A Clinical Lecture

ON

THE PRINCIPLES OF TREATMENT OF TYPHOID FEVER.

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GENTLEMEN,—To you this may perhaps sound too elementary a theme for a clinical lecture, but graver critics are much more likely to regard its selection as a presumption. "First principles" are given to us in the pure sciences at the beginning of our schooling, but in our clinical studies they are too often not to be reached until near the finish, if ever; and as that has been my own experience, I can wish you no better wish than that you should begin where I am ending. I cannot pretend to give you the "principles of cure." The direct, rapid, germicidal method which will some day supersede all previous gropings is not yet within our grasp. Nevertheless, even in this temporary makeshift treatment addressed to the clinical condition rather than to the cause, there is a more stable side—that which is measured out upon life itself, upon the obvious perversions of the functions, and upon the visible alterations in the structures—in a word, upon physiology, clinical pathology, and morbid anatomy. Sound principles are the only lasting part of our therapeutics; all the rest shifts like the sands. Therefore, although there is a definite therapeutic formula appended to the method to be laid before you, I attach no final importance to the individual agents employed, and I should be the first to replace them by better remedies if any could be procured.

The Typhoid Ulcer.—Formerly we were taught that the typical lesion of typhoid fever was to be found (as in the specimens placed before you) in "the longitudinal ulcer of the ileum, close to or at the valve, with thickened and sloughing base and faecal staining"—a grim comment upon our therapeutics. But some of your seniors can also remember the time when the phagedaenic chancre was regarded as a genuine expression of the syphilitic process, and hospital gangrene as a normal development in pathology—views which are no longer held. Possibly some similar change of opinion may be in store for us in connexion with the typhoid ulcer. Indeed, we are already aware that the lesion does not in all cases proceed to the stage of ulceration. I may then, for the practical purposes of this lecture, venture upon assumptions, and state it as my opinion that the classical description in question is a picture, not of that which constitutes the essence of the typhoid lesion pure and simple, but of that which it should never be allowed to become, and that the "foul" typhoid ulcer is a preventable condition, the product of bad forms of infection combined with worse sanitation.

The Line of Treatment.—As the clinical aggregate includes every degree of severity, and every variety of type, the adoption of any one uniform method seems almost impracticable: yet thoroughness of treatment is always essential, if not for the safety of the patient, at any rate for our own; and the early stage is the only season for success. Our need, then, is a practical treatment, so effectual as to safeguard the bad cases, and so harmless as to be suitable even for the mildest ones. That to be described to you is my best attempt in that direction, but one much open to improvement. Most of the suggestions upon which it is based are free from the reproach of being novel or heterodox, since they are variously stamped with such good names as Jenner, Brunton, Bouchard, Gee, and others. The chief novelty is their practical combination in the service of simple and straightforward principles, for well-defined purposes of action.

To put before you at once the heart of the matter: The two generally approved aims in the treatment of typhoid are also our aims, namely, to (1) feed the patient, and (2) starve the disease.

The first, largely represented under the heading of "diet," should also include any indirect help towards nutrition and "general support." The second will include all measures tending to check the morbid process, and among them a special endeavour to apply the neglected principle, "local treatment for the local disease." How this may

be attempted will need some further explanation; but a general idea will at once be suggested by the following heading:

THE EMPTY BOWEL TREATMENT.

("TRAITEMENT À VIDE.")

RETROSPECTIVE REMARKS.

The French name is already identified with the method, thanks to my having recently enjoyed in France the privilege of explaining the latter to *compères* who are perhaps more often called upon than we now are to treat typhoid. Both names are used, not in metaphor, but in their plain practical sense, "no faeces." Inasmuch as this method is a development of previous ones, it is opportune to preface it with a brief retrospect, particularly in connexion with diet, medication, and other therapeutic measures.

Diet.

This has long been the question of vital importance. "Milk only," the now prevailing alimentation for typhoid, is a compromise between two dangerous extremes which have had their day, namely, "no food" and "solid food."

1. The "starvation plan" would have been more popular had typhoid fever been identified as a disease prior to the decline of the old idea that the *ens* of a fever could be starved out like a beleaguered garrison, or that in a mutual-devouring struggle the famished forces of health might outlast the foe. The so-called water cure was advocated and practised for many years by M. Luton of Rheims,¹ water only and water *ad libitum* (supplemented by water enemas when necessary) being allowed until after the appearance of the exanthem, and afterwards chiefly milk. For this plan Luton gave some good reasons and claimed excellent results. But the practice has not survived in its extreme form, and we have probably heard the last of it in an interesting paper by Yandell of Louisville.² He himself had fasted for seventeen days for rheumatism, and he gives an account of five cases of typhoid fever satisfactorily treated for two or three weeks on plain water. This is a diet better adapted for goldfish in a bowl than for man in a consuming fever; though it may be excellent for the bowel it is not good for the patient, except during the early "typhoid" stage of invasion, when, as long urged by various authorities, and recently in this country by Dr. Fred. Smith, it is the most suitable of diets and of treatments. So great may be the advantage then secured in respect of the local lesions that this alone may explain the successes obtained by Yandell, in spite of the undue prolongation of the fast.

2. "Mixed solid food" might, with the kindest intention, be really the worse evil of the two. Both issues are obscured by the fact that the average "mild case" is proof against most dietetic errors. All typhoid cases are essentially cases of bowel disease, but the "well-regulated case," once safely steered through the early period, is one of bowel disease only, often coupled with an excellent gastric digestion. This happy possession does not, however, in itself warrant a diet of square meals. High feeding is not a safe cure; it cannot *per se* save life, and it is fraught with great risks. It is quite right to say in its support that, although strictly speaking the patient's death may never be directly due to starvation but to toxæmia, still he has been usually much reduced by the virtual starvation of fever so as to fall an easy prey to toxins; and to say that his resistance would have been vastly increased if he could have digested food, and had had it supplied to him. But how is this to be worked in the severe cases? And if a milder case is making good progress why should we not leave well alone, rather than introduce uncalled-for elements of danger? My own contention some years ago was that milk might not be nutritious enough, or sufficiently varied for the ideal nutritional requirement; instalments of the fresh principles of vegetables and fruit were suggested, as well as cream and malted preparations; but I never discovered sufficient reason for the solid diet so warmly advocated by various writers.³

3. Exclusive milk diet—that *medio tutissimum*—is not, after all, a middle course of absolute safety. Nay, in the evil stage of the worst cases milk is a danger so great that we should take warning against the use of milk in any of them. This danger had been clearly perceived by some of our great authorities, in particular by Sir William Jenner,⁴ although he did not draw from his observations their full conclusions; and Burney Yeo⁵ subsequently pointed out the advantages of whey as an alternative to milk in some cases, whilst Gee and a few others have entirely substituted whey for milk. This is the practice which I have adopted for some years, after

reading in one of our journals the cogent advocacy of "exclusive whey" by a *confrère* whose name I should like, if I could, to honour by remembrance. But it really dates further back. Dr. Mackenzie of Normanton informs me that in the Highlands whey has long been in use as a routine in fevers, "because milk was found too heavy," and that he himself has prescribed it for more than forty years. The point is this, that when digestion is paralysed, whilst even whey will leave minute flaky residues in the intestine, pure milk loads it with massive curds which breed intestinal putrefaction and ultimately favour the intragastric fermentation of the fresh milk supplies. Each feed will aggravate the tympanitis when the putrefactive process has once gained the upper hand over the aseptic fermentation of normal digestion. Even whey may have to be diluted; but usually complete absorption of the small amount of albumen which it contains occurs within the upper bowel, except during the afebrile stage of typhoid prostration.

Stimulants.

This has always been a delicate question in disease as well as in health, but it is not a difficult one in typhoid fever. Stimulants are not often necessary, and in the majority of cases should not be given. We have all known cases where brandy had been prescribed because of the apparent exhaustion of the patient, and where it had to be abruptly withheld just in the hour of added peril and weakness, on account of severe hæmorrhage, and yet the patient did not succumb. The moral is obvious. Emergencies may call for the help of "eau de vie" in any of our cases; but the generality of patients may be classed into two categories. Those able to take food do not require alcohol, although quite able to digest both food and wine. The others are so ill that they cannot digest, and they must of course be kept up; but in view of the severity and coming duration of their attack, it is not the temporary stimulant which they most need, but the permanent support—that of food, not alcohol. The urgent indication is therefore to regulate their condition, to cleanse away their septic encumbrances, and to restore their function of absorption. But we must admit that there is a useful place for alcohol either as a substantial help or as a placebo, namely, in the early as well as in the late toxæmia. In the initial "typhoid" state, food is certainly worse than alcohol; and if concessions have to be made to secure for the patient the blessings of water or of whey, a little alcohol may be prescribed to tide over the situation for two or three days. And again at a later stage, if all our assiduous efforts to treat and to feed the patient should prove to be futile, brandy skilfully used may prolong and perhaps may save life in moments of danger.

Recent Therapeutics.

Medication.—The chapter of symptoms has always occupied a large share of attention in the treatment of typhoid, although the great aim has been to limit their occurrence by improving the general state. If we take it as read, an outline of the rest of the history of medication is quickly told. The primary causal indication pointed by Eberth's discovery may be some day fulfilled by bacteriological agency. Professor Wright's method is a considerable step in that direction. But the power to arrest the disease does not, so far as known, reside in any drug; none has been put forward as a direct germicide.

The secondary causal indication has been the object worked at—namely, to moderate the march and limit the inroads of the disease by making a direct attack upon its essential processes—fever and infection. It is upon those two lines that the more "specific" forms of treatment have been conceived. But the two sets of remedies employed, the antipyretics and antiseptics, are not before us to-day for detailed enumeration or valuation. Experience has given its verdict, and the attention of observers has turned to other quests. *Antipyretics* have rightly fallen into disuse as inferior to other antifebrile measures through combining greater risks with less efficiency. *Antiseptics*, also open to similar criticism, are still used by some, who might with some truth argue that the trial hitherto given has not been quite fair. Anyhow, the results have not succeeded in establishing a reputation for any single member of the group, nor in recommending the system itself for universal adoption. Nevertheless, Dr. Foord Caiger's recent good accounts of oil of cinnamon encourage a hope that there may yet be a future for medicinal antiseptics. That excellent bowel remedy is free from risks in moderate doses, although it cannot claim to

be a very powerful germicide. It was given in one of my cases, and I expect to resort to it again on suitable occasions for the sake of its carminative and stimulating properties; but meanwhile the continued administration of small doses of mercury— $\frac{1}{2}$ gr. of calomel three times daily—represents the antiseptic intention in my treatment without much of the effect. Pending further observations, I lay more stress upon "diet" than "medicine," and I prescribe little beyond such drugs as may help to "regularize" the gastro-intestinal situation, the best, so far as I know at present, being a daily routine of castor oil, of mineral oil, and of vegetable charcoal. I doubt whether this alone could ever shorten an attack, but I believe that future medication, including antiseptics, will be much assisted by the empty-bowel condition as a basis. Incidentally, we may note that, according to Dr. Secheyron,⁷ so long as charcoal is supplied it is relatively useless to give medicines by the mouth, so many of them being neutralized by contact with charcoal.

Non-Medicinal Treatment by Nursing and Hygiene.—These aspects of treatment have received during recent years an increasing amount of attention. If I should dwell but briefly upon them it is not from any underestimate of their value. As adjuncts they are indispensable if the best results are to be secured from any treatment, and among them *pure air and sunlight* are first requisites, urgently needed in proportion to the acuteness of the affection.

Cutaneous Hygiene.—Scrupulous cleanliness is almost of greater value to the nurse and the surroundings than to the patient. But the regulation washings contribute a definite instalment of active treatment in promoting the cutaneous excretory function which is conspicuously torpid. Greater still is the help to be got from a cultivation of the nervous function of the skin. Systematic cold spongings and friction can therefore claim a prominent place among our therapeutic agents, quite apart from their antipyretic properties, which more immediately concern the heat-regulating function. Fever heat, though part of Nature's cure, is demonstrably harmful when excessive, and therefore to be checked. You will realize, however, that its forcible repression gains an advantage over a symptom only, doubtless a major symptom, but not over the cause. Three methods have been practised to secure peripheral refrigeration: (a) The *cold atmosphere method* carried out either (1) by continued exposure of the surface to the cool air, in winter under very light coverings, or under a single sheet in summer; or (2) by artificially cooling the air of the bed by means of the ice cradle, or some equivalent device; (b) the *cold-water method*, by which surface heat is periodically abstracted by cold-water spongings, by successions of cold or even of iced compresses, or by rubbing with ice; and, lastly, (c) the most active method of all, the *cool-bath method*, to which we must presently devote separate consideration.

Hygiene of the Bowel. which forms the chief theme of this lecture, stands foremost among our principles of treatment but has been the last to receive its due share of attention. The duty of intestinal sanitation, at any rate so far as it consists in keeping the lower bowel free from any septic accumulation, is too obvious not to have been attempted repeatedly by separate observers. Suitable systematic irrigations of the colon as a direct means of limiting the absorption of toxic fluids were not, however, brought forward until relatively late, and they have never obtained a place in the routine of treatment. As they may not be in the future so much called for, we may defer for a while their consideration, whilst specially noting their importance in relation to all septic cases.

SYSTEMATIC REFRIGERATION.

THE CURRIE-BRAND COOL BATHING TREATMENT.⁸

The late E. Brand has deserved well in our day as an observer and as a healer, but the least that can be said of Currie is that he was a prophet; for he preached the remedy long before the disease was known. Prophet-like, he has reaped the homage of silent imitation elsewhere, and, in his own country, scanty recognition. Happily, his claims as a pioneer need no better proof than the title of his work:

"Medical Reports On the Effects of Water, Cold and Warm, as a Remedy in Fever and Febrile Diseases; whether applied to the Surface of the Body or used as a Drink: with Observations on the Nature of Fever; and on the Effects of Opium, Alcohol, and Inanition. By James Currie, M.D., F.R.S., Physician in Liverpool and Fellow of the Royal College of Physicians of Edinburgh. Liverpool. 1797."

But it needed Brand's staunch belief in those strange workings which he never quite succeeded in explaining, and Brand's strong clinical instinct, to endow us with a practical method.

Whilst we look in vain elsewhere for some active plan of treatment

commanding general recognition, this plan is not only active, nay, even heroic, but successful. Its credentials, which are not disputed, are a reduction in the mortality of typhoid, estimated by Osler at 6 per cent.,* and at an even higher figure by Francis E. Hare,† to whose labours so much of our information is due. Even if we adopt the least valuation which has been made of its life-saving advantages—namely, a lower mortality by 2 per cent. than that under the best of any other treatment, there is clearly much to say for a method which will rescue 25 per cent. of the otherwise doomed, without material damage to the interests of those in less danger. How shall we explain that its adoption is not a conscience clause with all of us—nay, that it has been abandoned by some of those who had used it? Surely this cannot be on the score of any lack of familiarity with the dangers of the disease and with its treacherous character. More probably there is a lurking impression that in this treatment, brilliant as are its results, we have not yet the true treatment of enteric fever, and that it lacks directness of attack. Perhaps, too, at bottom there is the “practical excuse” that in the vast majority of individual cases the advantage is disproportionate to the trouble entailed upon the patient and the attendants, although we are assured by Hare that the alleged trouble is much less than that of systematic spongings; and, again, an exaggerated estimate may have been formed of the precautions necessary for safety. In this country it has been a canon of practice to secure for typhoid patients the most absolute repose in bed, and the absence of a suitable lifting apparatus to save the patient from any exertion may have checked the action of many practitioners. Abroad less anxiety prevails, and the risks which have been taken have not had the effect of reducing the statistical rate of success of the method. In many foreign hospitals—as, for instance, to my personal knowledge, in those of Geneva and of Montpellier—patients, with few exceptions, are allowed to step from their bed into the bath, only the worse patients being lifted by hand. A French gentleman whom I recently saw in consultation with Dr. Dardel of Gisors in Normandy was able, throughout a severe attack, to walk from his bed into the adjoining bathroom for his bath every three hours without any evil effect. This more liberal rule as to locomotion might go far to facilitate the bathing plan, though nothing will probably render it quite popular. It is, unfortunately, impracticable in the absence of a sufficient water supply—as sometimes in the severe epidemics in war. Much nevertheless may be done under adverse conditions by enterprise and energy. I was much struck by Dr. Dardel’s statement that since he first tried the treatment he has for several years applied it in every case, even in distant country cottages, and that he has since then never lost a patient. Personal testimony of this sort, added to the evidence of statistics, may be trustworthy as a guide for individual practice; at the same time, it belongs to clinical and therapeutic progress that we should learn more about the physiological *modus operandi* of the remedy.

The Claims and the Limitations of the Cool Bath Treatment.

All are agreed that the reduction of high temperatures is in itself an important boon in the treatment of fevers. Brand’s system claims to do more than alleviate the discomfort and mischief of over-heat, namely, to influence the disease by a persistent repression of the latter. Yet, in spite of it all, bathing does not succeed in shortening the attack—a result which would have been a sure sign of a germicidal effect.

Brand had further claimed for his treatment that if begun sufficiently early it would save every case. This sanguine undertaking is unfortunately nullified by the fact that the early diagnosis which would be necessary is almost unattainable. As in the series treated and studied by F. E. Hare, the percentage of the mortality from perforation has not differed from its percentage under other treatment, the most favourable estimate is that whilst bathing may be capable of preventing the occurrence of severe complications, it is powerless to obviate the fatal developments of the worst lesions which have been started before the application of the remedy. Special stress must also be laid upon two other facts which F. E. Hare’s statistics claim to have proved:

1. The average duration of the pyrexial period is not diminished, although the average degree of pyrexia is lowered.
2. The incidence of hæmorrhage is not decreased, although according to F. E. Hare its fatality is slightly diminished.

The absence of any appreciable reduction in the duration of the pyrexia in a series of cases which include so many relatively mild ones is consistent with a view that the local lesion is not arrested, even when relatively slight. At any rate, the marked saving of life effected is obviously not due to any arrest of the worst forms of local disease, but only due to a mitigation of those which are rather less extreme; and above all to the extraordinary improvement brought about in the vitality of the patient. It might then be argued that the chief value of the Currie-Brand treatment is its vitalizing

effect, and that if some more effectual check could be found for the local lesions the need for that laborious restorative process would have lapsed.

An imperfect acquaintance, such as mine, with the practical use of the method does not carry any “conclusions,” but impressions only, and they are these:

1. It is strange beyond any ordinary explanation that a treatment recognized as capable of saving life in so high a proportion—however difficult or irksome it might be in the performance—should not have imposed itself for universal adoption.

2. If, as it may be assumed, the benefit of “bathing” is chiefly in the direction of “raising the vital powers,” as a large majority of cases do not present serious depression, all-round bathing would in the event prove to be for the larger number a superfluity.

3. On the other hand, any cases unmistakably severe from the first must claim the life-saving benefit of Brand’s system if no equally good substitute for bathing were to be available.

4. But what of the Ingravescens “treacherous” cases which begin with the mildest complexion and end with the worst? They are, happily, on the whole, uncommon. These are just the cases which are deprived of their chance so long as bathing is not made a universal rule, but reserved only for the fully-declared bad attacks. This risk could be expressed statistically by the relative rate of occurrence of the insidious cases in question, and it would probably work out at a low figure. This small risk is usually taken in this country in all mild cases in preference to the trouble involved in “bathing.”

5. A larger risk is obviously incurred when “bathing” is not used at all, even for severe cases; and, in view of the percentage of deaths capable of being prevented, this complete neglect still calls for an excuse.

6. Until the principles set forth in this lecture shall have had an adequate clinical trial it is not for me to discourage the fullest application of the Currie-Brand treatment. Some rational explanation of its mode of action has yet to be given. For my part, I am not a sceptic as to reflex nerve interactions between the general and the visceral periphery; and, although my present concern is with a more direct local treatment, I fully recognize and favour their utilization for the purpose of stimulation in ordinary cases of typhoid, over and above the life-saving value to be secured in bad cases.

7. If I may venture to draw a practical conclusion it is this: That we need some other less irksome method which shall at least equal and if possible surpass Brand’s favourable record of cures, and that if no alternative is found “bathing” should if possible be rendered less trying, and capable of general adoption in all cases where it can be of any use.

8. Should, as we may hope, its results be surpassed by some other plan in the future, we shall still benefit by the clinical lesson it has given us in demonstrating how great is the reserve of cardiac energy in typhoid as compared particularly with pneumonia, and to what extent the heart is able to respond to most searching vasomotor stresses.

CLINICAL CASES.

Having said so much let us turn to this afternoon’s main business, which is to explain to you those principles and that practice which may help to render systematic refrigeration unnecessary, and which are illustrated in the following cases:

The cases treated have been few because few have been admitted. I need not dwell at any length upon the clinical progress, which was uneventful and satisfactory, and is fully recorded in the *Medical Register*.

CASE I (St. George’s Hospital Medical Register, No. 1,382, of 1904).—F. B., hotel clerk, aged 24, was admitted on November 28th, 1904, after two weeks’ illness, with dry and brown-furred tongue, a history of diarrhoea preceded by some constipation, of nocturnal restlessness, and of delirium.

Pulse 120, respiration 30, temperature 104.6°. The chief features in the temperature chart during the remaining three weeks of his fever (five weeks presumably in total duration) were as regards temperature: (1) During the third and fourth week high level readings (maxima often 104°, minima as low as 101°, rarely); average oscillation between 102° and 103°; (2) during the last week no great oscillations of remission or of intermission, but a gradual sloping descent (occupying nine days) down to normal; (3) thereafter a continuous, almost absolutely level, normal temperature, without any subnormal period. Pulse: High readings throughout; even during the first five days of deferescence (fifth week) it remained above 120; at 100 for the first

*“In general hospitals from 6 to 8 patients in every 100 are saved by this plan”: Cf. *The Principles and Practice of Medicine*, by William Osler, M.D., etc., 6th edition (London and New York, 1905).

†According to Hare, the hospital death-rate from typhoid under the bathing system, including all cases admitted in all stages of the disease, and including also those which are too bad to bathe, is about 7 per cent.

six days of apyrexia, and finally at an average of 90. Respiration: A gradual rise to 48 and a gradual fall again to 30 occupied half the third and half the fourth week. Then a few oscillations up to 35 or 40, and finally a slow return to a rate of 20 per minute.

The severity of the attack was further evidenced by the cyanosis, copious exanthem, dry tongue, tremulousness, nocturnal deliriums, and diurnal semi-stupor or drowsiness which persisted; by the abdominal distension; by the slight albuminuria; and by the embryocardial action and weak sounds of the heart. The cardiac weakness at the beginning was so marked as to call for repeated doses of brandy; and for four days four-hourly injections of strychnine were given under the skin. The existing looseness of the bowels was maintained under treatment, and the fluid evacuations after a few days presented the appearances which I have described.

Treatment.—For diet, 4 pints of whey to which one-sixth part of lime water was added. Spongings were ordered three times daily. To relieve the tympanites, which was then considerable, a dose of castor oil, cold compresses, and the long tube were used. A mixture containing oil of cinnamon (mij) and liquid paraffin (3ss, soon increased to 3j, to 3jss, and to 3ij, every four hours) were prescribed on the fourth day of his stay; and next day vegetable charcoal (gr.30 every four hours) in addition. Oxygen inhalations were still required that day, but not the next day, when, after a small dose of castor oil (which was then ordered for daily or frequent repetition), there was marked decrease in the tympanites, which the following day had completely disappeared, the abdomen henceforth remaining flat or slightly retracted. The patient's condition from that time became satisfactory and the routine uneventful. He was thin, but his energy and muscular power were better than might have been expected after so severe an attack. His convalescence was slightly lengthened by a gluteal abscess and its surgical treatment.

The medicine was suspended on December 20th, and the charcoal on December 22nd.

The maltine, of which 3j had been given since December 5th, four times daily, was now supplemented with the hypophosphites of calcium, sodium, and iron (8gr. of each of these salts at a dose). In the diet the following gradual additions have to be recorded:—December 2nd—loaf sugar— $\frac{1}{2}$ lb. daily, also three eggs (the whites in the whey, the yolks with brandy); 6th—one egg additional, jelly, 3j of raw meat juice; 13th—3ij meat juice, and cream 3ij daily; 16th—burgundy, 3viii daily; 19th—honey, sugar, and beef-tea (strained); 21st—the strained juice of grapes and oranges; 23rd—peptonized milk instead of whey; 24th—bread and butter; 27th—pounded fish and a solid diet.

CASE II (*St. George's Hospital Medical Register*, No. 1,261 of 1905).—J. N., aged 11, was admitted on August 9th, 1905, with marked typhoid aspect and torpor, feverishness, prostration, slight sordes and partly dry tongue, and tumid abdomen. The date of onset was not clearly made out, but headache and constipation had existed for three weeks. Pulse, 88; respirations, 36; temperature, 101° to 103° . The temperature chart presents no striking features, the pulse varying between 90 and 100, the respirations between 24 and 26, and the temperature between 100° and 102.3° , rarely up to 103° . Remissions nearly to the normal began on August 20th, and subnormal intermissions on August 30th; complete apyrexia (with little subnormality) setting in on September 4th.

The diet and treatment prescribed were almost the same as in Case I, but no oil of cinnamon was given, and castor oil certainly not often enough. The abdominal distension, which had decidedly improved at first, recurred and varied together with the constipation. I was well satisfied with the early progress of the case, my own entries being on August 11th, "abdomen less"; on 12th, "breath perfectly sweet"; on 13th, "abdominal respiration now free."

I left for my holiday three days after the onset of the remissions, which continued to occur daily as stated, and the charcoal and paraffin treatment was stopped the next day, August 23rd. On August 26th three-hourly doses of brandy (3ij) were ordered and continued until 29th; but no permanent aggravation was put on record, and the morning remissions and the general progress of the case appear to have been maintained.

Comment on the Cases.

Both cases did well, though they might have done better had I had more experience of the use of the method. This applies particularly to the second case, where the chief indication—the constipation—was not sufficiently studied. As neither the charcoal prescribed (3ss 4^{is} h^{is}) nor the liquid paraffin (3j 4^{is} h^{is}) are competent to set up flatulence, the persistence of distension must have been due to the diet. Too much whey (Oij) was ordered on the first day, and the orders for sugar (2 $\frac{1}{2}$ oz. on August 10th), for albumen (3 whites of egg on the 13th), and for cream (1 oz. on the 16th) were probably premature in the face of the imperfect bowel relief. But all might have been well had I given day by day the needful small morning dose of castor oil.

THE PRINCIPLES OF LOCAL TREATMENT.

Surgery and Local Treatment.

Failure to employ local treatment had not been an oversight, much less intended neglect, but only postponement of an urgent study from lack of leisure and of cases. It is not now a regret that I should have appealed in vain to surgeons

for some means of continuous irrigation of the diseased loop of bowel, as their assistance no longer seems to be indispensable for topical curative measures. Nay, I have not only ceased to think of any form of treatment by early laparotomy, but I expect in the future a considerable reduction in the necessity for late, urgency laparotomies "for rescue."

On the other hand, I still look to surgery for its teachings, and endeavour to copy its methods, prophylactic, protective, and curative, for the local treatment of the lesion.

How do surgeons deal with a simple ulcer? Locally, not from a distance. It is true that we are not dealing with a common, but a specific ulcer, and we may conceive of its not yielding to purely local measures. But it is equally true that any advantage which the latter can confer is much needed and in conscience not to be neglected; for if ever there was a lesion crying for help it is the typhoid ulcer with its dangers of haemorrhage, of perforation, of peritonitis; with its evils of necrosis and of resulting secondary septic absorption—a common cause of death in fatal cases; and with its fearful multiplication of the germs of disease. More was wanted of the physician than had been accomplished; but in the absence of any practical suggestions, the principles of local surgery were in vain present to mind and close to hand, because, as it then seemed, hopelessly inapplicable. We may now at last endeavour to turn them to account. Those which are in daily use for ulcers of the leg are the following:

1. To cleanse the ulcerated surface;
2. To keep it clean and free from septic contact;
3. To protect its delicate repairs from any destructive irritations; and
4. By suitable stimulations of the local circulation to induce the growing tissues to appropriate the nutriment supplied in a liberal diet.

Sanitation.

1 and 2. The necessity for an initial cleansing is now generally recognized. Calomel is used, or castor oil; or, better still, both together at one dose, or with half an hour's start for the calomel. This simple cleansing is a boon, but from a Listerian standpoint it would hardly pass muster as sufficient to establish and maintain internal sanitation. Much more is needed than casual enemas or aperients. Not alone in cases of persistent constipation, but particularly in that vicious circle of diarrhoea where over-assiduous feeding aggravates the foulness which needs cleansing, a frequent, sometimes daily, repetition of the small morning dose of castor oil is indicated, and it must therefore form part of our method.

Postural Treatment of the Bowel.

An elementary measure of local sanitation had suggested itself to me some years ago in default of the wished-for surgical help. It is explained in a paper on "Suggestions for the Practical Treatment of Typhoid Fever,"⁹ on a principle slightly different from that for which Dr. R. W. Leftwich¹⁰ has since claimed under the name of "Intermittent Syphonage of the Colon," a still wider application. The object intended and apparently attained was the automatic drainage by posture of the caecal cesspool, to save the ulcerated and paralysed bowel from continuous maceration in foul warm juices. If percussion has not deluded me, the caecum can be easily emptied and kept empty by an occasional inclination of the bed so slight as to be unnoticed by the patient. The suggestion remains a good one, though I now have much less occasion for its use: I have not yet discovered its disadvantages; but this is an open chapter, as the method has not hitherto received either criticism or comment.

Asepsis and Antisepsis.

The notion of a "clean bowel" is incongruous except in the case of the fetus, where little adventitious matter enters the tract. Some recent investigations by Rolly and Liebermeister¹¹ have shown that in rabbits the small intestine has a remarkable bactericidal power which is entirely lost when its mucous membrane is injured or inflamed. But it is probable that after birth a strictly aseptic condition can never be restored, even by absolute starvation, much less when the bowel is kept charged throughout its length with relays of fermentables, as any antiseptics, before they could disinfect its surface, would have to sterilize the bulk of its contents. This thought has discouraged most clinical workers, the doses of antiseptic medicines being much too weak for bowel disinfection even when too strong for the patient. Nevertheless, short of the *summum bonum* of asepsis, antisepsis remains as a partial fulfilment to be steadily pursued, and with that view I had long advocated and practised Wedgwood's¹² treatment by mercury and iron, though largely, too, for its general usefulness. From time to

time mercury itself has repeatedly been put forward by a series of writers whom I need not enumerate, and I still use small six-hourly doses of calomel throughout the attack.

No Faeces.—As it is hopeless to disinfect the faeces, the only course is to suppress them. Is this conceivable, is it feasible, is it wise? Scepticism may carry the argument, but the patient should be allowed the benefit of the practice. A not unreasonable objection is that the presence of faeces is part of the normal state of the intestinal tract in health, and as such to be preferred; but can this contact be equally suitable for the intestinal surface when ulcerated? Again, it cannot be disputed that undigested and indigestible food residues are not the only constituents of the faeces; epithelial debris and other off-castings of the mucous membrane, mucus, and the various glandular secretions, including bile, pancreatic juice, and succus entericus, must all contribute an appreciable solid residue, even if all food remnants should have been eliminated. But an important distinction has to be made. None of these strictly physiological constituents are in themselves prone to fermentation, though, according to Rolly and Liebermeister,¹³ bile, pancreatic and intestinal juice are efficient culture media. It is mainly in the remnants of the ingesta that the putrefactive process is started and kept going; and their absence, although not providing ideal conditions, would be of great sanitary advantage.

The Agents Employed in the Local Treatment.

3. The "surgical" standard of cleanliness might be still further approached if the surface of the ulcers could be covered by some protecting layer analogous to the antiseptic dressings applied to external wounds and ulcers. This would no longer be unattainable if the faeces could be eliminated or reduced to their physiological elements. A further realization, too, might then be contemplated—that of bringing antiseptic agents into working contact with the ulcerated surface; a responsible question the immediate discussion of which is not opportune. Not feeling quite convinced that they are necessary I am not at present tempted to complicate with their risks the simplicity of our method which is limited to the use of absolutely harmless and mainly protective substances.

Liquid Paraffin.—The choice of safe agents of this class is much narrowed by the requirement that any substance intended to reach the distant seat of the lesion must be neither soluble nor capable of absorption. Oil, the natural protective and lubricant for dry and for wet surfaces, fails us here, special provisions existing in the small intestine for its saponification and absorption. Moreover, it is not always well tolerated in large and continuous supplies. Mineral oil, on the other hand, such as petroleum or paraffin, is neither absorbed nor dissolved; therefore, after all absorbable ingesta are taken up by the lacteals it will still remain within the bowel. In this way pure liquid paraffin is valuable, precisely because it is inert; moreover, it might some day, perhaps, be made the vehicle for effective topical remedies. The internal use of petroleum was strongly advocated some years ago by William Duffield Robinson in phthisis, as well as for tuberculous and other forms of diarrhoea,¹⁴ but does not appear to have obtained recognition. In proof of the non-absorption of these products he refers to the observations of Samuel G. Dixon and Archie Randolph, who published in 1885 their results of the administration of vaseline, "in doses of from four to eight drachms daily, every grain of which was reclaimed unchanged from the stools, save the minute loss attributable to separating and purifying"; and Robert Hutchison¹⁵ has also arrived at the same results in connexion with the petroleum contained in "petroleum emulsion." Liquid paraffin is as tasteless as it is harmless, and is therefore acceptable to all patients in almost any dose. Two teaspoonfuls every four hours, equivalent to 1½ oz. in twenty-four hours, is the maximum daily amount which I have hitherto used for adults, but this amount might easily be increased. Frequency in the repetition of the doses is part of the indication, both for the sake of lubrication and of cleansing. And it need hardly be said that paraffin in sufficient doses is in itself a non-irritating mechanical laxative.

Vegetable charcoal in fine powder is a much older remedy of well-known properties. It was long ago prescribed in conjunction with magnesia as a remedy in typhoid fever by M. Dille¹⁶; and Bouchard found good results from the continuous administration of as much as a tablespoonful of it every three hours.¹⁷ Morel¹⁸ also praises its use because of its disinfecting and deodorizing power, and of its beneficial effect upon the ulceration, an influence which Constantin

Paul considered to be of a mechanically stimulating nature, in agreement with Sir Lauder Brunton's¹⁹ view of the mode of relief procured by it in gastric flatulence. Sir William Jenner²⁰ had previously in 1879 dwelt upon its probable action in preventing pyaemic absorption from the ulcers.

But the therapeutic study of charcoal is to be traced much further back. To P. F. Touéry²¹ is due the credit of having discovered and utilized the power of animal charcoal to fix alkaloids and various inorganic substances such as arsenic and phosphorus, in addition to its condensing power for gases, and of having subsequently demonstrated its virtues as a safe and effective antidote for a considerable number of poisons, including strychnine, of which, to prove the fact, he swallowed a large lethal dose with impunity. Touéry's grandson, Dr. Secheyron of Toulouse, to whom I am indebted for these particulars,²² advocates its use as a general household antidote. He is of opinion that, although not a germicide, it absorbs the toxins, as held by Sir William Jenner; and this also agrees with Professor Bouchard's observation that sleep is restored to bad cases of typhoid fever by the administration of charcoal.

Non-germicide and Inert.

In spite of these good opinions charcoal seems to have been forgotten, and so little mention is made of it in recent literature that I had not realized that my use of it was a mere revival. It is a fact fully recognized by Bouchard that the virtues of charcoal do not include any germicidal action. Dr. Slater kindly undertook at my request an independent investigation into this question. The results, which I hope he may publish, are to the effect that the presence of charcoal in any quantity in a moist or in a fluid medium does not interfere in any degree with the growth of Eberth's bacillus. Incidentally I may also refer to Dr. Slater's investigation now in progress as to the action of liquid paraffin, and I may state the broad fact that it does not exercise any bactericidal action in cultures to which it is added, although bacilli cannot be made to grow in it. It could only influence the growth of the cultures in any fluid media by forming an upper layer which might exclude air from them. In short, neither paraffin nor charcoal is capable of arresting the growth of Eberth's bacillus in the bowel.

As regards charcoal we may conclude that, in spite of its wonderful properties as an absorbent for animal poisons and effluvia, it behaves as an inert body towards microbes as it does towards animal tissues. In typhoid I first used it some years ago in suspension of water as an irrigation for the colon. At that stage of my observations, not having succeeded in getting into touch with the lesion itself, I regarded irrigation as an indication of primary importance—and I still regard it as such—because of its ability to lessen the evil of septic absorption by keeping the entire colon and the caecum free from the foul products of gangrenous ulceration; and I imagined that the deodorizing action of charcoal would be a useful addition to the mechanical cleansing by enterocolysis. I have been well pleased with the result, but I hope in the future to have less and less need of this method, which, though it refreshes the patient, is a disturbance and a source of fatigue. I now give the charcoal internally in free and frequent supplies (hitherto a maximum of two teaspoonfuls every four hours, suspended in a little water) as a suitable solid adjunct to the equally inert and insoluble liquid paraffin. I have discovered only good effects from its employment; but I need hardly state that its continued administration calls for intelligent and assiduous attention to the action of the bowel. A systematic inspection of the faeces, which is *de rigueur* in enteric fever, coupled with a daily examination of the abdomen, will supply the necessary guarantee that the powder is doing its office without any tendency to accumulation and concretion. This is a risk which might give trouble if any insoluble mineral powders, such as magnesia were combined with the charcoal; but it is almost completely guarded against by the fluid and oily character and by the laxative tendency of the paraffin with which it travels down the bowel. Moreover, an important part of the treatment is the frequent or daily administration of a small morning dose of castor oil (5j or ʒij) if the bowel should fail to act at least once every day.

An additional reason for the daily administration of oil is the desirability of keeping the upper section of the alimentary tract as free from charcoal as possible lest this should, perhaps, exercise upon some of the valuable constituents of food that selective fixation to which Dr. Secheyron²³ has again directed our attention. Indeed, we may have to reckon with various chemical actions, which should be more completely

studied. It hardly needs to be again emphasized that under empty-bowel conditions the paraffin and the charcoal are brought into direct contact with the diseased surfaces, and therefore realize in some important measure one of our great therapeutic principles—the local treatment of the lesion.

THE EMPTY-BOWEL ALIMENTATION.

We must now return to the practical consideration of those two great principles—"plenty of food" and "no faeces"—seemingly incompatible but really easy to combine, which are able to secure perfect nutrition together with absolute safety. A lump of loaf sugar melts in the mouth and is gone without a trace. Let every ounce of the food that we give equal the solubility of sugar, its direct absorption, and its inability to yield a precipitate, and the problem is solved. The food that needs no digestion, but only to be absorbed, is the ideal for a disabled alimentary tract. Just for awhile the typhoid patient is to be brought back to the régime of the ovum, namely, "alimentation by imbibition." The recognized vital requirement that there shall be within the bowel a sufficient bulk of solid insoluble material, is to be met in the present treatment not by food but by the charcoal supplied. The whole question, therefore, narrows itself down to a skilled selection from the group of foods which leave "no residue."

The Dietary.

Typhoid patients can ill afford to spare from their dietary two essential groups apt to be forgotten under the régime of pure milk in which these are not sufficiently represented: (1) the mineral salts and (2) the organic acids and essences contained in fruits and vegetables.

Common salt is not, as in nephritis, a complication—the typhoid kidney not being impervious—but a help to digestion and to metabolism. It should be given in the whey in the proportion of 10 to 15 gr. to the half-pint in addition to sugar. The phosphates are not less important, and a more abundant supply than is contained in the milk can only do good. This additional amount may be conveniently given in syrup as a medical food. But we possess in vegetable diet a natural source for their derivation and for that of other mineral and organic salts.

Neither vegetables nor fruit should be administered in bulk, although, as I realized many years ago, clarified vegetable soups are specially indicated in typhoid fever, as they also are in rheumatic fever. I have therefore ceased to allow baked apple—as I had done since Dr. F. Dickson suggested it to me—in view of the bulky residue which apples leave. This objection, which applies to all fruit and vegetables, cannot be made against their watery extracts duly strained, especially when freed by boiling from any excess of coagulable albumen. The juice of various fruits may be relished in this way, and a standing item is the daily cup or two of vegetable soup or broth lightly flavoured with fresh beef or bacon and scrupulously clarified.

Most acceptable, too, is a frequent rotation of fruit jellies, among which apple jelly is probably the most salutary. The pectose which these jellies contain is probably absorbable without precipitation, and there is no other precipitable element in them.

As to the comparative bacteriological merits of the "meat" and of the "vegetable bouillons" I must leave it to experts to decide which of the two is the more favourable menstium for pathological cultures in the intestine. From a merely clinical standpoint I regard an attack of typhoid fever as a fine opportunity for the blessings of a vegetarian course, particularly for the purin-encumbered patients past middle age, who are so often rejuvenated by their long illness; and I prefer to derive most of the needful nitrogenous income from other sources than meat.

The nitrogenous supply is represented by peptonized whey, and, if thought desirable, by genuine artificial peptones, but more simply by white of egg diffused in the whey before peptonizing. Eggs are (in the absence of any adverse idiosyncrasy) a most valuable part of the dietary. The egg may be regarded as "chicken milk" at the same time as the "fetal pabulum" of the chick. Its albumen is most diffusible, and when dissolved in the whey in small and progressive quantities, and peptonized, it is probably absorbed in the upper part of the intestine. As to the diffusibility of the yolk, enough that we should remember that it fulfils the same office as the maternal plasma in the placental mode of fetal nutrition, in feeding the tissues by direct penetration. A yolk a day in divided portions may be added to the dietary at a fairly early date without fear of unabsorbed sedimentation. Egg is

thus a complement to the whey, making up for some of its deficiencies in albumen and in fat, and something more, inasmuch as it is in itself a complete storehouse of all the constituents of the animal body.

The carbohydrate supply is most easily managed, sugars and dextrines being all absorbable without residue. In addition to saccharose and lactose, which are fermentable, but nevertheless usually well tolerated, we have the animal glucose in a non-fermentable form as clarified honey, a favourite member of the typhoid dietary. Sugar and glucosides are also abundantly present in the fruit jellies. Maltine, too, is an additional resource. Not one of the members of this large contingent is capable of furnishing a residue so long as there is enough water to keep it in solution in the alimentary tract.

Among the fats the least likely to yield any residue is oil itself. But cream is more acceptable. It may be taken alone or added to the whey. One ounce a day is a sufficient amount, to be worked up to progressively from smaller doses.

Although it is not mathematically accurate to say that no organized remnant and no chemical precipitate can be left in the jejunum by the foods enumerated, this is substantially true. It is for the physician to suit the proportion of each of the latter to the stage under treatment, bearing in mind that it is a mistake to attempt much feeding during the first few days. Even whey may yield more coagulum than can be digested. Two pints and a half of salted whey may be quite sufficient, in addition to plenty of water, pure or flavoured. The whey should not be fortified in the manner described until the turgid abdomen has subsided and the mucous membrane has recovered from its early typhoid disabement. Sugar, albumen, and cream may then be supplied, singly at first, but afterwards jointly, with due regard to the indications afforded by a daily inspection of the stools. As soon as it is quite clear that the fortified whey, which is the basis of the diet, is suiting the digestion, the soup and the spoon-food delicacies—such as honey, fruit, jelly, and the rest—may be added to the dietary one by one; and in a short while the arrears of nutrition will begin to be made good; but the growing total of food supplies will make it the more essential to provide for a daily evacuation.

The Contents of the Lower Bowel, and the Evacuations.

No opportunity has arisen for an examination of the bowel contents *in situ*, but a description may be given of the dejecta voided day by day under the gently laxative influence of the paraffin, or after the administration of small doses of castor oil. The stools, in accordance with the hygienic rule now invariably practised, were passed into a carbolized or mercurial disinfecting solution, and then transferred for subsidence and inspection into a conical glass receiver. So long as the treatment is in force their chief feature is the thick, jet-black layer of clean, unmixed charcoal at the bottom. Above this is a slightly turbid, flaky fluid with a few almond-sized blobs, and a thin, scummy, flaky upper layer. The black, semi-floating blobs, examined one by one, prove to be made up of charcoal and of a very soft, semi-fluid base—apparently paraffin. This is perhaps mixed with mucus; but I have failed to find any mucous shreds in the stools examined.

These details are not unimportant, as with them rests the vindication by actual demonstration of the special claims of the "empty-bowel method;" and in this direction the charcoal fulfils a useful purpose as an index. Doubtless if any scybala were formed its intense blackness might possibly disguise the presence within them of a good deal of faecal matter; but the loose stools obtained under the influence of paraffin and of castor oil do not leave room for any doubt on that score. As just now stated, the thick layer at the bottom, the "coal-mine" as it might almost be termed, consists of loose charcoal powder only, the unmixed state of which can at once be verified by running it out on a flat white surface. If it is fair to assume that the composition of the dejecta does not materially differ from that of the contents of the ileum at the valve, then we may safely infer on the strength of the chemical evidence as regards the paraffin, and of the ocular evidence in the case of the charcoal, that they must both enter into contact with the diseased surfaces, and that the contact of the latter with any faecal matter must be very slight, or *nil*. Moreover, since any small amount of faecal matter that may be present other than oil, is mainly composed of granules and of cellular débris, it does not possess that mechanical tendency to cling to soft surfaces so characteristic of vegetable charcoal powder. It is, therefore, not a figure of speech to say that this form of local treatment

realizes the capabilities for better or for worse of the surgical treatment of ulcers by the charcoal poultice; only the poultice is kept on, not for so many hours, but continuously for two, three, or four weeks, and is kept constantly refreshed. This reminds us that, half a century ago, G. M. Jones,²⁴ of Jersey, used with much success for sloughing sores and wounds a rather thin paste of vegetable charcoal and fresh yeast.

Whatever the therapeutic value of this bowel treatment may be, there is no doubt as to the fact that local treatment is being applied, and that the main object in view, which was to save the diseased intestinal surface from coarse mechanical irritations and from the septic contact of faeces, is in large measure secured. It is perhaps not too much to hope that any pre-existing gangrenous process may be benefited, that any threatenings of gangrene may be discouraged, and that any fluids undergoing absorption from the lower bowel may have been largely deprived of their toxic properties.

Very few words will suffice to indicate some of the collateral advantages accruing from the empty-bowel conditions to the patient and to the surroundings.

1. Provided, of course, the bowel is not allowed to remain unrelieved, any marked decrease in the frequency of the evacuations and in their quantity must obviously be a gain, as it means relative physiological rest for the bowel, and as it saves the patient from much unnecessary disturbance and fatigue.

2. From the nursing side of the question there is an economy of labour which *ceteris paribus* is well worth securing.

3. Not the least important aspect is that of preventive sanitation. *Verbum sapienti*: "The less the bulk of faeces so much the less the amount of infective material."

4. Finally, as regards the disposal of the faeces, combustion, which is so much the better way (also for the urine), is facilitated, not only by the quantity of charcoal present, but by the fact that, owing to their relatively aseptic and odourless condition, a much less dilution with disinfecting fluid is needed in the pan.

What are the Prospects of the Method?

This is a question which cannot be answered to-day, and which I must leave to others with wider fields of observation. I believe that, being absolutely harmless, it is worthy of a trial, and that its publication is the only means of securing for it an adequate trial—a trial not only extensive but thorough. The success of any treatment largely depends upon the amount of attention bestowed upon its details, and I cannot disguise from you that this method makes larger claims than some others upon the assiduous supervision of the physician. If the hopes that I venture to entertain should not come true, and that, even with the help of any future improvements in the application of the method, we should fail to obtain a better control over the disease, a check to the downward progress of the inveterate cases, a mitigation of the worst features of the bad cases, and a perceptible reduction in the mortality, there will be no choice but to recommend the adoption of the Currie-Brand treatment on the strength of its recognized efficacy. *Habeant sua fata*—whichever way the experiment should turn out, and whatever form of treatment you may ultimately be led to practise, I believe that the principles which we have considered to-day will fit in with the scheme, and that they will form a useful part of your practical management of typhoid fever.

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An Address

ENTITLED

ARE THE PROBLEMS OF CANCER INSOLUBLE?

Delivered before the Brighton and Sussex Medico-Chirurgical Society, December 7th, 1905.

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REFERRING to du Bois-Reymond's discussion of the limits to physiological inquiry, Mach, in his *Analysis of the Sensations*, points out that those problems which are insoluble from their very nature should be outside the domain of scientific thought. He suggests that their insoluble nature depends on the form in which they are stated—depends, in short, on an erroneous formulation. Rational thought must devise a re-statement of such problems in a way that makes their investigation profitable.

More than other problems of medicine, the problems of cancer present a varying facies, according to the number, the variety, and the nature of the facts which we take into our purview in attempting to formulate them, and the conflicting standpoints of different investigators are the natural result. Experience and discussion have, however, already provided for the proper formulation and solution of some of those problems, but the history of the investigation of cancer presents many instances of problems still baffling solution, because, as I believe, having been originally formulated on insufficient data, they have been wrongly formulated. Nevertheless, their direct solution continues to be freshly attempted.

I propose to indicate my present conceptions of some of the problems of malignant new growths, and the means by which their solution is being attempted. I shall restate some of the problems which have long baffled solution, in a form which makes their investigation profitable and their solution more hopeful.

I shall express my opinions on the progress made towards the attainment of these ends as definitely as possible; and in reply to any criticism that I am not dogmatic enough, I shall contend that the investigation of cancer has suffered, and suffers to-day, from a too great readiness to hold dogmatic opinions on a subject of which we know so little, and regarding which hitherto unsuspected facts have accumulated in recent years and are still accumulating.

Some three years ago the investigations of the Imperial Cancer Research Fund commenced. Those actively engaged in the task essayed to grapple with the disease, not as a problem of human pathology only, but as a comparative biological problem and one requiring experimental treatment. Dr. Murray and myself have striven to place the exact knowledge of the nature and incidence of the disease on a basis commensurate with its ramifications in men and animals. For on the one hand those facts which were matters of common knowledge to the medical profession were drawn from an extremely narrow field of investigation—namely, the study of the disease in man—and, on the contrary, the hypotheses explaining them ranged over the full field of biological knowledge and speculation. To preserve an attitude sufficiently free from bias was no easy matter, because all co-ordinated investigation must be conceived in terms of a working hypothesis of some sort.

OLDER HYPOTHETICAL EXPLANATIONS OF THE NATURE AND GROWTH OF CANCER.

At that time various hypotheses were prominently before the medical profession—three especially contested for favour. In the Cohnheim hypothesis and its variants an embryonic origin was postulated, and to the minds of many the only alternative to an awakening of latent powers of growth in "embryonic rests" was the acquisition of new powers of growth by adult differentiated tissue. What was the amount of growth requiring explanation? It was the amount which sufficed to cause a patient to succumb to cancer, and the explanations were formulated accordingly. The energy with which growth proceeded showed no diminution up to the time of death, and was loosely described as "limitless." How was this amount of growth to be elicited in either