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PROGNOSIS AND THERAPEUTIC PRINCIPLE*

BY

JOHN A. RYLE, M.D., F.R.C.P.LOND.

REGIUS PROFESSOR OF PHYSIC IN THE UNIVERSITY OF CAMBRIDGE; CONSULTING PHYSICIAN TO GUY'S HOSPITAL

It has sometimes occurred to me to wonder with what criticism a man of scientifically judicial mind would head his list if called upon to scrutinize and report upon the daily work of doctors. Perhaps we may safely assume that our method or lack of method in therapeutics would at least receive prominent censure. Even after allowances are made for the difficulties under which we work, the rushed and frequently exhausting conditions of our lives, and the complexity and variability of our human material, we must confess that modern therapeutics in practice are still sadly lacking in system; that many of us are curiously uncritical and susceptible to the blandishments of the proprietary chemist; that we are pessimistic sometimes, but as hopeful often about the new remedy or operation as the untutored laity, and as slow almost to distinguish between "post" and "propter" in assessing the results of treatment.

Vogues in treatment come and go, introduced without experimental justification, and accepted without the application of any crucial test, without comparisons between a treated and an untreated series, without inquiries into mode of action or even a display of curiosity as to whether the remedy includes an active principle at all. Sometimes, even, harmful treatments flourish for a time. The others exhibit a waning curve of popularity, and early exalted claims suffer a gradual extinction with little attendant commentary or reflection on the time and money wasted and the disappointed hopes. We should be very shy of meeting members of other scientific professions, but, in point of fact, in matters therapeutic, and particularly when they themselves are the patients, even eminent scientists are sometimes as gullible as we are.

Is it some survival of the old association of ideas between medicine and magic that allows this state of affairs to continue? Many patients would still seem to believe (and we are not, as a rule, at pains to correct them) that we have hidden powers of healing, and that our medicines, vaccines, rays, and operations, and our psychiatric jargon are expressions of a magical wisdom which recent science has only served to exalt or modify. Actually, of course, we are concerned with highly complicated physical, chemical, and psychological adjustments, and our powers, though ever extending, are still strictly limited. The *vis medicatrix naturae* does, and will always do, far more for our patients than we can.

These self-criticisms notwithstanding there is no real cause for despondency. Through physiology and pathology and clinical observation our understanding of the *vis medicatrix* continually enlarges, and we become better able to condition the lives and actions of our patients

and to apply mechanics, remove diseased parts, and prescribe drugs and regimen to their advantage. From time to time a great discovery, based usually on experiment, gives us a new advantage. The benefits conferred by Pasteur and Lister are immeasurable. Rickets and scurvy, small-pox, typhoid, and diphtheria, even syphilis and tuberculosis, are preventable and coming under our therapeutic control. Acute abdominal diseases and many chronic surgical conditions are far less dangerous and disabling than they were. Surgery and radium have in some degree lessened the menace of cancer. Myxoedema, pernicious and other severe anaemias, and diabetes can be efficiently countered. Malaria and amoebic dysentery have their answers. Psychology is beginning to make a more genuine and useful contribution to healing. Anaesthesia has developed out of recognition. The relief of pain and of many other symptoms is becoming rationalized even when cure is still impossible.

"Credulities and Empiricisms"

What a pity that, in parallel with these advances, we should have to record credulities and empiricisms and follies in therapeutic fashion by the score.

In the last quarter of a century we have witnessed the therapeutic vaccine craze based, not on experiment and the vast experience of war-time as in the case of Wright's prophylactic antityphoid vaccine, but on haphazard speculation and ill-considered enterprise. Organisms isolated from the throat, dental sockets, stools, and elsewhere, and hailed as the cause of the rheumatism, the catarrh, the colitis (and sometimes of the undiagnosed anaemia, cancer, tuberculosis, or gout) have been injected in various combination in their millions of millions—the prescription being at last discontinued when it failed or the patient, after months or years, got better in spite of it. The polypharmacy of the Middle Ages was no more absurd. "Endocrines," "rays," exploitations of surgical procedure, injections of chemical substances vaunted to cure influenza and pneumonia, intravenous chemotherapy for septicaemia, have all been allowed to have their day. In each case it has been the same story. The treatment has been launched with no adequate preliminary experiment, without controls, without clinical trials, and employed without criticism and often, alas, without an adequate diagnosis and to the exclusion of a rational conservative therapy, which, although not miraculous in its effects, at least has the virtue of encouraging or not delaying natural recovery.

Most treatments of the kind I am criticizing are aimed at chronic diseases of variable duration and commonly with a tendency to remission or slow natural recovery. As Gull said: "Medicines do more good when there is a tendency to recovery without them." The remissions

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and recoveries give the upholders of the treatment their opportunities to "claim results." They are never true students of disease. But unless we study disease and its natural variations, how can we ever accept that variations occurring during a treatment are due to it? Other debatable treatments are concerned with acute and alarming illnesses. Here anxiety and a disinclination to dispense with anything which "might do good" provide the common impulse to the employment of the remedy. I have frequently mentioned my indebtedness to the writings of Sir William Gull, who, at a time when various cures for rheumatic fever were being boomed in the profession, made (in collaboration with Dr. Sutton) the simple experiment of treating a number of cases with mint-water in order to prove to himself and others what was the course of the disease uninfluenced by other factors than rest in bed and nursing. He thereby demonstrated to the profession that the new remedies were incapable of shortening the disease or of modifying its pathology. That is a simple form of experimental control which might well be applied in other diseases as a preliminary to reports upon the new "specific."

To-day I propose to select for particular discussion certain treatments which may be allowed to come within my sphere of criticism either because of the manner in which they have been launched and the credulity with which they have been accepted, or because they have already been employed for a long time without adequate justification or proofs of efficacy, or because I see a danger of their becoming accepted as general rather than occasional therapeutic measures. In each case, it seems to me, there has been acceptance without due criticism or proper clinical trial or without a fair determination of scope. In each case the chief criticism of the method is to be found in a simple study of the prognosis of the disease or a fuller understanding of what Sydenham would have called its "natural history."

I shall consider in turn: (1) a recent treatment of peptic ulcer by the injection of histidine; (2) a recent suggestion that surgical intervention for bleeding peptic ulcers should be extended; (3) the employment of serum in streptococcal septicaemia; (4) the employment of type sera in pneumonia; and (5) the use of certain much "boomed" subcutaneous remedies for pneumonia, influenza, and other febrile diseases. Some of these treatments have had their origin in genuine scientific endeavour and in animal experiment, or have derived from wide clinical experience and the growth of technical skill. Others have had no such initiation. In the case of (2) and (4) I would make it clear in advance that I fully appreciate that there are certain circumstances in which the treatments are justified. I am apprehensive only lest their advocacy should be too generally and thoughtlessly or too rapidly approved.

The Histidine Treatment of Peptic Ulcer

A year or so ago, on the basis of animal experiments¹ in which ulcers produced by gastro-intestinal anastomoses were said to be benefited by injections of amino-acids, and especially of histidine, this treatment was advocated and widely adopted, both in this country and abroad. It was indicated at an early stage that the treatment could be carried out without strict dietary or strict rest, a concession which was naturally very acceptable to ulcer-dyspeptics. Soon letters appeared in the journals from doctors who considered that they had had success with the new method, and reports were published on series treated at hospital with more or less inadequate controls in respect of the criteria of healing, and of the time allowed to elapse after the treatment, and with no parallel untreated series for comparison. The stage of criticism

and disappointment is now arriving, but not before there has been a great expenditure of time and money on the treatment and some ulcers have perforated or bled during or soon after its employment.

What should our grounds for initial scepticism have been in this instance, and what criteria of effectiveness should we have demanded? In the first place, even conceding that certain not very convincing animal experiments with recent artificial ulcers could be allowed to persuade us of the justification for a clinical trial with chronic naturally occurring ulcers in man, it seems highly improbable that injections of minute quantities of an amino-acid subcutaneously could promptly influence the activity of a chronic gastric or duodenal lesion, a type of lesion notoriously slow in its response to physiological rest, whether supplied by medical or surgical measures. Secondly, to claim that this physiological rest, which has some degree of proved efficacy, could be dispensed with should at once have suggested ignorance or opportunism on the part of the advertisers of the treatment.

When we come to the therapeutic trials themselves, as reported, our knowledge of the prognosis or natural history of peptic ulcer at once compels dissent. Symptomatically peptic ulcer is a disease well known for its natural fluctuations. In the case of duodenal ulcer particularly it has long been recognized that any small change of circumstance, such as rest in bed or going on a holiday, will cause the symptoms immediately to disappear; that even in the absence of treatment it is usual for the symptoms to remit after two to four weeks, and commonly for weeks or months at a time; that disappearance of symptoms may occur in the presence of a large crater; that some ulcer-craters disappear very readily and in response to varying treatments; that radiological and clinical criteria of healing are themselves not infallible; that cases must be carefully followed for many months or even years (not for a few weeks or a few months) and then reinvestigated before sound healing can be surmised; that apparent recovery after a treatment does not necessarily mean recovery because of treatment; and that recovery in cases in which histidine, diet, and alkalis were simultaneously prescribed proves nothing in favour of histidine.

In none of the commendatory letters or papers which I have seen has there been a sufficient appreciation of the very strict observances necessary before a genuine claim on behalf of histidine can be submitted. The writers have had no conception of the conditions of an experiment. I have seen a number of cases in hospital and private practice in which, on clinical and radiological evidence, histidine treatment seemed to me to have been worthless. I have seen none in which I was convinced that periods of improvement attributed to it were due to it. But I am not allowing myself to be unduly biased by this experience. Histidine may have some beneficial effect, but no one has yet proved it by experiments which satisfy me, and in the meantime a large number of patients have been deprived of treatments whose benefits are widely accepted on the basis of old-standing experience and close observation, while a few have suffered perforation or haemorrhage that might have been avoided. Should not we and our patients demand a better method of assaying the value of a new remedy than this very unscientific, "hit or miss" performance? A small committee to investigate and report on the substance itself, its pharmacological and biological properties, and the experiments upon which its production was based, and then (if a therapeutic trial seemed justifiable) a series of fifty or more cases studied by competent observers in a group of hospitals would soon provide the answer to our question.

This answer might or might not please the manufacturer, but it would at least satisfy our critical sense and do service to therapeutics and justice to our patients. A reinvestigation of histidine with animal experiments by Barry and Florey² has now thrown doubt upon the original animal work upon which the treatment was based.

The Treatment of Bleeding Peptic Ulcer by Immediate Surgery

In the *Lancet* of October 19th, 1935, Mr. Gordon-Taylor,³ for whose surgical skill and resource I have the greatest admiration, advocated a more extended trial of surgical measures in cases of severe bleeding from a gastric or duodenal ulcer, basing his advocacy first on the gravity of the complication itself, and secondly on the improvement in the prospects of operation due to such accessory measures as continuous drip transfusion. In his own words: "Finsterer's first forty-eight hours" is still the optimum period for surgical attack in haematemesis, and the golden age of gastric surgery will have been attained only when all cases of haemorrhage from chronic ulcer come to operation within that space of time." He quoted mortality figures for severe haemorrhage ranging from 2.5 to 12.7 per cent. Other writers give even higher figures, up to and above 20 per cent.

That there should be such divergences in itself suggests that we are too uncertain about prognosis to justify embarking upon a new treatment involving considerable risk. There is no settled statement at present as to what should be understood by "severe haemorrhage." Clearly the more we segregate the "very severe" from the "rather severe," the higher the mortality becomes. The larger figures might well seem to justify a consideration of alternative methods to those in common use for the treatment of gastric haemorrhage, but they were so much in excess of ordinary experience that they prompted Dr. Hurst and me to make independent inquiries into private and hospital figures. Dr. Hurst also circularized a number of general practitioners of large experience, and the common verdict was that gastric haemorrhages, however alarming, have a low mortality. The accompanying Table I indicates the widely varying mortality figures that have been quoted.

TABLE I.—Mortality Rates of Haemorrhage from Ulcer given by Various Authors

Author	Place	No. of Cases	Death Rate per cent.
Aitken ...	London Hospital	255	11
Bulmer ...	Birmingham	578	10.7
Burger and Hartfall	Guy's Hospital	137	22
Chiesman ...	St. Thomas's Hospital	191	25
Conybeare ...	Guy's Hospital	600	2.5
Crohn ...	Mount Sinai Hospital, New York	101	4.2
Cullinan and Price	St. Bart's Hospital	105	18.1
Davies and Nevin	St. Thomas's Hospital	391	21
Eggleston ...	Michigan	95	1
Gordon-Taylor ...	Middlesex Hospital	Not stated	21
Hellier ...	Leeds	202	13
Hinton ...	Bellevue Hospital, New York	52	20
Lynch ...	Canada	31	12.9
Meulengracht ...	Copenhagen	251	1
Paterson ...	London	Over 100	4
Ross ...	Australia	187	6.5

(From Babey and Hurst, *Guy's Hospital Reports*, 1936, lxxxvi, 129)

Here are my own private figures. My "severe" cases were definitely described as such in the notes, or the patients were in bed for a period of weeks, or were recorded as having haemoglobin figures of 50 per cent. or less.

TABLE II.—Mortality from Uncomplicated Haemorrhage Expressed in Relation to: (a) Total Cases of Ulcer; (b) Total Cases of Ulcer with Haemorrhage; (c) Total Cases of Ulcer with Severe Haemorrhage

	Per cent.
(a) Mortality from uncomplicated haemorrhage in ulcer (754 cases) ...	0.5
(b) Mortality from uncomplicated haemorrhage in cases of ulcer with haemorrhage (258 cases) ...	1.6
(c) Mortality from uncomplicated haemorrhage in cases of ulcer with severe haemorrhage (128 cases) ...	3.1

(Private series)

Babey and Hurst⁴ at Guy's Hospital, in another recent series of cases of peptic ulcer admitted for haemorrhage, found a mortality from haemorrhage of 4.8 per cent. A combined general practice series (525 cases) gave a mortality of 1.5 per cent. Meulengracht,⁵ employing a much more liberal diet in the early stages, claims a mortality of only 1 per cent. in 256 cases of severe bleeding. Christiansen⁶ in Denmark, in an inquiry into "massive haemorrhage in peptic ulcer," found a mortality of 7.9 per cent., but remarks that the case mortality has almost doubled since blood transfusion became a frequent addition to treatment.

Now Finsterer,⁷ whom Gordon-Taylor rightly acclaims as the modern master of gastric surgery, remarkable though his successes are, and employing such refinements of technique as are not yet at the command of the generality of surgeons, has shown in a series of fifty-nine cases a mortality of 5 per cent. with immediate operation—that is, within forty-eight hours. In other words, taking the great risk which an operation in a case of gastric haemorrhage must always involve, and employing his own wonderful technique, he still cannot improve upon these medical figures obtained from three sources of practice and based on an analysis of a much more extensive series.

But that is not all. A full study of natural prognosis requires a consideration of the influence of sex, age, length of history, the previous state of the patient, and such factors. Gastric haemorrhage from an ulcer in young adults is so rarely fatal that it is just to ask whether surgery should ever be employed in the first three decades, however severe the bleeding. In the older group, although the natural prognosis is worse, the risks of surgery must also be the more carefully weighed, because the risk of intervention is greater. Hospital patients, for economic reasons and because they have been moved to hospital, are apt to be in poorer condition than private patients treated in their homes. Of my four cases of death from uncomplicated haemorrhage—that is, uncomplicated by old age or illnesses which would have precluded operation—the ages of the patients were 55, 50, 36, and 26. All gave long histories of dyspepsia, and the two younger patients both gave histories suggesting the presence of a chronic penetrating ulcer. Deaths are usually due to erosion of a large vessel by a very chronic and often adherent ulcer—the hardest type to deal with surgically even in a patient who is not shocked and exsanguinated.

Briefly the present situation is this. The discrepancies between mortality figures from various sources are so great as to suggest incomparable methods of analysis or treatment in the different groups. A more careful study of prognosis is clearly necessary. Taking the lower estimates of many experienced observers, the mortality from bleeding peptic ulcer treated medically by conservative methods is found to be not greater than 5 per

cent. Surgery in the most skilled hands has not effected a lower mortality. With very great skill and modern improvements lives can be saved by surgery, but the mere fact that they can be saved by an alternative method does not in itself justify the general adoption of that method. Surgery may save a few lives which medicine would have failed to save, but, equally, surgery may lose a few lives which medical treatment would have saved. An extension of surgical treatment as recently advocated, and its wide adoption by surgeons of varying grades of efficiency, will, almost without question, increase the mortality.

Although I am prepared to accept that I may yet have reason to modify my views and to counsel surgery in particular circumstances, reflections of this kind and a recent review of prognosis in hospital, general, and consulting practice seem to me to call for a continued support of conservative treatment in gastric haemorrhage from chronic ulcers.

Finally, we have yet to decide whether transfusion has improved or damaged the prospects of recovery in medically treated cases. We have yet to understand more intimately the factors endangering life, for, in addition to anaemia, dehydration and, in some cases, alkalosis with uraemia, are known to be contributory.

Serum in Streptococcal Septicaemia

For more than a quarter of a century it has been customary to employ anti-streptococcal serum, given subcutaneously, intravenously, or intramuscularly, in cases of streptococcal septicaemia. Many isolated cases and small series have been recorded in which recovery has followed and sometimes been attributed to the treatment, and yet the general anxiety which the disease promotes has never been appreciably influenced by the treatment. Few individuals, perhaps, see enough cases to allow a settled opinion in regard to the efficacy of serum, and as it is generally given (if for no stronger reason) for fear of omitting something which might have a beneficial effect, comparisons between a treated and an untreated series are rarely possible. In a given case we have no certainty that the available sera are specific for the particular infecting organism. It is improbable that most sera are anti-bacterial, although some of them—notably scarlatinal serum—have an antitoxic action. Serum may not only fail to do good; it may do actual harm by causing anaphylactic symptoms. Even in very grave cases recovery can undoubtedly occur without it. If it were possessed of any outstanding potency we should, after a quarter of a century, have welcomed and approved it more unanimously, as we have welcomed and approved the antitoxic sera employed in diphtheria and tetanus.

Why have streptococcal and pneumococcal antisera been so much less dramatic in their influence than the antitoxic sera for diphtheria and tetanus? In the first place the latter are employed to counteract an intoxication and not a septicaemia—a very different proposition. Secondly, with both of these antitoxic sera the attack is launched when the intoxication is still local and before it has spread to distant tissues, or if it is not launched early—that is to say, within a few days—the treatment is ineffective. In the case of a septicaemia the disease is usually active and generalized before the indication for the serum arises, so that even if the remedy possessed an anti-bacterial or antitoxic potency it comes into play unduly late. But let us leave these theoretical considerations and consider some results of serum treatment.

In 1931 Dr. R. E. Smith and I⁸ contributed to a symposium in the *Guy's Hospital Reports* a joint paper on "The Natural History, Prognosis, and Treatment of Streptococcal Fever." My own observations were based

on experience chiefly obtained in private practice. Dr. R. E. Smith examined the reports of cases of streptococcal septicaemia admitted to Guy's Hospital over a period of ten years. A careful study of the case histories and temperature charts gave us no conviction that serum, often given in very large doses, ever contributed towards the recovery. Subsides of pyrexia rarely appeared to follow directly after the treatment. A fall in temperature following drainage of abscesses or a natural subsidence after the serum treatment has been discontinued for some time are apt to be claimed by the uncritical as effects of the serum. I can recall one case only in which the patient, a medical man, was convinced, while I myself remained sceptical, that the serum made a sudden difference and helped his recovery from a general septicaemia. In this case I employed a mixture of various brands of sera, hoping for specificity in one of them. More recently Colebrook,⁹ writing on puerperal septicaemia (*Streptococcus haemolyticus*), has concluded that there is no evidence that these sera are of any value, and that they may do harm. The mortality was higher in the treated than in the untreated control series analysed by him. It cannot, however, be concluded that the serum was the cause of the higher mortality in the treated series.

TABLE III.—Death Rate of the Serum-treated Cases and of the Cases which had no Serum

	Cases	Deaths	Case Mortality (per cent.)
All cases treated with serum before admission	69	21	30.4
All cases which had no serum ...	932	108	11.6
Haemolytic streptococcus cases:			
Treated with serum ...	40	18	45.0
Treated without serum ...	346	70	22.3

(From Colebrook, *Lancet*, 1935, i, 10, 85)

Serum treatments are expensive, their administration may be very disturbing to very ill patients, and they are capable of causing immediate and remote anaphylactic symptoms which only add to misery. Until the laboratory worker and the clinician, working in collaboration and imposing upon themselves the strictest rules of observation and control, investigate and report further upon these problems, we are, I believe, entitled to withhold treatments so slenderly supported by common observation and by comparative prognosis in treated and untreated groups of cases.

Type Serum in Pneumonia

I come now to a more difficult judgement. Very careful work in the United States and in this country, based upon competent animal experiment and hospital studies, has demonstrated a reduction of mortality in lobar pneumonia due to infection with pneumococcus Types I and II. Cecil¹⁰ in America, in 422 untreated cases (all types), found a mortality of nearly 36 per cent. In 429 cases (all types) treated with serum the mortality was 28 per cent. The best results are obtained in Type I cases, some observers claiming a reduction of mortality by almost half when treatment is instituted within the first seventy-two hours. Type I infection accounts for approximately one-third of all cases. The mortality figures for pneumonia in the United States are higher than in England. Waterfield,¹¹ at Guy's Hospital, over a nine-year period, found a total mortality of 16 per cent. between the ages of 13 and 75 years. One-third of the deaths occurred above the age of 50. There were no deaths between the ages of 15 and 20.

Making the following allowances: that above infancy the mortality of lobar pneumonia in children is probably too low to justify drastic treatments of this kind; that after 50 the mortality is doubtfully influenced by serum; that the natural recovery rate taking all ages in this country is approximately 80 per cent.; that serum should probably not be given unless it be of appropriate type; that typing may take from twenty-four to forty-eight hours; that serum after the third day is of steadily diminishing value; that the diagnosis is often not possible until the second or third day; that serum must be given once or twice daily and intravenously; that serum reactions, in spite of improvements in the sera, still occur; and, finally, that minimal interference has long been accepted policy in this disease—where does our duty lie in connexion with this accessory treatment?

Pneumonia is one of the acute diseases in which a patient may seem to be desperately ill and yet make a complete recovery. How are we to judge whether serum may be necessary to tip the balance in his favour, or, when we employ it, that it has been the cause of a recovery? Serum treatment is clearly more suited to hospital than to private practice, owing to the demands which it imposes in the matter of investigation, close nursing, and watchfulness, and of the time and preparation expended on intravenous medication. The mortality is already lower, in all probability, in private practice than in hospital practice, and home treatment under good conditions is therefore, in ordinary circumstances, to be preferred to transportation for hospital treatment.

Knowing what we do of prognosis and the moderate contribution which serum has been shown to make, I would suggest, pending further studies, that serum treatment should be reserved for patients between the ages of 20 and 50 who appear to be gravely ill in the early stages, or are alcoholic, or whose blood shows no leucocytosis, who give no allergic history, and for whom a typing can be secured within the first seventy-two hours. Where the choice lies between good conditions and good nursing at home without serum and movement to hospital for serum treatment I should generally prefer the former, but judgement, as always, must be reserved for the individual case. It is a very hard decision to withhold a treatment which might just make the difference in the contest between infection and immunity, and so save a life. If serum could produce results like antitoxin in diphtheria or insulin in diabetes we should have no hesitation in advocating its extended use, but the judgement is, as I have sought to show, a much more difficult one, and in each case our general knowledge of prognosis and individual and local circumstances must be allowed to exert its proper influence.

Some Other Treatments

I have thus far chosen to discuss methods which have been widely advocated or used and which have had some scientific backing, but in regard to which it seemed desirable that we should pause and take stock. These methods must, I suspect, have set many conscientious men thinking. There are others in use which I have not yet discussed and which are so patently unsupported by reason or inquiry or results that one wonders how they retain their popularity at all.

I have frequently been asked in recent years, when called to consult over a case of pneumonia, septicaemia, "influenza," bacterial endocarditis, or other obscure continued fever, what my opinion was of substances which I will call X or Y, and which have been advocated by proprietary firms, and, more rarely, by medical men writing to professional journals, as capable of influencing humoral pathologies and expediting cure. Their vogue

is now, I fancy, declining. I have usually prophesied that it would do so, just as the use of vaccines and the application of ultra-violet rays for every kind of debility have suffered a gradual loss of favour. Why should I have been sceptical? The reasons are easy to state. First, the treatments were launched without preliminary trials; their boons, just like those of any quack remedy in the advertisement pages of the Sunday papers, were proclaimed in advance. Secondly, the claims for these substances were not, so far as I could learn, based upon any animal experiment. Thirdly, their pharmacological or biological actions, whether in animals or men, did not appear to be known, if, indeed, they had any such action. Fourthly, although they were clearly being used quite extensively in practice, in the teaching hospitals they had no vogue. Finally, when I examined charts and cases in which these remedies had been used before my advent I could not discover that anything had been achieved by them. Sometimes their employment had even seemed to stultify inquiry and postpone diagnosis. I remember a laudatory paper in a journal in which a doctor reported upon cases of "influenza" treated with one of these remedies. In the majority of his cases the fever terminated within three days. He quite overlooked the fact that that was the approximate course of the disease in the particular epidemic.

What are the reasons, apart from the subtle virus of advertisement, which impel doctors to employ such doubtful and unproved remedies? They may do so in an anxious or troublesome case with a forlorn hope that this time "it may do good." They may do so from a vague urge "to do something active" when at the end of their resources, and for some reason a hypodermic injection has come to be regarded as a more positive action than the prescription of a potion or a poultice. They even do so—and this has not infrequently, I believe, been the case with vaccines and with histidine—"because the patients demanded it."

But surely these are all motives unworthy of our art. Not only are they unworthy in themselves, but I would suggest that each time they lead to action they are liable to be accompanied by omission of rational symptomatic measures of importance to the patient. There is no case, however obstinate or grave, in which there is nothing left to be done. Sleep and rest must be secured; anxiety on the part of patient and relatives must be comforted or allayed; nurse and relative must be given instructions and "kept busy" in all such emergencies as haematemesis, streptococcal septicaemia, and pneumonia. For the patient posture, the administration of morphine or oxygen, the fluid intake and how it should be maintained and by what routes, the blood count or culture, and many intimate details of nursing must all be catered for. Close clinical scrutiny must continue with the mind as far as possible detached from its anxiety. Meanwhile the *vis medicatrix* is being assisted and the doctor is busy enough, without unwarranted or speculative interference, to satisfy patient and relative, who will be the first to appreciate the form and intent of his industry. Referring to the details of symptomatic treatment employed by him in rheumatic fever, Gull¹² remarked that "it required often more consideration than was requisite for prescribing any supposed appropriate drug treatment." The same could be equally well said of careful routine treatment in ulcer cases, gastric haemorrhage, septicaemia, and lobar pneumonia.

Accepted Treatments

Let us now contrast the study of new remedies which have been unanimously acclaimed. Banting's discovery of insulin was based upon careful experimental methods, its action confirmed in animals with experimental diabetes

and then upon patients with the natural disease treated under proper conditions in respect of control and observation. Only then was it presented to the profession. Within a few months its benefits were everywhere apparent. It had "come to stay" in every country in the world. It satisfied alike the credulous and the sceptical.

Minot's demonstration of the value of liver therapy in pernicious anaemia was partly dependent on earlier animal experiments by Whipple with artificial anaemias and then on careful clinical trials checked at every stage. Its refinements have depended equally on close clinical observation and intimate haematological study. As a consequence an intensive study of the blood diseases has followed and the value of massive iron therapy in microcytic anaemia has also been proved. As with insulin, so with these treatments acceptance was inevitable; the treatments were studied eagerly and employed actively but critically in the teaching hospitals from the first, and rapidly revolutionized practice throughout the world. In each case prognosis was at once and subsequently improved.

The experimental method of originating new therapeutic measures does not preclude the occasional empirical discovery like quinine and digitalis and prostigmin, but even such discoveries require and have received, sooner or later, what may be called "adequate clinical trial" or scientific assay, or both. The Therapeutic Trials Committee of the Medical Research Council does valuable work in arranging for proper trials of any new remedies which the manufacturing chemists are prepared to submit to it, but we are daily confronted with the advertisements of treatments launched as a commercial speculation and with no such scrutiny. I believe that our profession would gain nothing but respect and increased allegiance from the public if it were to insist on more frequent and judicial inquiries into all therapeutic innovations.

My remarks are not uttered in a censorious spirit, nor are they intended to apply to any one section of our fraternity. They are the expression of a mental discontent which I believe we all share in some degree. I put them forward alike for the consideration of the general practitioner, the consultant, the clinical and laboratory specialist, and the manufacturing chemist.

In addressing your old and honoured Pathological Society I may appear to have wandered too far afield and to have touched upon matters of conduct in practice which might, at first thought, be held to be remote from pathology. But, in fact, all I have asked for is a better appreciation of all that pathology, using the word in its broadest sense, implies. Only by the study of disease and its natural origins, processes, and progress can we learn how to influence its prognosis for the better, whether by active intervention or refraining therefrom. In the next stage of medical evolution the actions and uses of remedies, in common with other biological phenomena, must be determined not by advertisement or opinion, but by observation and experiment.

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SOME METHODS OF ANALGESIA DURING LABOUR*

BY

KATHARINE LLOYD-WILLIAMS, M.D., B.S.

HONORARY ANAESTHETIST, ROYAL FREE HOSPITAL AND ELIZABETH GARRETT ANDERSON HOSPITAL

Relief of pain during the second stage of labour has now become a fairly well-accepted practice, though even now, I regret to say, there are still some practitioners who consider the use of analgesics unnecessary for the normal case. Relief at this stage is usually obtained by the administration of an inhalation anaesthetic given intermittently with the pains, so that an analgesic effect is obtained. This method has much to recommend it, for the co-operation of the patient is retained and she is able to make voluntary efforts and so hasten delivery.

Inhalation Anaesthesia

Of the inhalation anaesthetics, chloroform and gas in combination with either air or oxygen are the most commonly used. Each has its adherents, and circumstance usually decides which is used. It is obvious that chloroform is often the only possible anaesthetic for use in domiciliary practice, more especially in country districts. Its cheapness, portability, and ease of administration account for its popularity.

The use of gas and air and gas and oxygen is steadily increasing, and rightly so, for wherever possible it should be chosen as the least toxic of the anaesthetics. In hospitals or nursing homes where portability is not a consideration gas and oxygen or gas and air is most certainly the anaesthetic of choice, and Dr. Minnitt has done a great service by the introduction of his ingenious gas-and-air machine, which is now making it possible to use gas much more widely in domiciliary practice. Though I consider gas and oxygen and gas and air to be of the greatest value throughout the second stage of labour, I am not fully convinced that either of these alone is, in many cases, really sufficient for the actual delivery. The addition of a small amount of ether or chloroform for the crowning of the head adds very much to the ease and comfort of delivery, both to patient and to obstetrician.

Relief from pain in the second stage does not really present a very difficult problem now where adequate assistance and instruments are to hand. I wish, at this time, to draw particular attention to the relief of pain during the latter part of the first stage of labour. This is often described by the patient as being the most wearisome and painful part of her whole labour. The cervix is dilating, often very slowly, and the patient can do nothing to help herself as she can in the second stage by her voluntary efforts. The form of relief which we should give her at this time differs essentially from that given for the second stage, in that an intermittent form of relief, such as is obtained by inhalation anaesthetics, is, to my mind, inadvisable.

It should be borne in mind that if an inhalation anaesthetic has been begun it must be continued until the time of delivery. It is obviously unwise to use chloroform in this way, for its toxic effects are most often seen in those cases which have received it over a long period, even in very small doses. Gas and air, or gas and oxygen, is sometimes used before full dilatation, but I do not approve of its prolonged use in the first stage, for the intermittent form of relief is often inadequate and very tiring to the patient. Though she may get relief with each pain, she

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