumothorax was too frequent a complication, and I now find removal of the twelfth rib a valuable adjunct.

Damage to renal arteries, and troublesome hæmorrhage, are ever-present dangers, and once I had to ligate what was almost certainly the main renal artery. I comforted myself, however, by the thought that heretofore these kidneys had almost always been subjected to removal, so, at worst, I was being but orthodox. Experience, too, has been limited by relative shortage of material.

In the eleven years prior to and including 1936, which I had investigated for a paper, only seventy-one cases of hydronephrosis were diagnosed in the wards of the Royal Victoria Hospital. Of these, only forty-seven came to operation, i.e., an average of a little over four a year, distributed over five surgical wards. Only seven of these had sympathectomies, six of which are in my series.

I count myself fortunate that I have been able to carry out sympathectomy in twenty-six patients between 1935 and 1943, and I am grateful to those of my colleagues who facilitated my collection. It is, of course, far too small a number from which to draw definite conclusions. I have excluded those done in the last year, as it is too early to assess results in them.

Mistakes and failures often teach much more than successes, and possibly best of all, post-mortem examinations, but, fortunately, there was no mortality. There were, however, failures.

Of the twenty-six cases on which I operated, I have been able to trace twenty last year. Five more were traced as long as one to two years after operation, but

can no longer be found. In some cases, the streets in which they lived no longer exist; in others, they have left, leaving no trace.

One I exclude, as the renal artery was almost certainly tied. She was quite well two years after operation, but her home, too, was destroyed in the raids.

Thus, all of the cases have been followed up for at least a year.

Seventeen of the series were females; nine males. The right side was involved sixteen times; the left eight times. In two cases the condition was bilateral, and in one of these, both sides were operated on. The average age was 41, but if the 68-year-old patient be excluded, as she subsequently turned out to have a tubercular kidney, and is included amongst the failures, it was 35.4.

I shall first deal with complete failures, i.e., those patients in whom the kidney was removed subsequent to the primary operation. There are three of these.

One was a woman of 68, and section of the organ showed it to be tubercular. Another was a pyelonephritis, as proved histologically. A third had a chronic infection, presumably of a similar nature.

The following I must regard as at least partial failures.

Mrs. L., operated on 26/5/35, still has some tenderness in the scar and pain in the opposite side. This, however, is a very minor degree of disability, and her original pain seems to have disappeared.

Mrs. B., operated on 12/10/36, had a recurrence of pain in 1942. As she was a rheumatic subject, and somewhat neurotic, this may not be related to her kidney. Intravenous pyelography a few months ago showed rather poor filling on the side of operation, but no hydronephrosis now present.

Mrs. F., operated on 29/3/39, now abdominal pain. She had, however, cholecystectomy since her first operation, and clinically, the pain appeared to be due to spasm of the sphincter of Oddi. Her intravenous pyelogram showed no gross hydronephrosis.

Mrs. M., operated on 27/1/40, still has a certain amount of pain, but as this was relieved for six months by curettage, she thinks herself it is of pelvic origin. Her intravenous pyelogram showed poor function on the right side.

Mr. P., operated on 25/10/41, has had great relief, but has slight frequency, accompanied by slight pain at times.

Mr. M., operated on 15/8/42, states he has been in hospital once or twice with attacks of pain in his left kidney region, but as he is serving in the army in England, I did not see him personally.

Mr. M., operated on 1/4/43, still has a very slight degree of pain, and occasional urgency.

The remaining fifteen were complete successes in so far as they were entirely free from pain or other symptoms in any way attributable to the hydronephrosis.

The final test of the value of this operation is the effect on the dilatation of the pelvis.

My records of this are much less complete than I would like—my first impressions were that probably this would not show a very striking change, because the musculature of the pelvis is relatively weak and might not recover its original

form. I was prepared to be content if the progress of the condition was stayed, because once back pressure ceased to operate, I considered that renal function would not be impaired any further.

My difficulty was to obtain comparable radiograms. I believe that only intravenous pyelograms, taken at approximately the same interval after injection, are fair criteria.

My earlier cases, in most instances, had only retrograde pyelograms, and many of these had been lost, only the reports being available. Some of the patients refused to have further X-rays of either type, especially if they had no symptoms. There was the further difficulty of asking an overworked X-ray department, with the present shortage of equipment, to undertake work of this nature. However, their help was never withheld, and I am deeply indebted to Dr. Montgomery and Mr. Leman for their ungrudging assistance, despite war conditions.

I have selected X-rays of a few cases to demonstrate that change does take place.

In conclusion, I feel I can say that in properly chosen cases, sympathectomy will relieve pain and restore normality to hydronephrotic kidneys, the result of sympathetic imbalance.

Sixty per cent. of the series were, up to date, completely successful. A further twelve per cent. had very slight disability. Sixteen per cent. continued to have symptoms, although it is not quite certain that these were entirely renal in origin. Twelve per cent. had subsequent nephrectomy, but, as I have already indicated, these cases, in the light of subsequent knowledge, were unsuitable, and should have had primary nephrectomy. One case, omitted from these statistics, had quiet necrosis of her kidney, following accidental ligature of the renal artery, and had, of course, complete relief from symptoms.

The selection of cases suitable for operation remains difficult. Infected cases require nephrostomy as well, if it is decided that an attempt to preserve the kidney is worth while. Large hydronephrotic sacs require plastic repair in addition, if the size of the sac is to be reduced, and this, of course, only if reasonable renal function remains. Advanced cases will, as always, need nephrectomy.

The best results would seem to be in small or moderate sized dilatations associated with a considerable amount of pain. When an aberrant renal artery is present in the neighbourhood of the upper ureter, it is probable that division of this alone will suffice, if Quinby's hypothesis be true. I have, however, in several of these, none of which are included in this series, done a sympathectomy as well, to make doubly sure.

I can only submit these conclusions as work in progress, as the number of cases is too small, and the time too short, to claim finality. I feel, however, that the results justify the attempt to save kidneys, which in the past had to be sacrificed.

Rat Bite Fever Due to Streptobacillus Moniliformis

A CASE TREATED BY PENICILLIN

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IT is unlikely that rat-bite fever will ever become a public health problem in this country, so the justification for publishing the following case lies rather in its rarity, its interesting course and investigation, and in the response to Penicillin.

PRESENT CASE.

The patient, D. G., born on 1st January, 1929, is the second child in a family of three sons and one daughter of well-to-do parents. There is nothing of importance in the family history or the previous history of the boy. Before his present illness he was in good health, was about 5 feet 9½ inches in height, and weighed, in his clothes, about 10½ stone. The family are city dwellers.

On the afternoon of 18th March, 1944, whilst hiking in a party along a country lane about fifteen miles from Belfast city centre, he was bitten over the terminal phalanx of his right index finger by a rat, which held on until pulled off and killed. The rat was described as looking old and sickly. The wound bled slightly at the time, but with ordinary domestic dressings it healed within a few days. Without missing a day from school and feeling normally well in the interval, the boy became sharply ill at lunch-time on 31st March, i.e., thirteen days after the bite. He had acute loss of appetite, with rigor, vomiting, and headache, and his temperature, when taken shortly afterwards, was 105°. He took to bed that day, but after about three days the malaise disappeared and his temperature returned to normal. He tried to get up, but was unable to stay, and returned to bed. Two similar attacks followed periods of apparent normality before he was admitted to a general hospital on 12th April, for investigation. This revealed a white cell count of 1,200 per cm., a negative Paul Bunnell, X-ray of chest and abdomen apparently normal, urine normal. The Widal was positive to a titre of 1/50 to B. typhosus (H) and negative to B. para. A, para. B, and abortus. On this finding he was transferred to Purdysburn Fever Hospital as a possible enteric infection.

On admission, although he was actually in an acute pyrexial phase, there was nothing outstanding to note in his clinical condition. He was dull, but not to the degree consistent with even a mild enteric infection. He could detail his story without confusion, and denied any disturbance of sleep, made light of his headache, and admitted rigors, so that altogether he was not clinically suggestive of enteric fever. His tongue was moist and lightly furred. He had a healthy throat and no palpable glands. His abdomen was distended without any tenderness. The spleen was not palpable. For some days he had difficulty with micturition, apparently entirely postural. He had been constipated since taking to bed, and for some weeks afterwards required enemata at intervals. There was a small well-healed scar on his right index finger where the rat had bitten, but there was no tenderness

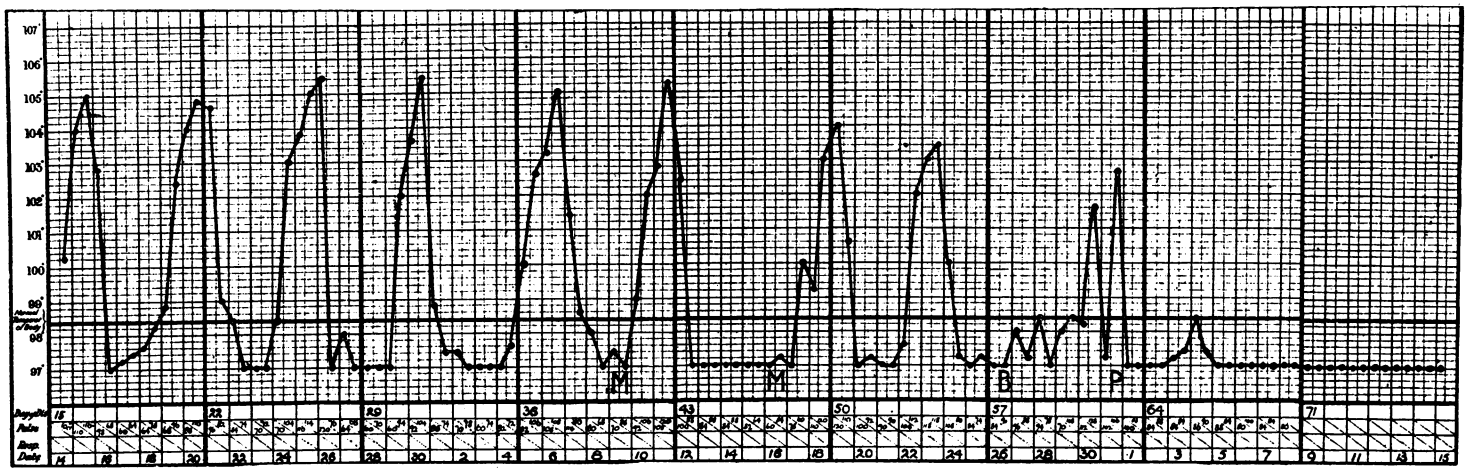

Fig. 1

Morning and Evening Pulse and Temperature Chart

M—Myocrisin. B—Blood transfusion. P—Penicillin.

or induration and no lymphatic involvement whatever. There were no abnormal findings in heart, lungs, or C.N.S., and there was no sign of any rash.

The temperature and pulse chart during the entire sixty-two days of his stay in this hospital indicates the course of his illness (fig. 1). The outstanding feature is the relapsing nature of the condition. At first relapse occurred at regular five-day intervals, but later became irregular, tending towards shorter and milder attacks with longer free periods.

In the afebrile periods the boy was bright and cheerful, completely without symptoms, with a rather fickle appetite, and a pale white skin. The approach of

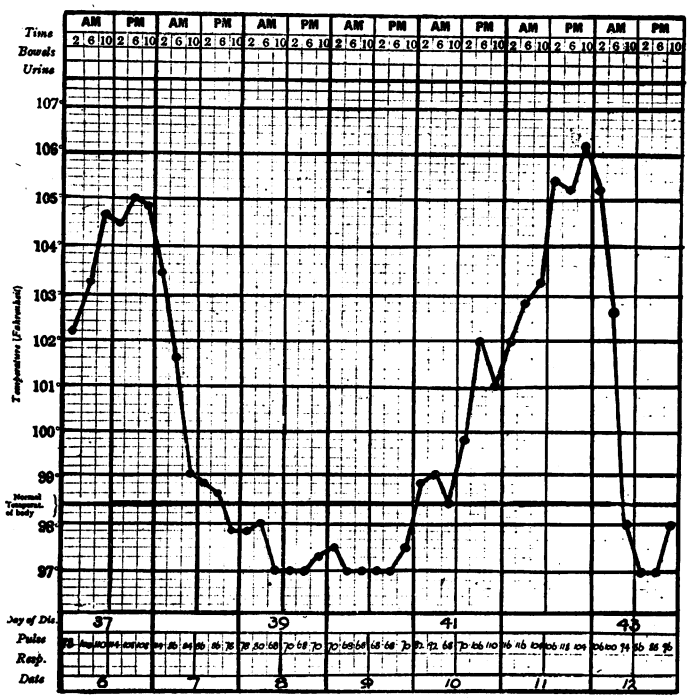

Fig. 2
Four-hourly Temperature and Pulse Chart of One Week
(6th—12th May)

a relapse became evident by his quietness, loss of interest in his radio and papers, a puffiness of his features, especially of the eyelids and nose, and a sharp loss of appetite. The dulness and loss of appetite were the only features common to all relapses. His temperature and pulse were recorded four-hourly throughout, and the second chart (fig. 2) shows a week's record with two typical relapses. It shows the temperature rising gradually over two days to a peak, with a sharp fall to subnormal terminating the relapse. (This contrasts with the impression of Douglas, Colebrook and Fleming,[13] who record the fall of temperature as being more gradual than the onset.) There was no disproportion between the temperature and pulse-

rate. Once epistaxis of mild degree occurred during a relapse. There were no chest symptoms or signs.

The boy's tongue remained moist and lightly furred throughout. On several occasions his lips inclined to crack and bleed. On only two occasions was his spleen palpable : thirty-second and fifty-sixth days, both immediately following the termination of a relapse. The viscus was only slightly enlarged and not tender. At no time while in hospital was there any reaction about the scar of the bite or in the lymphatics. Headaches were never severe and were easily relieved. Sweating was not a prominent feature, and rigors at the onset of the first few attacks were of a mild degree. Blood-pressure readings varied from 86/60 to 104/64. Sleep and rest were little disturbed at any time throughout the course. The fluid exchange, charted throughout his illness, was always liberal, from five and a half to eight pints intake and a urinary output varying from three and a half to seven pints daily. Only on three days throughout the course was a trace of albumen found in the urine, twice after his first injection of Myocrisin and once in convalescence. Loss of weight was not pronounced : his ward record shows that when first weighed on his twenty-sixth day of illness he was 9st. 5lb., his lowest was 8st. 6lb. at his forty-fourth day, and at his seventy-first day he had returned to 9st. 5lb. There was never any sign of arthritis as a complication, although he had a very slight degree of myalgia upon full extension of elbows and knees, but not more than could be attributed to his long spell in bed. There was never delirium, confusion was minimal, and giddiness was present only in the early relapses, when the boy was allowed to sit erect in bed.

It was not until the twenty-sixth day of illness that a rash was seen. Then the patient drew attention to what he thought were "hives" on his left arm, although at no time did the spots itch. During this particular exacerbation—the third in hospital—he was entirely without symptoms, apart from loss of appetite and dulness, and did not even feel feverish. The rash on this occasion comprised six dusky red, ill-defined spots of about $\frac{1}{4}$ in. diameter, not raised and without induration, and limited to the left arm. There were no lesions on mucous surfaces. Next day there were another six spots of similar nature distributed over chin, neck, and chest, which had faded the following day with the remission of temperature. In every subsequent relapse these spots reappeared, especially about the face, neck, and shoulders. They were always ill-defined and blotchy and accompanied by the puffy features, described as "measly," but bearing little resemblance to morbilli. There was no photophobia or conjunctivitis, although in these exacerbations the boy usually lay with closed eyes (plate I).

Investigations.

At first it was considered necessary to exclude the possibility of typhoid fever, and although the agglutination titre of 1/50 for B. typhosus (H) was confirmed, blood culture in trypsin broth was reported sterile and the stools showed no enteric organisms. Thereafter, with appreciation of the relapsing nature of the condition, steps were taken to exclude malaria and establish connection with the rat-bite.

The following investigations were subsequently carried out.

Blood film—daily from twenty-first to twenty-fifth days—showed no malarial parasites.

	Day of Disease	
Red blood cells	32	4,120,000 per cmm.
	40	4,225,000 Hæmoglobin approximately 100%.
	46	3,850,000
	57	4,000,000 immediately before transfusion.
	62	4,890,000 immediately before Penicillin.
	63	5,100,000
White blood cells	21	3,200 per cmm.
	23	3,200
	24	2,300
	25	2,200 polymorphs 66%, mononuclears 11%, lymphocytes 23%.
	26	2,100 polymorphs 72%, mononuclears 18%, lymphocytes 10%.
	28	2,104
	29	3,120
	30	2,808
	32	2,496
	35	3,800
	37	1,300
	40	2,900
	46	3,800
	55	4,056
	57	4,000 immediately before transfusion.
	58	4,900
	60	4,300
	62	4,300 immediately before Penicillin.
	63	3,500 polymorphs 39%, mononuclears 37%, lymphocytes 24%.
	64	4,600
	68	7,100 polymorphs 65%, mononuclears 15%, lymphocytes 20%.
	70	8,300
	75	8,500 polymorphs 45%, mononuclears 25%, lymphocytes 30%.
Blood sedimentation rate	26	5.5
	30	5.0
Widal	18	B.T. 1/50 (H), negative para A, para B, and abortus.
	21	B.T. 1/50 (H), negative para A, para B, and abortus.
	25	B.T. 1/50 (H), negative B.T. (0), para A, para B, abortus.
	75	Completely negative.

	Day of Disease	
Weil-Felix	25	Negative OX.K, OX.L, and OX2.
Paul Bunnell	26	Negative (also negative at 14th day before admission)
	75	Positive 1/2,560.
Serum test for syphilis	25	Harrison negative, Fleming negative.
	46	Harrison + +, Fleming negative.
	55	Harrison + +, Fleming negative, Dreyer 0.
	75	Harrison + +, Fleming negative, Kahn + + +.
Throat and naso-pharyngeal swabs	39	No growth of streptobacillus.
Fæces	18	No enteric organisms.
	25	No enteric organisms.
	39	No growth of streptobacillus.
Urine	...	Daily examination throughout course revealed a trace of albumen on only three occasions.
	25	No enteric organisms.
	33	Two guinea-pigs inoculated intraperitoneally without effect.
	39	No growth of streptobacillus.
Blood culture	21	No growth in Trypsin broth.
	25	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	31	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	36	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	37	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	40	No growth on Loeffler slopes or serum broth.
	46	No growth on Loeffler slopes or serum broth.
	47	No growth on Loeffler slopes or serum broth.
	50	No growth on Loeffler slopes or serum broth.
	62	No growth on Loeffler slopes or serum broth.
	75	No growth on Loeffler slopes or serum broth.
Blood by animal inoculation	22	Two guinea-pigs inoculated intraperitoneally.
	25	Two guinea-pigs inoculated intraperitoneally.
	31	Two guinea-pigs inoculated intraperitoneally. Six white mice inoculated intraperitoneally.
Agglutination tests	...	Deferred to obtain agglutinable cultures of the streptobacillus; meanwhile samples of the patient's serum are frozen.

Diagnosis.

Following the lines suggested by Brown and Nunemaker,[4] investigations included attempts to recover the causal organisms by culture and animal inoculation. The first blood culture at the twenty-first day in ordinary trypsin broth was to exclude enteric infection, and was reported negative. It is unlikely that the streptobacillus would grow primarily on an unenriched medium such as this. Next day, at the end of a relapse, two guinea-pigs were inoculated intraperitoneally with patient's blood.

The subsequent attempts at culture were made on Loeffler slopes and 50 per cent. serum broth. On the twenty-fifth day blood was withdrawn when the temperature was 103 and in the early phase of a relapse. The streptobacillus moniliformis grew abundantly on both media. Of the two guinea-pigs inoculated intraperitoneally, one died immediately and the other twelve hours later, and in neither was there any abnormal post-mortem finding.

The next cultures were taken in relation to the phases of the relapses, and those of the thirty-first, thirty-sixth, and thirty-seventh days, at peak, rise, and peak respectively of two successive relapses, all gave pure growths of streptobacillus. Further intraperitoneal inoculation of two guinea-pigs and six mice was done on the thirty-first day. One guinea-pig died seven days later, and the streptobacillus was cultured from its heart-blood and peritoneal fluid.

Blood culture at the fortieth day, i.e., in a trough or remission, immediately before commencing gold therapy was sterile. Further attempts to culture the organism on the forty-sixth, forty-seventh, and fiftieth days, i.e., twice in a remission and once on a falling temperature, were in vain. Another culture on the sixty-second day, immediately before starting Penicillin, at first appeared to give a growth, but was eventually reported negative. This was regarded as an important culture in relation to therapy, as was also that of the fortieth day. The ultimate culture on the seventy-fifth day, during convalescence, was also sterile.

Upon the evidence of four successive cultures of the organism from the patient's blood, together with its transmission by inoculation to a guinea-pig, and recovery therefrom, the diagnosis of septicæmia due to streptobacillus moniliformis is established. No evidence of simultaneous spirillary infection was found from the animals inoculated. Difficulty as yet in obtaining an agglutinable culture of the streptobacillus has prevented agglutination tests being carried out, but samples of the patient's serum are in storage, and the results of these tests will be recorded later. Details of the animal inoculations will also be reported later.

Treatment.

No specific therapy of any kind was considered until the diagnosis was established beyond doubt, meanwhile little treatment, apart from nursing care, was required. The boy was allowed full scope of his appetite, and his other treatment included vitamins A, B, C, and D, and ultra-violet radiation.

As spirillary infection had not been established, arsenical therapy was deferred, and following the experiences of Brown and Nunemaker,[5] and Heilman,[19] that

sulphonamides were without effect, gold therapy was chosen. Treatment was instituted with aqueous myocrisin and two intramuscular injections, each of 0.01G., were given on the fortieth and forty-seventh days. A faint trace of albuminuria was present on the forty-fourth and forty-sixth days only, otherwise there was no sign of intolerance nor was any change appreciated in the blood picture. At the patient's

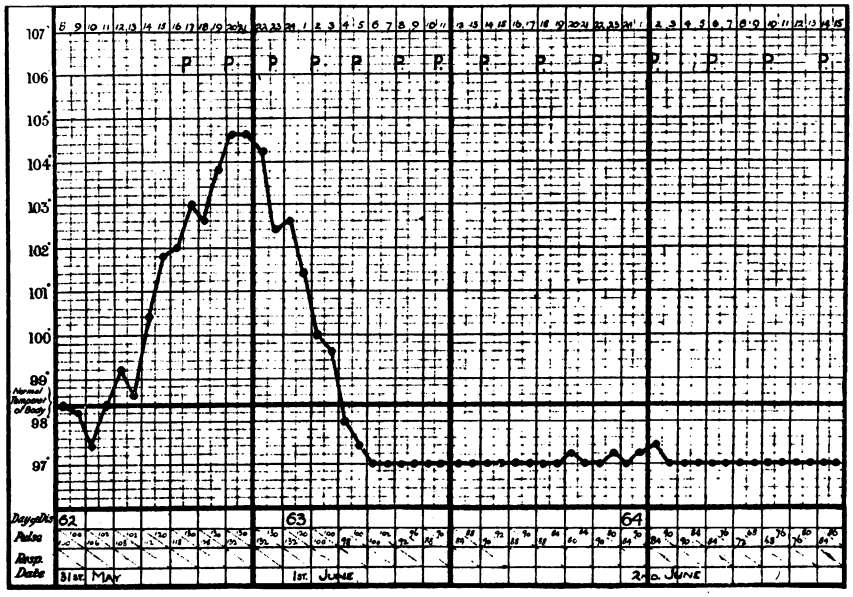

Fig. 3
Hourly Temperature and Pulse Chart at time of Penicillin Treatment

fiftieth day the streptobacillus was reported sensitive to Penicillin in vitro, and steps were immediately taken to procure a suitable preparation. Gold therapy was stopped, and, in an effort to boost the patient's leucocytes before starting Penicillin, a fresh blood transfusion of two pints of identical type (A) was given on the fifty-seventh day. The degree of success of this measure is indicated in the blood counts immediately before and following the transfusion. From consultation of the four-hourly temperature record of the case, it was decided to commence Penicillin therapy when the rising temperature reached 102. This condition obtained on the sixty-second day (31st May), and fig. 3 is an hourly temperature and pulse chart of this time. The preparation used was Penicillin sodium (Pfizer) in saline, given intramuscularly, 15,000 Oxford units three-hourly for eight doses, followed by the same quantity four-hourly to a total of 200,000 units. There was no unpleasant reaction of any kind, apart from a sense of numbness at the site of injection for a few minutes each time, and from the inception of this treatment the boy apparently determined to get well quickly. His temperature had returned to normal within twelve hours of starting Penicillin, and during the remainder of his stay in

hospital—fourteen days—was never above normal. Fig. 3 illustrates the amazing rapidity of his response to Penicillin in temperature, and his clinical improvement was similar. His appetite improved greatly, and he had a very pleasant sense of well-being. He was allowed up for increasing periods from his seventieth day, and left hospital seven days later (15th June), apparently completely well in every way.

Historical.

It is likely that human illness following rat-bite is as old as the association of the species, and from the literature it appears that in Japan, where the disease is common, the condition has been recognised for many years (Miyake[30]). Cases are also common in India (Das Gupta,[10] Dalal,[9] Surveyor[47]). Many reports of cases in America are available, and the review of the disease by Brown and Nunemaker[4] provided the basis of investigation of this present case. The review by McDermott[27] is concerned mainly with the spirillary form of the disease.

In Europe, Millot-Carpentier[29] first reported the condition in 1884, and in 1900 Miyake[30], and eight years later Ogata[36] described in detail the features of the disease under the title of "Rattenbisskrankheit." The Japanese term for the condition is "Sodoku": 'So'—rat, and 'doku'—poisoning.

Horder,[22] in 1910, was the first to record the disease in Britain with a report of three cases presented to the Association of Physicians. In 1909 von Ofenheim[51] described autogenous vaccine treatment of a septicæmia following a rat-bite, from which he recovered micrococcus tetragenus by blood culture. Since then cases have been recorded in Britain by Middleton,[28] Cruickshank,[8] Nixon,[34] Douglas, Colebrook, and Fleming,[13] Burton-Fanning,[6] Low,[25] Thorp,[48] and Hickling.[21] In 1912 O'Carroll reported a case in the west of Ireland.[35]

As the title implies, the disease usually follows the bite of a wild rat, but the literature records cases arising after bites by a laboratory rat (Caldwell and Templeton[7]), field mouse (Reitzel et al.,[41] Moore and Davis[32]), weasel (Dick and Tunnicliff[12]), ferret (Nixon[34]), cat (Mock and Morrow[31]), and squirrel (Schottmüller[44]), and from a dog (Ripley and van Sant[42]). It appears to have followed the bite of a monkey and also that of a parrot, and Walker[52] suggested the possibility of transmission by infected soil. There is, however, no record of rat-bite fever assuming epidemic proportions.

The relapsing nature of the fever probably led to the therapeutic transmission of Sodoku to patients suffering from general paresis, as recorded by Solomon et al.[45] in 1926. At that time Solomon wrote of this treatment that it was comparatively simple and harmless, less severe on the patient than malaria, and could be used in patients immune to malaria. Hershfield[20] found the disease was not transmissible from man to man, but through the medium of infected guinea-pig heart blood. He reported a further example of artificial Sodoku in seventy-two cases of paresis so treated. In his cases, after an incubation period of eight to fifteen days, he recorded paroxysms of fever up to 106°, becoming progressively lower and shorter, with an average total duration of thirty-two days. Nine of his cases recovered spontaneously from the fever, the others were controlled by .3G.

neoarsphenamine. The last report of this form of Sodoku by Neyman and Koenig[33] probably put an end to Sodoku-inoculata, as they found it difficult to control the disease, and much preferred diathermy for the treatment of their cases of paresis.

The bacteriology of rat-bite fever has been, and still appears to be, a subject of controversy. Text-books of medicine still identify the spirillum minus as the causal organism, and either ignore entirely the role of the streptobacillus or dismiss it as a common secondary invader. Ogata, in 1908, appears to have been on the trail of the causal organism, but to Schottmüller goes the credit for the first description of an organism he designated streptothrix muris ratti. In 1916, Blake[3] confirmed Schottmüller's finding, but later in the same year Futaki et al.[16] described as the cause of the disease an organism which they later named spirochæta morsus muris, and which was subsequently designated spirillum minus. Since then the controversy has been waged, and in their summary, Brown and Nunemaker[4] admit the evidence that spirillum minus causes an illness which may be indistinguishable from that produced by the streptobacillus. There is as yet no reported case of simultaneous infection by both organisms, although some cases are suspicious, but do not appear to have been followed to the degree necessary. Of recent years the majority of cases appear to be due to the streptobacillus, but this may be due to investigations being directed more towards that end. The streptobacillus can be cultured from infected body fluids, whereas, in spite of the claim of Joekes[23] and that of Futaki et al.[16] (subsequently withdrawn), the spirillum has not yet been cultured outside the body.

In 1926, Place et al. and Parker and Hudson[38] described the condition of erythema arthriticum epidemicum, or Haverhill fever, occurring in epidemic form, and in 1934 Place and Sutton[39] summarised the findings in the outbreak. Eighty-six persons were involved in the epidemic, which was established as a septicæmia, due to the Haverhillia multiformis, identical with the streptobacillus moniliformis. The source of the outbreak was traced to the consumption of unpasteurised milk, in one case taken as ice-cream, and the probable contamination of the milk arose in the udder of one cow of many concerned in the farms supplying the particular dairy. This cow alone showed specific antibodies in her blood and had lesions of two quarters, but further investigation was impossible, due to "the hostility of the farmer." Evans[14] records symptomless streptothrix infection of cows' udders with recovery of the organism from the milk. The main features of the outbreak of Haverhill fever were an incubation period of two to four days, abrupt onset with rigor, headache, vomiting, relapsing fever to 105°, rash probably in every case, with arthritis of the large joints the most persistent symptom. In the cases investigated the white cell count was from 5,680 to 19,000 per cmm., and as well as being present in the blood, the organism was cultured from the joint fluid. Agglutinins were present in the blood of cases to a titre of 1/100. All patients recovered spontaneously, and there was no response to any therapy. A similar epidemic of 1925 involving some six hundred persons is commented upon.

It appears that either spirillum or streptobacillus is harboured as a saprophyte by many rats and some other similar animals. Strangeways[46] suggests the naso-

pharynx as the site of the infection, while other authors suggest a blood infection transmitted by abrasion of the gums at the moment of biting. As well as the present case, where the rat is described as looking old and sickly, the rats in the cases of Cruickshank[8] and Low[25] were described as being "mangy." Individual susceptibility must play some part in the development of the disease, for in the cases of Miyake,[30] Dick and Tunnicliff,[12] and Thorp,[48] one alone of the persons bitten by the infecting animal developed rat-bite fever. In the case of von Ofenheim,[51] the dog bitten by the same rat as his patient suffered for six weeks afterwards with an uninvestigated illness, as did the cat, which ate part of the rat in Thorp's case. The disease has been transmitted experimentally by rat-bite to rabbits, as recorded by Savoor and Lewthwaite,[43] and likewise rat-bite is the likely path of infection of cows' udders. Topley and Wilson[49] mention as a fact the excretion of the streptobacillus in the urine of infected mice and possibly rats, and suggest this means of contaminating milk. A dog has been infected experimentally by the spirillum, and recovered after treatment with an arsenical preparation (Ripley and van Sant[42]).

The age-limits of susceptibility appear to be extreme between the infant of four days at the time of the bite, recorded by Tunnicliff and Mayer,[50] and the man of 79 years, reported by Leadingham.[24] Colour appears no bar nor is sex any deterrent to the biter. The two cases published by Ripley and van Sant[42] were both of medical students.

The incubation period in cases following a bite appears to be from seven to twenty-one days. In this case a thirteen days' period is established. In almost every case note has been made of bleeding at the time of the bite, followed by rapid healing of the wound, although in the case of Cruickshank[8] the bitten finger was eventually amputated on account of its gangrenous condition. The healed wound appears well during the incubation period, only to show local induration and lymphatic involvement during paroxysms of fever. In the present case no local exacerbation occurred after primary healing.

The onset of general symptoms seems to have been sharp in every case. It was frequently diagnosed as influenza, and in the case of von Ofenheim,[51] as well as the present case, the patient eventually came to hospital as suspected enteric fever. The case reported by Douglas, Colebrook, and Fleming was originally admitted to a sanatorium as possible phthisis.[13] Rigors with vomiting and a moderate degree of headache are the most constant symptoms. Sweating is not recorded as profuse, and there is no mention of disturbance of sleep. Allbritten et al.[1] seek to distinguish clinically between the disease due to the streptobacillus and that caused by the spirillum, and suggest in favour of streptobacillary infection a short incubation period, joint pains, fine petechial rash, and leucocytosis. In this case the attempted clinical distinction on these points would have been completely wrong.

The prominent constant feature of the fever is the paroxysmal nature of the temperature, very suggestive of a malarial infection. In the early stages the chart shows a regular five-day cycle. Later it loses its symmetry, with longer remissions and lower and shorter paroxysms. The bacteriology of the streptobacillus suggests

a life-cycle comparable to that of the malarial parasite, and it was hoped to be able to correlate the bacterial cycle with the clinical phases of the disease. The desire to get the patient well precluded this investigation. In this case the highest temperature recorded was 106.2 at the peak of the relapse immediately following the first Myocrisin. As mentioned earlier, the rise of temperature was always more gradual than the fall, which was invariably dramatically sudden, but without gross sweating. No disproportion between temperature and pulse-rate was noted and there was no alteration in respiratory rhythm. There was nothing of note in the blood-pressure readings. Daily blood films excluded malaria, and revealed the red cells to be apparently normal and hæmoglobin was likewise unaltered. The transient fall in R.B.C. count was reasonable with the clinical course of the illness. On the two occasions upon which the spleen was palpable it was not suggestive of a malarial infection. This palpable enlargement of the spleen following a crisis suggests the possibility of this viscus being the reservoir of infection.

The outstanding blood finding in the case is the extreme degree of leucopenia, for which no parallel can be found in the literature of rat-bite fever. The lowest count recorded before is 4,400 by Reitzel.[41] Rather is leucocytosis stressed in the majority of cases with counts up to 32,000 and increased polymorphonuclears characteristic. In this case the attempt to increase the white cells by transfusion was disappointing, and it is remarkable that only with apparent recovery after Penicillin did the W.B.C. count return to normal. The differential count varied throughout and presents no diagnostic feature.

The blood sedimentation rate in this case on two occasions was within normal limits. In a case by Beeson[2] a similar finding is recorded.

The Widal reaction, giving a titre of 1/50 to B. typhosus (flagellar), was obviously false and persisted for some time, but was eventually completely negative at seventy-fifth day. No agglutination of O strain typhosus or of the paratyphoid and abortus strains occurred. No former record of this false positive Widal in this condition is to be found. Many authors report negative findings.

Savoor and Lewthwaite[43] record positive Weil-Felix reactions in the blood of rabbits experimentally infected with spirillum minus, and suggest a polysaccharide common to the spirillum and proteus OX.K, with which the test was done. In this present case the Weil-Felix reaction was negative with OX.K, OX.L, and OX.2, and it might be suggested that on this single finding his was not a spirillary infection. Allbritten[1] records a negative Weil-Felix in his streptobacillary case, as does Beeson in one of his cases. Ripley and van Sant[42] report positive Weil-Felix reactions in their two medical students with spirillary infection.

The Paul Bunnell reaction, negative on admission to hospital, was still negative at twenty-sixth day, but on repeating at seventy-fifth day was positive to a titre of 1/2,560. The development of heterophile antibodies, not claimed as peculiar to glandular fever, has not been previously noted in rat-bite fever.

There are many references in the literature to the results of serum tests for syphilis (S.T.S.) in this condition. In most cases the complement fixation tests, such as Wassermann, Harrison, Fleming, and Kolmer, are negative or faintly

positive, whereas the flocculation tests of Kahn, Kline, and Hinton are frequently positive and often strongly so. Positive S.T.S. are familiar in yaws, leprosy, malaria, sleeping sickness, and tuberculosis in rapidly descending order of frequency, and rarely in other febrile conditions.[49] Apparently the reaction can develop with either infection, streptobacillus or spirillum. In Dawson's[11] cases, both due to streptobacillus, both complement fixation and flocculation tests became positive. Beeson[2] reports of his two spirillary cases that one was Kahn negative, the other, at first negative, eventually became + +. Two of Marshall's[26] cases are recorded as + + + + Kahn, one of them with a + + + + Wassermann. (He notes a negative Mantoux in this case.) In the case of the infant of eleven days, published by Greengard and Hess,[17] the Kahn, at first negative, became + + + before death. Woolley[53] deals largely with S.T.S. findings, and reports twelve out of fourteen Kahn tests in this disease, taken after at least four weeks from infection, showing some degree of modification, and suggests that the positive reaction fades with the conclusion of adequate therapy. He suggests the greater sensitivity, and as a corollary, lesser specificity of the flocculation test as the explanation of the findings of positive Kahn with negative Wassermann. In the case under discussion, the S.T.S. is traced from negative Harrison to + +, Fleming negative throughout, Kahn + + +, and Dreyer 0.

The examination of throat and nasopharyngeal regions for the streptobacillus was suggested from Strangeway's[46] finding of the organism in these regions in rats. Likewise, the investigation of stools and urine for the organism arose from consideration of the food-borne nature of the same organism in the Haverhill outbreak. [38 39] Attempts to identify the causal organism from these sources were in vain. Allbritten,[1] in addition to negative throat and stool findings, records a negative sputum in the search for the streptobacillus.

There were no complications to record in this case. Blake[3] mentions as important complications nephritis, severe anæmia, and emaciation, whilst O'Carroll[35] described hydrothorax as a sequel. In the case of Reid and Ritchie,[40] rat-bite fever developed in a child already in hospital suffering from nasal diphtheria without aggravation of either condition. The patient was bitten before admission to hospital!

The course of the illness to recovery usually occupies months. Surveyor's[47] patient suffered for eight years, and in one other case recovery took place after seventeen years. Mortality from the disease amounts to 10 per cent. in Japan, and is probably limited to the extremes of life.

Four cases recorded respectively by Blake,[3] Greengard and Hess,[17] Pappenheimer,[37] and Tunnicliff and Mayer,[50] died and came to autopsy. Tunnicliff's case, an infant of four days old, when bitten, survived a further twenty-six days, and at post-mortem gave a growth of streptobacillus from the heart blood without any significant pathological finding. Greengard's patient of eleven days old when bitten, displayed a hæmorrhagic broncho-pneumonia at death without bacteriological findings. Pappenheimer's patient, a man of 44 years, died after four months in hospital with streptobacillus septicæmia, and post-mortem examination revealed

a vegetative aortic endocarditis with demonstration of the organisms on section of the vegetations. Blake's patient, a woman of 67 years, died after fifteen days in hospital, and post-mortem revealed an acute ulcerative endocarditis of the mitral region only, with infarts in the spleen and kidney. Culture of heart blood gave the identical organism previously cultured during life, and a morphologically similar organism was pictured, on section of the mitral vegetations.

Treatment in the past has been largely empirical, and Farrell[15] actually writes: "In cases where there was continued fever, no therapy seems to have been effectual." Spontaneous cure must occur ultimately in some cases and, in others, hitherto no remedy applied was of avail. Most cases to date have had arsenical preparations exhibited, and as early as 1913 Hata[18] recorded eight cases treated with Salvarsan. Heilman and Herrell[54] report the results of their experiments with Penicillin upon experimentally produced infections by spirillum minus and streptobacillus moniliformis. Their results are most impressive, and suggest that Penicillin will prove effective in the treatment of human infections with either spirillum minus or streptobacillus moniliformis. It is of interest that no success is recorded with sulphonamides, and the present case affords the unique occasion to report cure of streptobacillus septicæmia by Penicillin.

Summary.

A case of septicæmia due to streptobacillus moniliformis, following a rat-bite, is recorded.

Detailed clinical investigations are discussed.

Treatment of this condition with Penicillin is reported, it is believed, for the first time. Complete recovery resulted.

I am happy to acknowledge the keen interest displayed, and the enthusiastic assistance given throughout the course of the case by the staff of this hospital and of The Institute of Pathology, Belfast. In addition, the help of Major J. Oliver, R.A.M.C., with Penicillin is warmly appreciated.

The pure bacteriology of the case will provide the material for further publication by Dr. N. C. Graham and colleagues of The Institute of Pathology.

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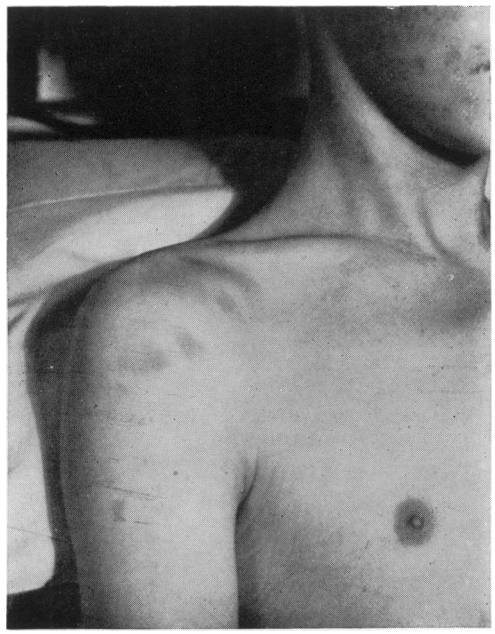

Plate I

Report on a Case of Staphylococcal Pneumonia with Staphylococcal Septicæmia

TREATED WITH PENICILLIN

By ALEXANDER JOHNSON, M.B., D.P.H.

PERSONAL HISTORY.

THE patient, a female, aged 10½ years, weighing 5 st. 6 lb., height 4 ft. 10 in., has a congenital heart lesion, recognised since birth and described below.

No disease in infancy.

Chicken-pox.

Measles and lobar pneumonia (consolidation both sides); all in sixth year.

Lobar pneumonia again at seven years.

Influenza age 8; nil since, apart from a mild catarrhal cold with no temperature, and only a few rhonchi in her chest for four to five weeks immediately prior to her present illness.

DETAILS OF THE CARDIAC LESION.

Electro-cardiograph (Dr. S. B. Boyd-Campbell) shows normal complexes (plate I). Age 6½ years. X-ray report (plate II), 11th April, 1944 :—"Heart not altered from usual outline."

SYMPTOMS.

A very loud blowing systolic murmur can be heard, with the point of maximum intensity at the sternal end of the third and fourth left intercostal spaces. The murmur is well conducted and can be heard over the entire upper two-thirds of chest, increasing in intensity as one approaches the third and fourth left interspaces in front, where a thrill can be felt on palpation. Murmur well heard up into carotids. On percussion, cardiac dulness appears to be normal. Her blood-pressure is 160/100, substantially the same as that recorded four years ago, when it was 160/90. The blood-pressure readings in either arm show a difference of 10 mm. Hg. (R. 150/100; L. 160/100).

Pulsation is visible in the interscapular region, indicating the presence of *coarctation of the aorta.*

The child leads a normal life, apart from playing no strenuous games, and at no time has shown any sign of decompensation either in health or illness.

PRESENT ILLNESS.

Began with a temperature of 104°F. There was nothing on clinical examination to account for it. Patient felt quite well and had no pain, headache, sore throat, or vomiting. During the next three days she had a total of 8 grm. sulphapyridine, but in the continued absence of any signs or symptoms by which a diagnosis could be arrived at, she was given sulphathiazole. Two and a half days later her

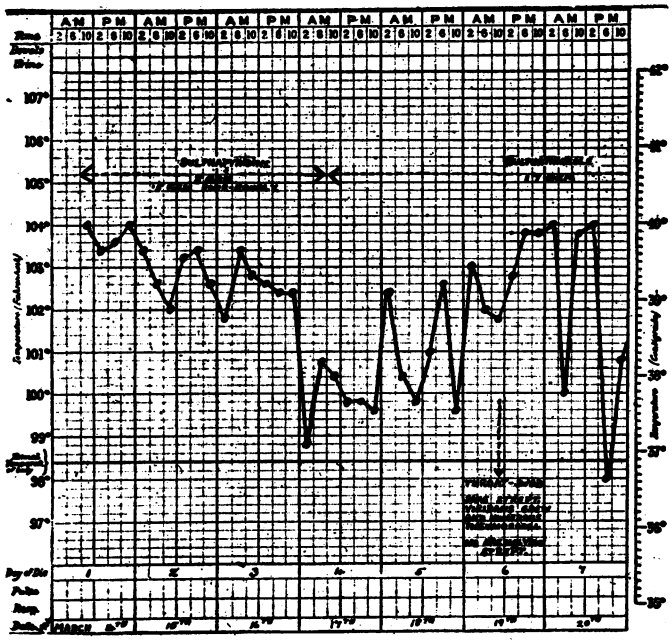

Fig. 1

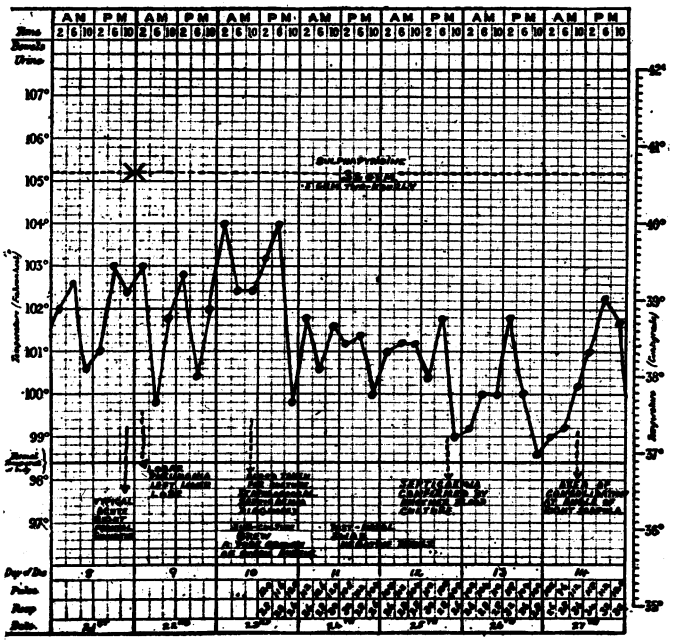

Fig. 2

condition remained unchanged, her throat swab revealed "no hæmolytic streptococci present, but quite a number of non-hæmolytic streptococci grew in company with pneumococci"; sulphathiazole treatment was continued. The first positive signs became evident two days later (eighth day of illness), when acute right frontal sinusitis developed (fig. 2), with severe frontal headache and photophobia; slight prominence of the eye, ptosis and tenderness over the supra-orbital ridge becoming evident the next day. Transillumination showed definite dulness in the sinus.

That evening (ninth day of illness), consolidation was found in the left base accompanied by a loud pleural rub. Sulphathiazole therapy was now discontinued —the total dosage given was 17 grm.—and sulphapyridine introduced again (0.5 grm. two-hourly).

Next day the pneumonia extended over the entire left lower lobe, and a blood culture was done (fig. 2). A profuse growth of staphylococcus aureus was obtained in both Hartley and Douglas media, and a pure growth of the staphylococcus aureus was found in sub-culture. There was a leucocytosis of 18,000—chiefly polymorphonuclears—no albuminuria. A post-nasal swab was sterile. No sputum could be obtained, as there was little or no cough. The diagnosis of staphylococcal septicæmia was confirmed by another positive blood culture two days later. No meningeal signs or symptoms were present, and although the temperature fell to a slightly lower plane, the patient became steadily more toxic in appearance, and dyspnœa more marked. The sinus infection, after its initial flare-up, began to recede, and in five days time had disappeared completely, there being no evidence of an inward spread to the cavernous sinus.

On the fourteenth day of illness a patch of consolidation appeared at the angle of the right scapula.

The only other signs of note at this stage were twitching of the limbs, hesitancy and confusion during speech, occasional lapse of memory, and cyanosis—all of which were probably due to the intensive sulphonamide therapy, as she had a total of 32 grm. sulphapyridine in seven days.

As the sulphonamides were not having the desired effect, there was a strong possibility of the congenital cardiac lesion becoming, if not already being, the focus of bacterial endocarditis.

The heart showed no signs of decompensation, although the condition of the patient was critical on admission to the Clark Children's Clinic on the fifteenth day of illness.

Penicillin was administered at once—initial dose 8,000 units intramuscularly (fig. 3), followed by 4,000 units three-hourly. The first sample of sputum was obtained the next morning, and grew a pure growth of staphylococcus aureus. Blood culture, taken after 56,000 units of Penicillin (fig. 3) had been given (thirty-six hours treatment) showed :—

First bottle clear—nil on sub-culture (blood agar).

Second bottle—staphylococcus aureus on direct examination and a good growth on sub-culture.

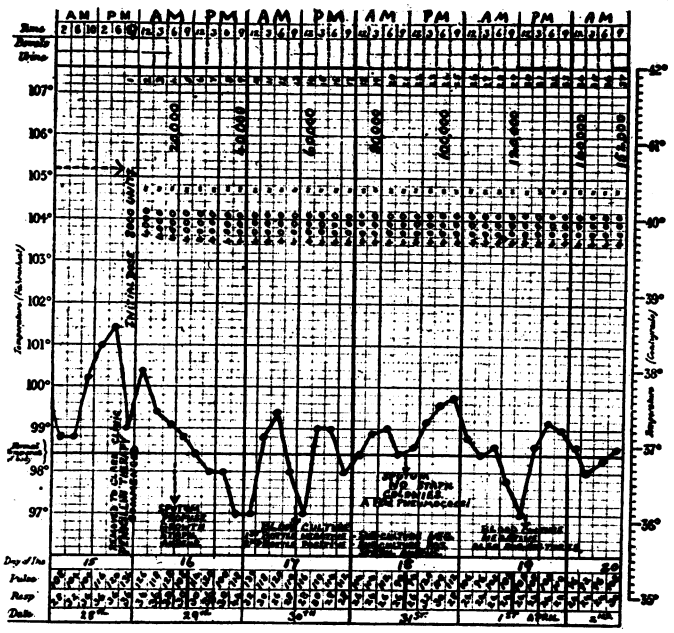

Fig. 3

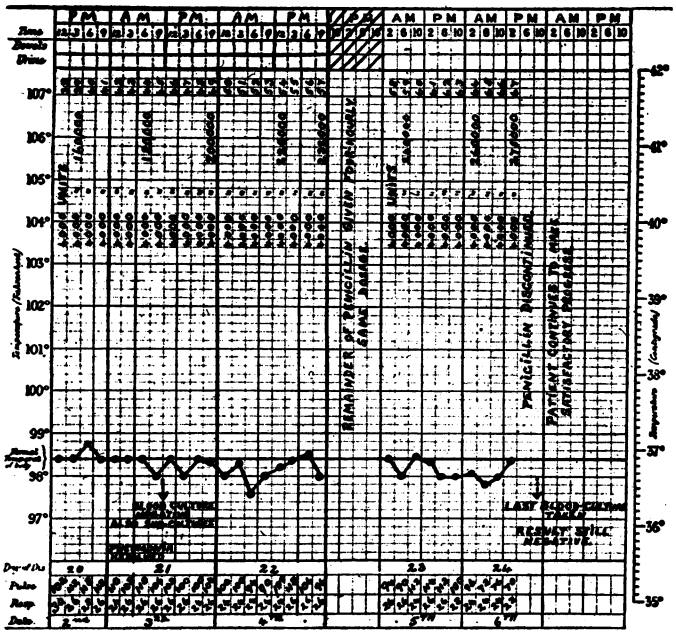

Fig. 4

On the third day of treatment—after 88,000 units of Penicillin—a sample of sputum showed *no staphylococcal colonies* (fig. 3), and patient's condition was improving rapidly.

On the fourth day—after 120,000 units of Penicillin—*blood culture was negative* and negative on sub-culture.

Two days later pneumonia disappeared from both sides (fig. 4), not by the gradual type of resolution by "lysis," but rapidly, as would be expected in "crisis" —the change over to normal breath sounds taking about twenty-four hours.

After six days' treatment—180,000 units—another negative result was obtained from blood culture.

When 232,000 units of Penicillin had been administered—eighth day of treatment—the last ten injections were given four-hourly, and concluded thirty-eight hours later—total of sixty-seven injections (fig. 4).

Eight hours after the last injection, another blood sample was cultured, and a negative result obtained.

Her total dosage was 300,000 units, although 275,000 is the figure given on diagram. The discrepancy is accounted for by the fact that in giving 1 c.c. per injection (100,000 units were dissolved in 25 c.c. sterile distilled water), a few extra minims were usually included.

Seconal $\frac{3}{4}$ gr. was given as a sedative eight-hourly during treatment and, together with ice-pack, was fairly effective in counteracting the pain which followed immediately after each injection, and in overcoming the restlessness associated with her toxæmia.

I am indebted to Dr. N. C. Graham of the Department of Bacteriology, Queen's University, Belfast, for the following investigations :—

Twenty-four hours after treatment with Penicillin was instituted, a sample of urine was tested by Fleming's "hole method" on an agar plate.

A dilution of urine 1 :100 inhibited staphylococci, and produced a ring 24 mm. in diameter.

The same sample caused complete inhibition in 1 : 640 when tested by serial dilution.

Other samples collected during treatment caused similar inhibition, even though the urine was more dilute, as patient was taking fluids in much more liberal quantities.

The first blood sample taken was thirty-six hours after treatment was commenced—56,000 units of Penicillin—and two and a quarter hours after the thirteenth injection. It was tested by the "slide cell" method in dilutions of 1 : 1 to 1 : 8. The result was a more marked inhibition of the staphylococci isolated from the patient's sputum than of a staphylococcus from a stock strain, but complete inhibition was not obtained in a dilution of 1 : 1 as compared with normal serum.

The second blood sample was obtained eighty-four hours after treatment was instituted—120,000 units of Penicillin—and one and a half hours after the twenty-ninth injection.

The result was almost complete inhibition of the staphylococcus strain.

Using the "hole method," no inhibition could be demonstrated by the patient's sputum or serum, as the test is probably not delicate enough.

X-ray report of antra and accessory air cells, 11th April, 1944 (five days after cessation of Penicillin treatment), shows nil abnormal.

X-ray chest (plate II), 11th April, 1944, report :—"Old infection of chest. Several heavily calcified foci on right side. Does not seem recently active."

The patient's progress is continuing satisfactorily.

I am indebted to Dr. J. A. Smith for the original diagnosis of staphylococcal septicæmia, and for the subsequent blood culture and sputum reports; and to Dr. N. C. Graham for his interest and reports; also to Dr. F. M. B. Allen for his supervision and advice during the patient's stay in the Clark Children's Clinic. No words of gratitude are adequate to the donors of the Penicillin, who must remain anonymous.

REVIEWS

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It seems a pity to begin such an ambitious little book with the statement that "The beginning of the study of medicine should be the consideration of the end of life." The whole trend of modern medical thought is precisely in the opposite direction.

The work is intended for "students and others interested in laboratory work," but by far the greater number of tests described are quite outside the province of a medical student's curriculum, and, on the other hand, the simple tests with all their possible fallacies, together with the accurate and strictly detailed technique necessary for their performance, are not explained with the clarity essential to the training of a student. Nevertheless, there is a great deal of valuable information contained in the pages of this small and very reasonably-priced book. It is too highly technical to make an appeal to the average clinician, but the young clinical pathologist will find a place for it on his shelves. He will probably not agree with all the author's statements and may dislike some of his terminology, certain obvious errors will catch his eye, but in the main the wide scope of the book will appeal to him, and he will feel that he has had very good value for his money. The book itself is well produced and compares very favourably with other war-time publications. E. M. H.

AIDS TO MATERIA MEDICA. By G. H. Newns, M.D., M.R.C.P. Third Edition. Pp. 211. Baillière, Tindall & Cox. 6s.

This is an excellent little book and can be confidently recommended to all medical students. It should also be of use to the average doctor, who is often glad to refresh his mind as to the action and doses of the less familiar drugs, and it would also enable him to keep his knowledge of the newer preparations up to date. Penicillin, however, has not been included in the text.

The book is well and clearly written, nowhere verbose, and never difficult to understand. The printing and spacing of paragraphs are remarkably good, making it an excellent volume for quick reference. The arrangement of the chapters appeals at once to common sense. It is much superior to the average war-time product and is very good value. E. M. H.

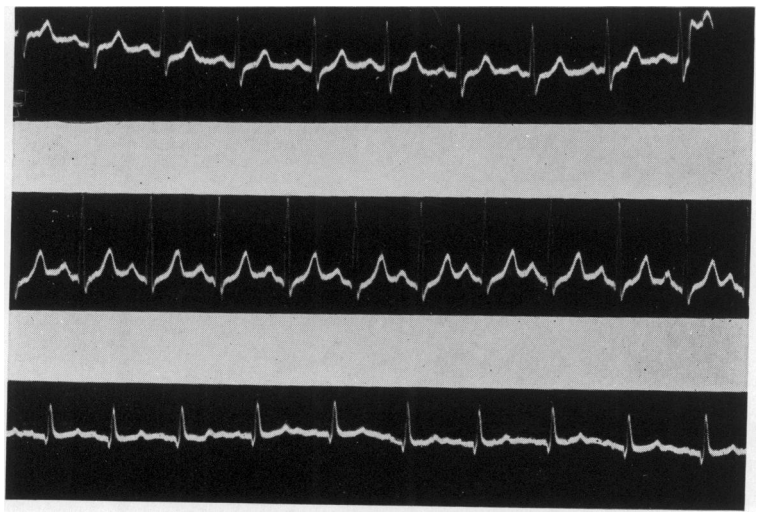

Plate I

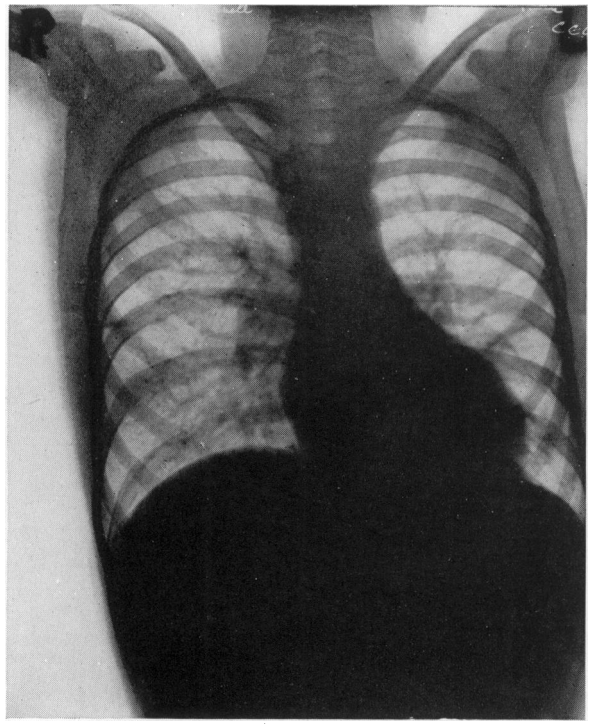

Plate II

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Forward Surgery

By IAN FRASER,

D.S.O., O.B.E., M.D., M.CH., F.R.C.S., F.R.C.S.I., F.A.C.S., F.R.S.EDIN., BRIGADIER A.M.S.

MANY articles have appeared on Forward Surgery, but mostly written by writers from their own points of view and dealing with scientific problems more often than with administrative ones.

The following is just an unconnected story of affairs as the writer found them.

HOURS OF WORK.

It took some time before agreement was reached on this subject. Many surgeons consider sixteen hours operating, with eight hours sleep, gave the maximum output: others preferred twelve hours work with twelve hours sleep. Finally, it was agreed that eight hours on and eight hours off, these times strictly adhered to, gave not only the maximum, but also the most efficient turnover, and this rate of work could be kept up indefinitely. At the end of sixteen hours continuous operating, the best work was not being done. Long spells of twenty-four, forty-eight, or seventy-two hours, which can be done in isolated incidents, are not practical when casualties may come in for days and weeks on end. This is a great contrast to the home air-raids, where the volume of work for a period may be severe, but usually one can see a rest period somewhere ahead. Food, and particularly tea, must be in constant readiness. Tea seemed to be equally appreciated in the heat of the desert or in the snows of Italy.

If the above held good for the surgeon, it applied even more so to the orderlies, who tire more quickly. The surgeon makes his own pace and is fully distracted by his work. The principle of having one orderly arriving early to get sterilizers, etc., working, and also naturally going off duty early, and another arriving late, but remaining afterwards to leave the place tidy, was found to be a great help. One felt that it was quite unfair to do a large surgical list, then walk off to rest, leaving the orderlies to get the place cleaned, and yet expect them to be on duty the next morning at the right time.

SELECTION OF CASES.

This was partially carried out by the surgeon prior to starting his operating session, but often a more serious case arrived later, and the decision then was usually made by the anæsthetist or the field transfusion officer. To keep operating upon serious cases gets tiring, and to alternate with a small case is a rest for all, particularly for the orderlies, who can get time to sterilize the main instruments while the small case is being operated upon with the debridement set of "knife, fork, and spoon."

A constant eye must be kept upon the pre-operation ward or tent to see that the waiting-list is not mounting up. If it is only five to ten hours to the next operating centre, it is unfair to hold cases whose turn for operation will not be less than twenty-four hours if retained. If the pre- and post-operative patients

who require resuscitation and transfusion are kept together, it is a great help, as it means that the transfusion officer has all his work centralized, and a quick visit can be paid by the surgeon between cases.

Notes.

On the field card notes must be kept carefully—the man's future treatment, his pension, or his widow's pension claim may depend upon them. The anæsthetist or one of the orderlies often writes more legibly than the surgeon. A rubber stamp with the necessary headings standardized gave good results—"Time of injury," "Site," "Missile," "Time of operation," "Complications," etc. Notes on the plaster of paris—plastograms—proved valuable, provided they were not written over the site of injury, which later became illegible from bloodstains. Forehead notes—theoretically a good idea—in practice did not always prove very valuable, as with sweating, dust, and a tired soldier rubbing his brow, little could often be made of them. The red-edged label around the neck showed times and quantity of sulphanilamide tablets, which were taken at 08.00 and 18.00 hours daily, proved very valuable. It ensured that, no matter where the casualty was on the lines of evacuation, he was sure of getting his required sulphanilamide dosage. The ship's envelope was specially marked, when necessary, with the appropriate coloured sticky label, if the case was to go to a special centre, such as "head," "chest," "facio-maxillary," etc.

Morphia.

There has been some misunderstanding in the use and value of morphia, but one thing is clear, and that is that with the shocked patient in pain, morphia must be intravenous, not intramuscular or subcutaneous. One often found that several injections had been given at intervals without effect, and then with resuscitation and transfusion, sudden overdosage occurred, as with the recovery of the circulation the morphia became absorbed.

Operating Theatre.

It is not the purpose of this article to give technical details, but it was found that two or three tables in the theatre at the same time prevented a delay. At table 1 the surgeon was working: at intervals the anæsthetist could examine case 2 as regards site of wound, blood-pressure, physical examination, and choice of anæsthetic. During this time the orderlies are bringing in case 3, getting him shaved carefully and comfortably placed for the operation, and verifying the question of micturition, dentures, etc. This allowed a smooth flow of cases and prevented the not uncommon sight of a case being hurried into the theatre, dumped on the table, whilst the anæsthetist and surgeon, competing with orderlies and stretcher-bearers, are pushing their way in to find the extent of the damage. The table itself in all cases was the plain army pattern, and in the forward area the patient was always left upon the stretcher. This also allowed a careful and gentle removal of the patient back to the post-operative tent, and prevented the orderlies in the rush and black-out from tripping over the tent-ropes and tossing on the ground the patient after a serious operation. It was found that first priority cases

(abdomens, etc.) took an average one hour and ten minutes, i.e., twenty cases in twenty-four hours, and the smaller cases fifteen to twenty minutes each.

X-Rays.

The mobile X-ray van was available with most forward units, and when required the surgeon had usually the wet film at time of operation. In many cases an X-ray was not considered necessary by the surgeon, whereas with others, e.g., the F.B.'s that had entered by the buttock, the final site of the F.B. was of paramount importance.

Transfusion Unit.

The mobile field transfusion unit with lorry and frigidaire was the greatest single life-saving factor. These units were filled up daily from the base with fresh blood, and the supply was always adequate. The transfusion officer could and did act at times as spare surgeon, anæsthetist, or triage officer, in addition to his main work of resuscitation. The unit carries all transfusion fluids in addition to fresh blood, its substitutes, and now has Penicillin in solution.

Transfusion Fluids.

Blood in forward areas is the fluid of choice. The battle casualty has usually lost a considerable quantity of blood, differing from certain air-raid casualties, where crushes and damage from bricks and mortar are the commonest injuries. There is no such thing as "a pint of blood." If a man only needs a pint of blood, he only needs a cup of tea! This is too obvious to require elaboration. Three, four, or five pints were the average quantity of blood and/or substitute at the most forward operating centres, and two, three, and four at the next point further back. For the strong soldier whose main disability is blood-loss, blood replacement cannot be too fast. First pint in five minutes, second pint in ten minutes, and the third pint in twenty minutes. A good heart muscle will stand up to this, and there are few, if any, reactions. With the war-wounded casualty at the base, the converse holds good; it is difficult to give whole blood sufficiently slowly—reactions, rigors, etc., were much more common and more serious. Saline was quickly reduced from normal .9 per cent. to half strength, and this has since been reduced further to one-third, as with continuous saline transfusion, œdema was found to develop from salt retention. With loss of chlorides by continuous gastric suction, however, intravenous saline replacements must take place. If nourishment could not be taken orally, then glucose 5 per cent. and plasma for its protein content and osmotic pressure value was given. For burns in the early stages with a hæmo-concentration, due to serum loss, plasma was the best replacement. Double-strength plasma, i.e., dried plasma, with half the normal quantity of fluid diluent, has not given conclusive proof of preventing the excessive exudate in extensive burns. As the sternum will absorb only a limited amount of blood slowly, so it has no value in forward surgery where massive and rapid blood replacement is required. At the base it can serve a valuable purpose. Saline absorption is more rapid, but it is doubtful if it offers any advantage over the old method, sub-cutaneously into the breast and axilla. For intravenous fluids, one should avoid

the flexures. The flat surface of leg, forearm, or arm do not limit joint movements and allow the needle to be strapped "in situ"; also it leaves the ante-cubital vessels for the anæstheist if necessary later. The value of blood or fluid transfusions in the case of diseased or injured lung must be carefully considered, and transfusion not started light-heartedly without thinking of the possible consequences—pulmonary œdema, etc.

Gastric Suction.

All abdominal injuries were put on continuous gastric suction as a routine. A Ryle's tube, Jacque's tube, or transfusion tubing, was all that was necessary. Suction was achieved by reversing the action of the army transfusion bottle. As the fluid from the bottle dripped into a bucket, the gastric contents filled the vacuum left behind. It worked very well. It prevented gastric and intestinal distention, took the strain off the newly-sutured areas, and, if fluid was replaced intravenously pari-passu, the patient was very comfortable and free from the distressing vomiting and distention often present with even a minor abdominal operation. The most fastidious will swallow and almost enjoy a Ryle's tube if allowed to suck an Anethine tablet first. Suction at the time of operation can be improvised by reversing the valve in a motor-tyre foot-pump.

Amputations.

As in rugby, the slogan was "go slow," and so leave room for the final definitive site. In all cases two small flaps were left, not sutured, but just loosely held to prevent retraction. The guillotine operation was not used unless in the rare case of amputation through the knee joint.

Conclusions.

As one who qualified after the last war and was trained in the surgical methods that evolved from it, the most striking contrasts that one notices are:—

(1) *Primary excision* and suture, which at that time was the main aim, is now entirely discarded, and wounds are left open and excision of the damaged soft tissues of the wound carried out with minimum trimming of the skin. This has proved an advance beyond doubt, and it has again been proved in recent casualties, when in one or two E.M.S. hospitals wounds were again sutured with bad results.

(2) *The septic wound* in 1914-1918 was left as an open gutter and with elaborate glass and rubber connections, Carrel Dakin irrigation with Eusol was carried out, either continuously or intermittently, thus causing pain, discomfort, etc., to the patient, wastage of multiple dressings, and much consumption of time and energy on the part of medical officers and dressers. The alternative now of occlusion of the wound in plaster of paris has saved pain to the patient, dressing materials, and time of those in charge, and has aided in evacuation.

(3) *Vaseline gauze,* with the inevitable swing of the pendulum, has now reappeared as the dressing of choice, where a non-adhesive dressing which keeps the wound open and yet allows free escape of serum or pus is necessary. Daily

dressing of the septic wound is no longer necessary, and it was found at the base hospital that the cases least frequently examined were the least heavily infected. This refers chiefly to infection with streptococci, which rarely go in with the missile, but are the result of human contamination—usually throat of patient, orderly, or medical officer.

(4) *Blood transfusion* has been superb—unlimited in quantity and foolproof in its simplicity. If the patient is not killed outright through immediate loss of blood, it is unlikely that he will die from lack of available blood. For such cases the forward surgeon has found that plasma is not a substitute, and that although the patient may be resuscitated medically, he is not necessarily in a suitable state to stand further surgery.

(5) *Sulphonamides,* especially by the oral route, have lengthened the safe period of delay before operation and cases have arrived back, untreated in the forward area, in which the absence of spreading infection in the wound can only be credited to the level of sulphanilamide in the blood. Its value as a local wound antiseptic is yet far from proven. Penicillin, if judiciously used with Penicillin sensitive organisms, is an epoch-making advance.

(6) *Gastric suction* used by all as treatment for distention, ileus, etc., for several years, is now used as a preventative of such complications. It gives physiological rest to the upper abdominal contents and relieves dangerous tension from the newly-sutured area.

(7) *Colostomy* is the absolute routine for all colonic injuries. It certainly has prevented the delayed intra- or extra-peritoneal leak, so fatal in the last war. Dividing the anal sphincter or stretching it has little to be said for it. Succinyl sulphthiazole has rendered the closure of the colostomy a procedure almost unattended with risk.

(8) *Mobile forward surgical teams.*—In this war the policy has been to bring the surgeon forward to the patient, rather than transport back the wounded man to the fixed operating unit. This has naturally saved many lives. It has resulted in certain cases being operated upon, which would not have stood the journey over difficult country. It has influenced some surgical statistics in an unexpected way, in that before only the cases that survived the journey were operated upon, whereas now, in certain hopeless cases, a forlorn chance is taken, which may adversely affect the statistics of the surgeon who is out to have a low mortality-rate, and previously refused to take a chance.

(9) *Evacuation.*—In the forward area and in mountainous areas the jeep could go where no other motor transport was safe, and saved the tedium of stretcher-bearers and the jolting of the mules. This proved particularly useful in Italy and in certain mountainous regions in Sicily. In the Sicilian campaign some sixty thousand cases were evacuated by air to the base. It must be remembered that it is a measure of expediency rather than necessity, in other words the man who

cannot stand an ambulance or other normal evacuation method will not stand air transport. High flying must be avoided in chest cases, cerebral cases, and post-operative abdomen cases. The writer, having been evacuated by this method, found it rapid but not comfortable, nevertheless it proved invaluable for the case which must reach a special centre for specific treatment in a given time.

REVIEWS

MODERN TREATMENT IN GENERAL PRACTICE YEAR BOOK 1944. Edited by Cecil P. G. Wakely, C.B., D.Sc., F.R.C.S., F.A.C.S., F.R.A.C.S. Pp. 211. The Medical Press and Circular, London, W.C.2. 15s.

THE title might suggest a résumé of recent advances in treatment. However, the volume contains forty-two articles by well-known authorities on the diagnosis and treatment of a wide range of medical and surgical conditions.

It is divided into two equal sections, the first dealing with diseases commonly encountered by the family doctor, and the second with war medicine and surgery. One read with pleasure the articles on coronary artery disease, carcinoma of cervix, vaginal discharge, ulcerative colitis, and malaria. These are written with lucidity and crispness of style admirably suited to the busy practitioner, who believes that medical authors should "write the vision, and make it plain upon tables, that he may run that readeth it."

In the second section the articles on ocular injuries, injuries of the large intestine, war wounds of the abdomen, and wounds of the head call for special mention.

This book is well produced, the type is large and clear, there are some excellent illustrations and a useful index. W. F.

DISEASES OF THE NOSE, THROAT, AND EAR. By I. Simson Hall. Third Edition. Edinburgh: E. & S. Livingstone Ltd. 15s.

WE welcome the appearance of the third edition of this admirable textbook for undergraduates and general practitioners. It has been thoroughly revised and brought up to date, additional diagrams and plates have been included.

The Appendix includes a concise chapter on the uses of sulphonamides in nose, throat, and ear diseases. It is pointed out that constant additions to this group of drugs make it impossible to standardise dosage and treatment, but certain principles are laid down to act as a guide. This has been very well done.

The chapter on tracheotomy states that "The anæsthetic of choice is local anæsthesia, but occasionally chloroform may be used." It is not pointed out that chloroform is definitely contra-indicated, if there is any obstruction to respiration.

In the paragraph entitled "Symptoms of Intrinsic Cancer of the Larynx," only one symptom is described, namely hoarseness, and great stress is laid on the fact that every patient who has suffered from hoarseness for a period of three weeks, without improvement, should have his larynx examined by a competent laryngologist. The addition of any other symptoms would mean that the condition was no longer intrinsic, and so the time for curative treatment would then be past. This could not be reiterated too often.

We have no hesitation in recommending this textbook to all students and practitioners. K. H.

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In the paragraph entitled "Symptoms of Intrinsic Cancer of the Larynx," only one symptom is described, namely hoarseness, and great stress is laid on the fact that every patient who has suffered from hoarseness for a period of three weeks, without improvement, should have his larynx examined by a competent laryngologist. The addition of any other symptoms would mean that the condition was no longer intrinsic, and so the time for curative treatment would then be past. This could not be reiterated too often.

We have no hesitation in recommending this textbook to all students and practitioners. K. H.

cannot stand an ambulance or other normal evacuation method will not stand air transport. High flying must be avoided in chest cases, cerebral cases, and post-operative abdomen cases. The writer, having been evacuated by this method, found it rapid but not comfortable, nevertheless it proved invaluable for the case which must reach a special centre for specific treatment in a given time.

REVIEWS

MODERN TREATMENT IN GENERAL PRACTICE YEAR BOOK 1944. Edited by Cecil P. G. Wakely, C.B., D.Sc., F.R.C.S., F.A.C.S., F.R.A.C.S. Pp. 211. The Medical Press and Circular, London, W.C.2. 15s.

THE title might suggest a résumé of recent advances in treatment. However, the volume contains forty-two articles by well-known authorities on the diagnosis and treatment of a wide range of medical and surgical conditions.

It is divided into two equal sections, the first dealing with diseases commonly encountered by the family doctor, and the second with war medicine and surgery. One read with pleasure the articles on coronary artery disease, carcinoma of cervix, vaginal discharge, ulcerative colitis, and malaria. These are written with lucidity and crispness of style admirably suited to the busy practitioner, who believes that medical authors should "write the vision, and make it plain upon tables, that he may run that readeth it."

In the second section the articles on ocular injuries, injuries of the large intestine, war wounds of the abdomen, and wounds of the head call for special mention.

This book is well produced, the type is large and clear, there are some excellent illustrations and a useful index. W. F.

DISEASES OF THE NOSE, THROAT, AND EAR. By I. Simson Hall. Third Edition. Edinburgh: E. & S. Livingstone Ltd. 15s.

WE welcome the appearance of the third edition of this admirable textbook for undergraduates and general practitioners. It has been thoroughly revised and brought up to date, additional diagrams and plates have been included.

The Appendix includes a concise chapter on the uses of sulphonamides in nose, throat, and ear diseases. It is pointed out that constant additions to this group of drugs make it impossible to standardise dosage and treatment, but certain principles are laid down to act as a guide. This has been very well done.

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The Pyloric Canal

By James Wilson Millen, M.D.
Department of Anatomy, Queen's University, Belfast

There is now a considerable agreement in the general descriptions of the form, subdivisions, and functions of the stomach. It is a specialised organ of the post-œsophageal region of the fore-gut, limited distally by the pyloric sphincter; and it serves for the temporary storage of the swallowed food, which undergoes changes in its physical constitution during its storage. These changes are produced (1) by physical processes, such as the saturation of the food with fluids and its physical comminution and division, which have as their end the trituration and suspension of the food in fine granular form in the stomach fluids; and (2) by chemical processes, at least they are usually so named, which begin the gross molecular disintegration of the food, and are steps leading to its solution.[1]

The fluids used in the physical processes are products of the gastric mucous membrane, while the physical division of the food is mainly effected by the pressure movements of the muscular wall of a part of the stomach, which is always recognisable and usually is a distinct region of it. This region is generally known as "the mill of the stomach"; the musculature of its walls is thicker, usually it is specialised in its arrangement and often it is distinctive in its structure; and its

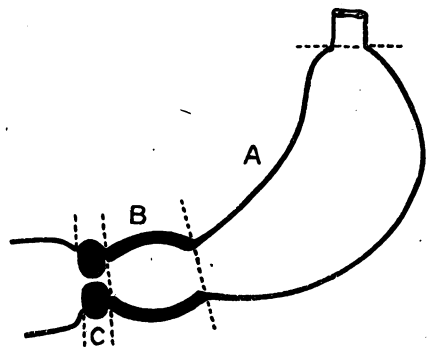

Fig. 1
The primary parts of the stomach.

mucous membrane is usually different from that of the receptive "non-milling" region, sometimes grossly so, sometimes only in the type of its glands. The "milling region" is always at the distal end of the stomach, immediately previous

1. I am not now concerned with the discussion of which processes are phylogenetically the older or fundamentally the more important; or of the different forms of "the reciprocal balance" of the two processes in different animal groups, so that now the one process and now the other plays the larger part in the food changes; or of the relation of this balance to the nature of the food and the treatment to which it is subjected in the mouth.

to the terminal "storage closure mechanism," the Pyloric Sphincter. There are, therefore, when its physical functions alone are considered, three distinctive parts of the stomach (fig. 1) :—(a) The purely receptive storage non-milling region, into some part of which the œsophagus opens, the Body or Cardiac Part; (b) the active 'milling' region, the Pyloric Part or, since it is commonly tubular in shape, Pyloric Canal; and (c) the terminal Pyloric Sphincter, which, by its tonic and active contraction, maintains the storage in the whole stomach and, especially, prevents the escape of the food while it is being milled in the pyloric canal.

This description of the stomach is essentially that of Willis (1674), who, apparently, was the first to describe the most distal part of it as a distinct region; he named it the Antrum (to the pylorus). It is now generally named the Pyloric Canal, and is considered, with the Pyloric Sphincter, to constitute the Pyloric part of the stomach; and to this part there is ascribed not a simple storage function, as for the cardiac part, but the final physical reduction of the food to a fluid pulp and, through its sensitiveness to food masses not so reduced, the retention of the food by the pyloric sphincter until the reduction is completed. It is as such I propose to consider it, a distinctive independent part, structurally differentiated and functionally specialised; as Cunningham (1906) stated of it, "There is no part of the organ which is more definite and distinct." It is therefore a constant and

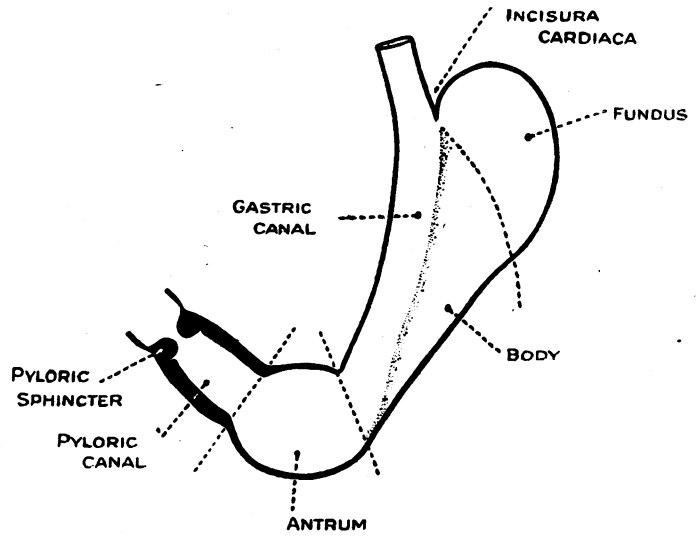

Fig. 2
The divisions of the human stomach.

remarkably uniform region in comparative anatomy, sometimes longer, up to one-third the total length of the stomach (as in some elasmobranchs and the six-months human fœtus), sometimes very much shorter (as in the adult human and most carnivores).

The body, or Cardiac Part, of the stomach varies much in its size and form;

sometimes it seems a single simple sac (as in rodents), sometimes it is a series of distinct chambers (as in ruminants). I believe, however, that three parts of it can usually be distinguished, and that as a rule they can be recognised in the human stomach (fig. 2) :—(a) the Body (or body proper) of the stomach is the part into which the œsophagus directly opens. It consists of two regions: (1) the Gastric Canal, which continues the canal of the œsophagus along the lesser curvature of the stomach and ends below in the antrum; the musculature of its wall, especially of its lower edges, is thick; and (2) a dilatable region below (to the left of) the gastric canal, for the reception and storage of food after the antrum has been filled. (b) The Antrum or Vestibule (to the pyloric canal) is the terminal part of the cardiac part of the stomach; in the literature both names are used for it, even though antrum was applied by Willis to what is now known as pyloric canal. The antrum, the first filled part of the stomach, is directly filled from the œsophagus along the gastric canal. It forms the lowest part of the human stomach; usually it is marked off from the pyloric canal by upper and lower grooves (*sulci intermedii superior et inferior of His*), and between it and the ending of the gastric canal there is the incisura angularis on the lesser curvature and sometimes (especially in the empty stomach) a notch on the greater curvature. (c) The Fundus is a diverticulum, to the left of the œsophageal orifice, from the lower dilatable storage part of the body of the stomach with which is its normal communication. It is shut off from the œsophagus and the gastric canal in the contracted stomach by the septum of the incisura cardiaca and the muscular wall of the upper end of the gastric canal,[2] but in the relaxed distending stomach it has communication with them.

It is to the pyloric part of the stomach, the pyloric canal, however, that I wish to direct attention. It is easily recognised and defined, in at least two-thirds of dissecting-room subjects and apart from the state of contraction or relaxation of the stomach, as a tubular part about 3 cm. in length, beyond the antrum and previous to the pyloric sphincter. It has a much thicker muscle wall than the parts of the cardiac part of the stomach, even than the gastric canal, and its mucous membrane is in longitudinal folds along its whole length. It has its blood supply from the right gastric and right gastro-epiploic arteries, branches of the hepatic artery, a supply distinct from that of the cardiac stomach, which is from the left gastric, splenic, and left gastro-epiploic arteries; its veins and lymph vessels are also distinct; and its nerve supply, at least from the anterior gastric nerve, is by special branches. In the fœtus and the new-born it forms a relatively larger part of the stomach (fig. 3), and the musculature of its wall is relatively thicker.

The canal can be demonstrated in the living subject by giving a small amount (℥ ss - ℥ i) of a thick suspension of Ba. (Horlick's shadow food) on the empty stomach; my best results were obtained on young adult male subjects in the early morning. The meal passes along the gastric canal to the antrum, which fills and increases in size by expansion downwards and to the left; and relief pictures of

2. It is the maintenance of this closure, I believe, that constitutes some forms of 'cardiospasm.'

these parts may be secured. By manual pressure and manipulation over the antrum, the work being done under the screen, some of the meal can be made to enter the pyloric canal; a radiogram taken at this stage is shown in plate I. The pyloric canal appears as a tubular region about 3 cm. long, distal to the antrum and ending at the pyloric sphincter, and the longitudinal folds of its mucous membrane are shown in relief. The passage through the pyloric sphincter is closed, but a small amount of the meal has reached the duodenum, and is seen on the front of the body of the second lumbar vertebra; the pyloric sphincter must have been relaxed, therefore, at some time while the canal was filling.

The pyloric canal is rapidly filled when a large amount (℥ vi) of the meal is given (plate II); its cavity loses its tubular form, apparently very readily, and becomes spherical and remarkably large; there must be a considerable relaxation of its muscular wall. There is, at the same time, some relaxation of the pyloric

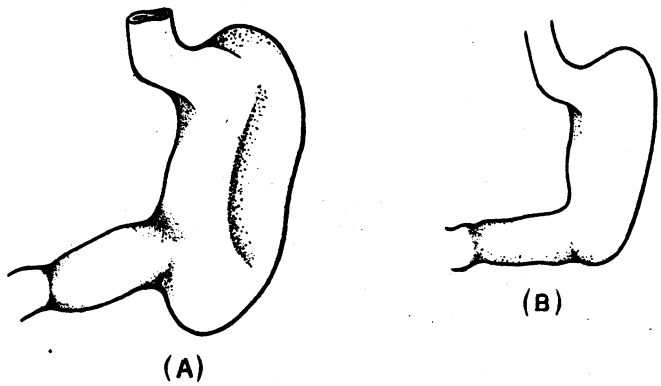

Fig. 3

The stomachs of (a) seven-months human fœtus and (b) five-months fœtus.

sphincter, and some of the meal passes through it into the duodenum, so that the amount in the duodenum is increased (cp. plates I and II) (the upper edge of these regions is artificially outlined in plate II); there is in plate II a narrow connecting shadow between the masses in the pyloric canal and the duodenum.

The pyloric canal having been filled,[3] it begins the movements of its "milling" function. These movements are distinctive of the canal and, as seen on the screen, different from those of the cardiac stomach, which end at the lower end of the antrum. They consist of concentric contractions of the pyloric canal wall, sometimes termed pyloric canal systole, whereby the cavity of the canal is concentrically diminished in size until finally it is, for a short time, completely empty (plates III and IV).[4]

3. The canal becomes even slightly more full, and larger, than in plate II.

4. I was unsuccessful in this subject in 'timing' the change from screen to film exactly enough to record the completely empty canal at the end of canal systole; but I reproduce, with permission, a tracing of this phase of canal activity from fig. 84 of "A Text-Book of X-Ray Diagnosis by British Authors" (1938).

It is well shown in plate III that during the systole of the canal, the pyloric sphincter is fully contracted and the passage through it completely occluded; that is, that during its systole the food is returned from the pyloric canal to the antrum and body of the stomach, which are increased in size. There is also some opening of the œsophageal orifice and a sharper definition of the fundus region; and, further, the duodenum, contracting with the pyloric canal, has altered the shape of the duodenal 'cap' to an elongated mass and defined very accurately the distal surface of the pyloric sphincter.

When the food is sufficiently "milled" and the stomach is to be emptied, the "milling" function of the pyloric canal must cease; the pyloric canal must become

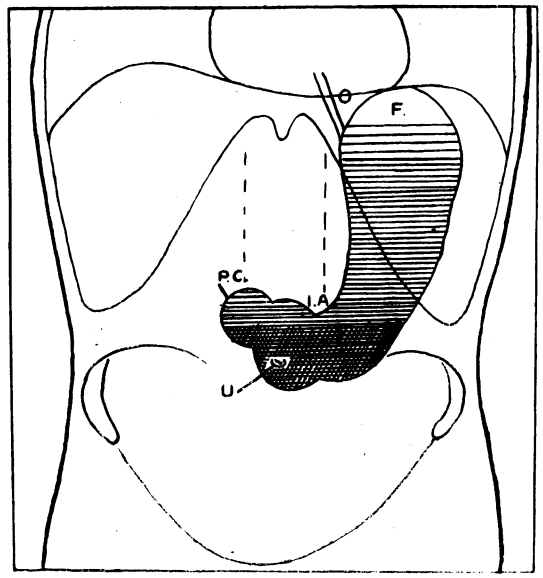

Fig. 4

Normal stomach in vertical position (from Hertz).
O—end of œsophagus; F—fundus of stomach, containing gas;
I.A.—incisura angularis; P.C.—pyloric canal; U—umbilicus.

functionally associated with the cardiac part of the stomach; and, the whole stomach acting as a single emptying mechanism, the movements of the two parts must become harmonised.[5] I am not now concerned with this phase of pyloric canal function, for in this paper I have wished only to define the pyloric canal and to recognise it as a distinctive part of the stomach; and, if this description is accepted, to make a plea for the recognition of it in the literature, especially of physiology and radiology. Best and Taylor (1939) and Bard (1941), for example, describe the pyloric canal as a narrow passage 3 cm. long, forming the lumen of the pyloric sphincter, and Hertz (1910), whose account is followed by Starling

5. Congenital pyloric hypertrophy (of the pyloric canal) is, I consider, the result of the non-association of the two parts and the non-harmonising of their movements as a single emptying mechanism.

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I suggest that antrum be the name of the most distal chamber of the 'non-milling,' storage, cardiac part of the stomach, pyloric canal the name of the distinctive and specialised terminal 'milling' part, and pyloric passage the short passage through the pyloric sphincter; these are the recognised anatomical terms.

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THE MEDICAL ANNUAL, 1944. Editors: Sir Henry Tidy, K.B.E., M.D., F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S. Pp. 404. John Wright & Sons. 25s.

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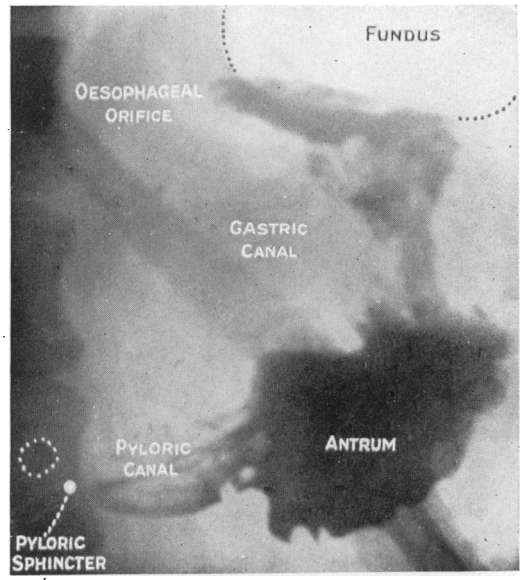

Plate I

The pyloric canal in a young adult: ʒ i of Horlick's shadow food given at 8.15 a.m., on an empty stomach.

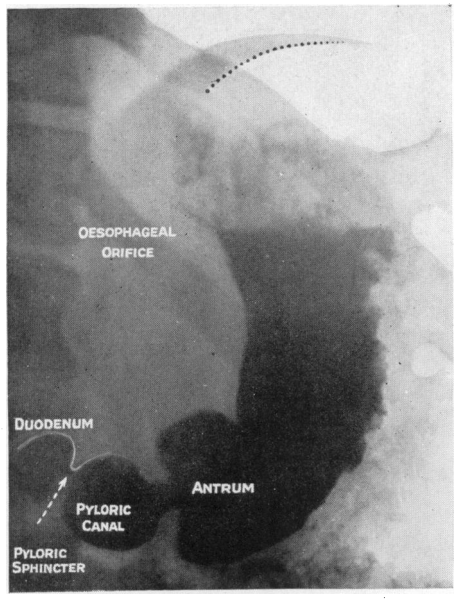

Plate II

The filling of the pyloric canal after ʒ vi of meal: same subject as Plate I: upright position.

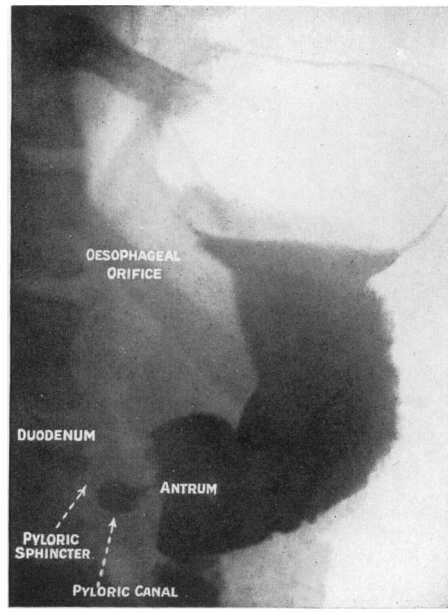

Plate III

Systole of the pyloric canal: same subject as Plates I and II: upright position.

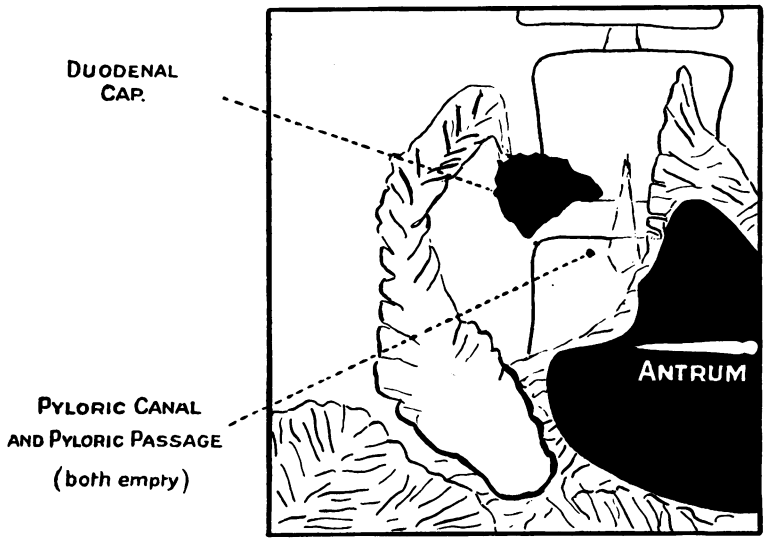

Plate IV

A tracing from fig. 84 of "A Text-book of X-Ray Diagnosis" (with permission), to show the empty pyloric canal at the end of pyloric canal systole.

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Suppurative Pancreatitis

A REPORT OF TWO CASES

By AGATHA R. CRAWFORD, M.D., B.SC.
Royal Victoria Hospital

IN view of the comparative rarity of cases of subacute and chronic abscesses in the pancreas, it may be of interest to report two cases which have recently come to post-mortem.

CASE I.

CLINICAL HISTORY.

The patient (R. G. S.) was a man of 55. There was no relevant history of previous illness except a transient attack of pyrexia, vomiting, and diarrhœa in May, 1943. The patient's final illness, which lasted sixteen days, began on 23/7/43 with vague upper abdominal pain. Pulse and temperature were normal, and there were no abnormal physical signs. Two days later the pain became severe, there was some epigastric tenderness, and his tongue was much furred. During the next two days the pain improved greatly, but returned on 30/7/43. For the next eight days the patient had very severe pain in the back and upper abdomen, but examination only revealed a slightly increased pulse-rate, a furred tongue, and sometimes slight epigastric tenderness; the temperature on 3/8/43 was 99.8°F. It was not until 7/8/43 that he first looked really ill. On 8/8/43 he collapsed suddenly, and was dead within half an hour.

AUTOPSY.

At autopsy, a few ounces of turbid yellowish fluid were found in the abdomen, but the surface of the viscera was smooth and shining. The transverse colon was closely adherent to the head of the pancreas, which formed a mass about six inches in diameter and three inches antero-posteriorly. This mass was pale with some irregular reddish blotches, and felt firm except for some fluctuant areas. It contained a cavity about three inches by five inches in size, with shaggy walls completely filled by blood-clot, and one or two smaller cavities full of thick pus. The duodenum, near the junction of the second and third parts, showed a rupture of its wall, so that the blood-filled cavity communicated with the lumen. The duodenum was completely filled with blood-clot, the stomach contained about one and a half pints of clotted blood, and the jejunum and ileum also contained much blood. The probable source of this hæmorrhage was an artery (from its position probably the inferior pancreatico-duodenal), which was found in the blood-clot near the opening into the duodenum. The tail of the pancreas appeared normal in size, shape, and on section. No calculi could be felt in the pancreas, and none were found on sectioning it.

The origin of the portal vein was embedded in the œdematous fibro-adipose tissue at the back of the inflammatory mass, and was filled by ante-mortem

thrombus. In spite of the portal obstruction, the spleen was not enlarged and felt flabby. The malpighian bodies were indistinctly seen against a pinkish-grey pulp.

The liver weighed 4 lb. 4 oz. It was rather pale, but the lobular pattern was normal. The gall-bladder was not thickened, and contained no calculi.

Other findings were benign nodular hyperplasia of the prostate and bilateral œdema and congestion of the lungs.

Histology.

Sections of the head of the pancreas showed cavities filled by pus, with walls of œdematous fibrous tissue infiltrated by large mononuclears, lymphocytes, and polymorphs. The amount of fibrous tissue surrounding the abscesses, and its content of well-formed collagen fibres, suggested that the pathological process had been going on for several weeks at least. Where pancreatic tissue survived, there were a few dilated ducts containing tiny calculi and some acini were also slightly dilated. A section from the tail of the pancreas showed a similar degree of chronic obstruction. The islets appeared normal.

A thrombus in the portal vein filled the lumen, but had not yet undergone any organisation. The vessel wall showed extreme œdema, with a network of fibrin and many large mononuclear cells and some lymphocytes and eosinophils.

The spleen was not unduly congested. There was hyaline change in the splenic arterioles.

In the liver there was a rich lymphocytic infiltration of the portal tracts, and slight fibrosis round some of the small bile ducts. The liver cells showed no fatty change.

In the kidneys there was cloudy swelling and well-marked pyelitis cystica.

The lungs were congested and œdematous, and some alveoli contained free red-blood cells and a few hæmosiderin-containing phagocytes.

Anatomical Summary.

Purulent pancreatitis with abscess formation :
Hæmorrhage into pancreas and lumen of duodenum :
Thrombosis of portal vein :
Cholangitis.

CASE II.

Clinical History.

The patient (S. S.), a man of 63, had been treated for diabetes for twenty years. For some years he had been troubled at intervals with epigastric pain, which was relieved by food and by "powders," and was admitted to hospital on 30/3/42 complaining of generalised abdominal pain. His urine contained no sugar. After three weeks he developed very severe abdominal pain and rigidity of the abdominal wall. At laparotomy, some free fluid was found in the abdominal cavity. The head of the pancreas was enlarged, and formed a firm mass adherent to the second part of the duodenum. A small fistulous opening in the pancreas near these adhesions

was closed. His temperature never rose above 100°F., but he required morphia daily for relief of pain, and died twelve days after operation.

Autopsy.

The body was poorly nourished, with considerable œdema of limbs, scrotum, and penis. The abdomen contained one and a half pints of creamy pus, which was loculated by fibrinous adhesions between loops of bowel. The pancreas was enlarged. On section, the main duct was dilated to about one inch in diameter, and a probe could not be passed from it into the duodenum. Near this dilated duct were numerous cavities up to a half inch in diameter, containing pus and mucoid material. Fibrous tissue throughout the gland was increased. No calculi could be found.

The liver weighed three and a quarter pounds. There were patches of fibrin on its surface, but the cut surface looked normal. The gall-bladder was not thickened and contained no stones. Just above and below the entrance of the common bile duct into the duodenum there was some ulceration of the duodenal mucosa.

The other abdominal organs were normal. The lungs showed œdema and a confluent broncho-pneumonia.

Histology.

In the pancreas no normal acinar tissue could be found. The abscesses were filled with pus and remnants of columnar epithelium, which suggests that they had arisen in relation to ducts. There had been very extensive proliferation of connective tissue, which had formed large areas of dense collagenous fibrous tissue infiltrated by lymphocytes and plasma cells. Imbedded in it were scattered islets of Langerhans, which appeared normal. There were some groups of small ducts, which were somewhat dilated and appeared to be actively proliferating.

A section of the region of the ampulla of Vater showed dense fibrosis just outside the muscle layer of the duodenum. This contained dilated pancreatic ducts with desquamated epithelium and inflammatory cells in their walls. The duodenum, especially the mucosa, was also infiltrated by lymphocytes and plasma cells, but at the level of section was not ulcerated.

Anatomical Summary.

Obstruction to pancreatic duct:
Chronic suppurative pancreatitis with abscess:
Generalised peritonitis:
Terminal broncho-pneumonia:
History of diabetes.

Commentary.

In neither case is it clear what factors produced the abscesses in the pancreas. In Case I there was an illness lasting sixteen days, but the degree of fibrosis suggests a pathological process of longer duration. This patient had an attack of gastro-enteritis three months before his death, and it is possible that at this time there was invasion of the pancreas by ascending infection. If so, it is remarkable

that the patient had no symptoms between this attack and his final illness. This patient had no cholecystitis, and there is little evidence of chronic obstruction to the pancreatic ducts. The terminal collapse is readily explained by the discovery at post-mortem of a massive intestinal hæmorrhage from rupture of an artery involved in the destructive process. The thrombosis of the portal vein is, histologically, very recent, and has not had time to produce secondary changes in the intestine or spleen.

The condition found in this case, where the head of the pancreas is occupied by one large cavity with shaggy walls, corresponds to what Kaufmann describes as a "pseudocyst," due to progressive autolysis following an attack of acute pancreatitis. He mentions the possibility of superimposed bacterial infection with the formation of pus. The clinical history of this patient, however, provides no episode which resembles an attack of acute pancreatitis, as he showed no objective signs of severe illness until the day before his death.

In Case II there is evidence of long-standing obstruction to the main pancreatic duct, causing great dilatation. The marked fibrosis near the ampulla of Vater suggests that a pancreatic calculus may have been impacted and later discharged into the duodenum, leaving the fibrosis to perpetuate the stricture. At the time of death there was no cholecystitis, so it is unlikely that the original blockage was due to a gall-stone. The obstruction has resulted in dilatation of the ducts with disappearance of the acini, the islet tissue being relatively unaffected. Stasis of pancreatic secretions has probably resulted in the escape of enzymes into the tissue with autodigestion, and the necrosis so produced would form a suitable nidus for bacterial infection. Rupture of one of the abscesses into the peritoneal cavity resulted in the severe pain and rigidity, which necessitated laparotomy. Generalised peritonitis supervened and was complicated by broncho-pneumonia.

The occurrence of diabetes in this case is of interest. In the reported studies of disturbances of carbohydrate metabolism in pancreatitis, most of the cases have been of acute pancreatitis. In Schmieden and Sebening's analysis of 1,278 cases of acute pancreatitis, 18 (or about 1.4 per cent.) later developed a true diabetes, and transient hyperglycæmia was common. Cases in which chronic pancreatitis preceded the development of diabetes are rare, and the causal relationship doubtful; one such case, in which a chronic abscess caused extensive destruction of the pancreas, has been reported by Beller and Nach. In the present case, however, it seems very improbable, in view of the long history of diabetes, that the association is anything more than a coincidence.

Beller and Nach's case of pancreatic abscess was associated with very marked fatty change in the liver. He suggests that this was due to deficiency of lipocaic, the substance which Dragstedt has described as of importance in controlling fat mobilisation and storage. In neither of these cases is there any such excessive fatty change in the liver.

The causes of acute pancreatitis are still debatable. Hence it is not surprising that the ætiology of chronic inflammatory conditions, like those described here,

in which the clues to the earlier events are destroyed or masked by destruction and fibrosis, should be obscure.

SUMMARY.

1. Two cases are recorded of chronic abscesses in the pancreas.
2. One case died suddenly from massive intestinal hæmorrhage, the other from generalised peritonitis.
3. The ætiology in both cases was obscure. In one there was marked chronic obstruction to the pancreatic ducts.

My thanks are due to Professor J. H. Biggart and Dr. J. E. Morison for their help; to Professor W. W. D. Thomson and Mr. H. P. Malcolm, M.Ch., for permission to publish their cases; and to Mr. D. McA. Mehaffey, for the photographs.

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REVIEW

TEXTBOOK OF MEDICAL TREATMENT. Edited by D. M. Dunlop, B.A., M.D., F.R.C.P.(Edin.), M.R.C.P.(Lond.); L. S. P. Davidson, B.A., M.D., F.R.C.P.(Lond.), F.R.C.P.(Edin.); J. W. McNee, D.S.O., D.Sc., M.D., F.R.C.P.(Lond.), F.R.C.P.(Edin.). Third Edition. Pp. 1218. E. & S. Livingstone. 1944.

IT is not surprising that a third edition of this work should have been required only two years after the second edition and its reprint. When originally published in 1939, the editors expressed the hope that it would "fill the therapeutic gap left by the majority of textbooks on general medicine, in which . . . the section on treatment is often inadequate." This hope has been amply fulfilled in successive editions, with an admirable sense of proportion and a high level of performance. While various aspects of treatment are discussed, the reader is guided in his choice by one who writes "having authority, and not as the scribes." In the third edition nearly all of the sections have been extensively emended, and completely new matter has been added on the following subjects: meningococcal septicæmia; spontaneous hypoglycæmia; male hormone therapy; deep X-ray treatment of certain blood-diseases; patent ductus arteriosus; the effects of cold; the rhesus factor. An excellent feature of this book is the section which describes in detail the technique of certain essential medical procedures, such as lumbar puncture, venesection, blood transfusion, and oxygen therapy. In an appendix there is an interesting list of proprietary equivalents for official preparations. Altogether, this is a most valuable addition to any doctor's library.

R. M.

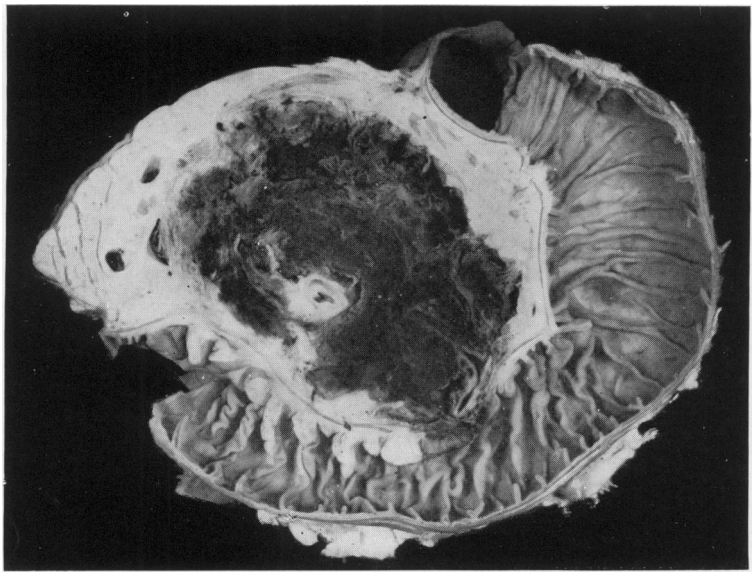

Plate I—Case 1

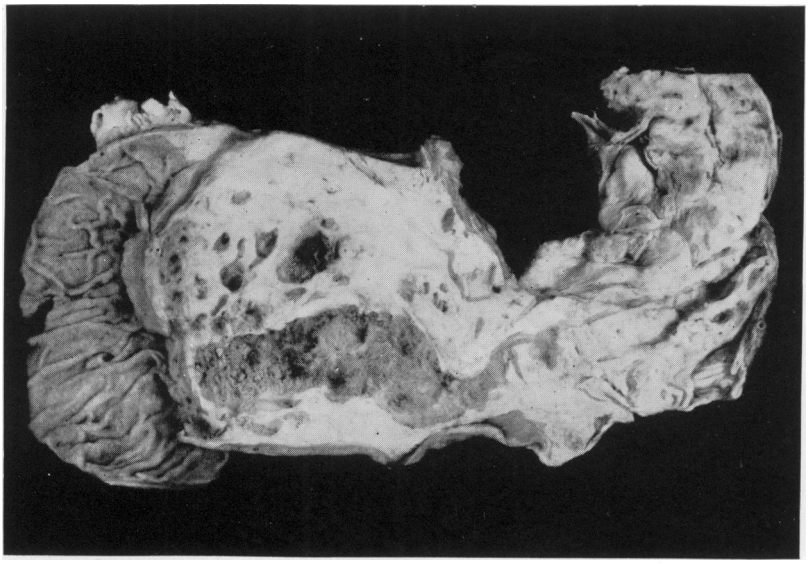

Plate II—Case 2

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DISEASES OF THE CHEST. By Robert Coope, M.D., B.Sc., F.R.C.P. Pp. 524. Edinburgh: E. & S. Livingstone. 1944. 25s.

IN this book Dr. Coope sets out to write an essay on medical education with a description of the first principles of the diagnosis and treatment of respiratory diseases. He has succeeded in his object, and has produced a book in which these principles are described lucidly and concisely, though the reader who desires more detailed information will have to go elsewhere. Dr. Coope leaves us in no doubt that the patient is at least as important as his disease, and his reinstatement of general principles is very helpful, particularly in chronic chest diseases, in which a balanced judgment is so necessary in deciding whether any proposed treatment may not be worse than the disease.

The author holds the view that too much reliance is placed on radiological examination, and lays great stress on physical signs, the chapter on which is excellent, is well worth careful study, and should be particularly valuable to the student. While he rightly condemns the use of radiology to the exclusion of other methods of examination, he perhaps allows the pendulum to swing too much in the opposite direction and places a disproportionate emphasis on the value of physical signs. Illustrations of radiograms are placed at the end of the book, and it is regrettable, especially in a book which lays great emphasis on the distinction between the normal and the abnormal, that the only two radiograms—those of the normal chest—which appear in the section on radiology are not well reproduced. In a book of this kind there must of necessity be many omissions, but it is surprising to find that the work of Seibert on purified tuberculin (purified protein derivative) is not mentioned in the section on the tuberculin test. It is, however, refreshing to find that Dr. Coope lays such strong emphasis on rest in bed as the main principle in the treatment of pulmonary tuberculosis, at the same time pointing out its limitations both psychological and physical.

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COMBINED TEXTBOOK OF OBSTETRICS AND GYNÆCOLOGY. Revised by J. M. Munro Kerr, R. W. Johnstone, James Hendry, Dugald Baird, James Young, Donald McIntyre, E. Chalmers Fahmy, et alia. Fourth Edition. E. & S. Livingstone Ltd. 42s. net.

This book, by several well-known teachers and practitioners of obstetrics and gynæcology, houses these two subjects under one roof. This is not only of importance in emphasising the close relationship between the two subjects, but will also make its appeal to the student, who feels, perhaps not without justification, that he already has too many books to read.

Several chapters have been revised, for example that on Sterility. This is an excellent chapter, and it might interest many doctors and lay husbands, who lay the flattering unction to their souls that the fault is with their partners in cases of childless marriages, to know that in at least 25 per cent. of sterile marriages the husband was incapable of procreation. A useful addition to this chapter is a section on contraception, but it could be improved by more detailed instruction in the methods of estimating the correct size of occlusive appliance.

Functional disorders have been excellently considered. The physiology of the ovary, the implantation of the ovum, and the development of the embryo are particularly well treated.

A note on the Rh Factor, to which attention is drawn in the preface, is, like the donkey's gallop, short and sweet, and the reviewer wonders if this section is of much practical value.

The toxæmias of pregnancy are clearly and adequately discussed, and the points in treatment well made. This is a particularly useful chapter.

The section on heart disease in pregnancy is well done, but the reviewer notes with much interest and not a little surprise, the following:—"In the Third Stage.—Free bleeding should be allowed to occur, especially in cases of Mitral Stenosis." He has frequently had the advantage of the assistance of the editor of this Journal in dealing with cases of heart disease in pregnancy, but so far he has not advocated this line of treatment.

The chapter, "Dystocia due to faults in the Passage," is carefully and usefully written, although the reviewer questions if it would not have been better to classify pelvic contraction more after Caldwell and Moloy, than to use the somewhat cumbersome classification given in this chapter.

The authors of this textbook do not consider that minute details of surgical technique should form part of the training of medical undergraduates. With this expression of opinion, the reviewer is in complete agreement, but he is mildly surprised to find so much detail on Wertheim's operation and a description of Pfannenstiel's incision. The average student will, no doubt, be pleased to know that a modification of this incision is known as "Bardcläben's incision."

Apart from this appeal to the emotions, will the fact be of any use to the medical undergraduate?

However, enough of this criticism. The book is usefully and carefully illustrated.

It is a most useful book for the undergraduate and the young doctor, whose book-shelves would be incomplete without this excellent treatise of modern obstetrics and gynæcology.

As a teacher of these subjects, the reviewer gives this book a strong recommendation. H. I. McC.

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COMBINED TEXTBOOK OF OBSTETRICS AND GYNÆCOLOGY. Revised by J. M. Munro Kerr, R. W. Johnstone, James Hendry, Dugald Baird, James Young, Donald McIntyre, E. Chalmers Fahmy, et alia. Fourth Edition. E. & S. Livingstone Ltd. 42s. net.

This book, by several well-known teachers and practitioners of obstetrics and gynæcology, houses these two subjects under one roof. This is not only of importance in emphasising the close relationship between the two subjects, but will also make its appeal to the student, who feels, perhaps not without justification, that he already has too many books to read.

Several chapters have been revised, for example that on Sterility. This is an excellent chapter, and it might interest many doctors and lay husbands, who lay the flattering unction to their souls that the fault is with their partners in cases of childless marriages, to know that in at least 25 per cent. of sterile marriages the husband was incapable of procreation. A useful addition to this chapter is a section on contraception, but it could be improved by more detailed instruction in the methods of estimating the correct size of occlusive appliance.

Functional disorders have been excellently considered. The physiology of the ovary, the implantation of the ovum, and the development of the embryo are particularly well treated.

A note on the Rh Factor, to which attention is drawn in the preface, is, like the donkey's gallop, short and sweet, and the reviewer wonders if this section is of much practical value.

The toxæmias of pregnancy are clearly and adequately discussed, and the points in treatment well made. This is a particularly useful chapter.

The section on heart disease in pregnancy is well done, but the reviewer notes with much interest and not a little surprise, the following:—"In the Third Stage.—Free bleeding should be allowed to occur, especially in cases of Mitral Stenosis." He has frequently had the advantage of the assistance of the editor of this Journal in dealing with cases of heart disease in pregnancy, but so far he has not advocated this line of treatment.

The chapter, "Dystocia due to faults in the Passage," is carefully and usefully written, although the reviewer questions if it would not have been better to classify pelvic contraction more after Caldwell and Moloy, than to use the somewhat cumbersome classification given in this chapter.

The authors of this textbook do not consider that minute details of surgical technique should form part of the training of medical undergraduates. With this expression of opinion, the reviewer is in complete agreement, but he is mildly surprised to find so much detail on Wertheim's operation and a description of Pfannenstiel's incision. The average student will, no doubt, be pleased to know that a modification of this incision is known as "Bardcläben's incision."

Apart from this appeal to the emotions, will the fact be of any use to the medical undergraduate?

However, enough of this criticism. The book is usefully and carefully illustrated.

It is a most useful book for the undergraduate and the young doctor, whose book-shelves would be incomplete without this excellent treatise of modern obstetrics and gynæcology.

As a teacher of these subjects, the reviewer gives this book a strong recommendation. H. I. McC.