On the relations between disease and regulating nerve centres : the Cavendish lecture for 1889 : delivered before the West London Medico-Chirurgical Society, on Friday, June 7th, 1889 / by James Andrew.

ON THE

RELATIONS BETWEEN DISEASE

AND

REGULATING NERVE CENTRES.

THE CAVENDISH LECTURE FOR 1889.

DELIVERED BEFORE THE WEST LONDON MEDICO-CHIRURGICAL SOCIETY,

On Friday, June 7th, 1889.

BY JAMES ANDREW, M.D.OXON, F.R.C.P.,
Physician to St. Bartholomew's Hospital.

LONDON:
ILLUSTRATED MEDICAL NEWS COMPANY, LIMITED.

1889.

ON THE RELATIONS BETWEEN DISEASE AND REGULATING NERVE CENTRES.

πάθει μάθος.

THE choice of a subject for such an occasion as this is no easy matter.

After much hesitation I determined to lay before you some views, rash speculations, if you like to call them so, which have long interested me as to the influence of certain physiological arrangements on the causation and development of disease, and I do so in the hope that some of you, out of the fulness of your knowledge, will be able to correct or confirm them. The subject also is one which has a direct bearing upon our daily work.

Modern investigations have very largely modified our views as to the causation of diseases. Some diseases which a short while ago were looked upon as intrinsic, diathetic, or constitutional, *e.g.*, tuberculosis, have been shown to be due to a specific exciting cause, and with regard to many others it is certain that, great as must be the difficulties of actually demonstrating their exciting causes, they also will sooner or later be proved to be infective, extrinsic.

Again, the so-called predisposing causes, *i.e.*, the modifications of structure, composition, and function, which render the organism

susceptible of disease, are in like manner, naturally, and to a great extent justly, held to be themselves due to external causes. Thus it comes about that, although we no longer look upon pathological processes as something different in kind from physiological processes, still, so far as causation is concerned, disease is generally looked upon as something which comes to us from without.

The exciting external cause may be so powerful that the most healthy organism is unable to resist it, or it may be that it must be aided by predisposing causes, *i.e.*, that it can produce no effect unless there exist some bias, some taint, some weakness, which in its turn has been brought about by the agency of external influences.

Thus, in fact, all disease begins mediately or immediately in the environment.

As an abstract proposition this is undeniably true. Both physiological structure and function and pathological structure and function are ultimately due in large measure to the external conditions under which the organism exists; change those conditions, and neither structure nor function would be exactly what they are. Indeed, so far as my present subject is concerned, I have no objection to make to the still stronger statement which you will find on page 332 of Dr. Harry Campbell's recently published learned work upon the causation of disease. "The environment," he says, "is in the last resort the sole cause of disease. This will be clear if we keep before us the formula, Structure + Environment = Disease. If it can be shown that structure is the outcome of structural modifications wrought through the environment, then it becomes obvious that structure + environment, or disease, is produced by the environment, and by the environment alone."

But it is not true if it be held to imply that the normally healthy body will remain healthy if it do not meet with some special (not necessarily specific) injurious surroundings, that the

normal body in a normal environment will remain healthy, the chief exception being that the normal degenerative changes of old age may make our bodies unable to resist certain external influences which in our period of vigour may have been actually beneficial to us, *e.g.*, exposure to cold.

Now it seems to be worth while to inquire whether this theory of the external origin of diseases may not be, has not been, pushed too far. In opposition to it I shall endeavour to prove that normal physiological action, however perfect, nay, perhaps because it is perfect and in a normal environment, may be the starting-point, the exciting cause of disease, independently of any directly injurious external factor whatever.

And, again, that physiological action, so far from neutralising, in many cases aids and intensifies pathological action. In fact, he who wrote, "I bring to life; I bring to death;" "I care for nothing; all shall go," had at least as true an insight into the workings of nature as those who talk of the *vis medicatrix naturæ*. Were the learned designer of Hygeia himself perpetual dictator of that happy city, deaths from disease would still occur within her walls.

In the arrangements of the outer world one cannot fail to notice, as indeed man has always done, and has openly recognised by the use of such common phrases as to conquer, to subdue nature, a curious imperfection, a perverse inadequacy to human requirements. Nature makes lavish promises of ease and comfort, but if left to herself rarely, if ever, fulfils them. The woes of him who inhabits the handiwork of the modern jerry builder must have been more than equalled in the experience of pre-historic cave man. In one of his novels, "The Toilers of the Sea," Victor Hugo discourses eloquently upon the evidences in Nature, not of design, but of imperfect execution. Our unfortunate ancestors sought in their caves a refuge from the elements; their distorted bones, and those of their dangerous

rivals the gigantic extinct carnivora, prove to this day that they found them veritable caves of the winds, with a constant but uncontrollable water service. In one chamber Nature supplies the cave-dweller with a perfect bath-room if only the floor would hold water, in another with a soft bed of moss which can only be used as a wet pack. Or, again, she constructs the semblance of an easy chair, in which, from its hardness and inequalities, ease is impossible.

The same perverse inconsequence defaces also some of the very highest of man's achievements; *Summum jus summa injuria* neatly expresses the same fault in the operation of human law which exists in that of the laws of nature. Surely, the history of civilisation, of human progress, is but the tale of man's efforts, too often fruitless, to remedy the defects of nature and of his own organisation, physical and moral.

Now these disappointing, these perplexing shortcomings, I had almost said practical jokes, of nature are found, I believe, in some at least of the physiological arrangements of perfectly healthy living creatures, and here as elsewhere they may, and do, lead to serious results. Before, however, entering on my main argument it is necessary to define as accurately as I can the precise sense in which certain terms will be employed in it.

What is the meaning of a perfect organ, a perfect organism, of perfection, of health, and of perfect health? Now, if these terms, as they very commonly, though unconsciously, are, be taken to mean ideally perfect, ideal perfection, ideal health, I have propounded, not a paradox, but utter nonsense in stating that the first beginnings of disease may arise in a perfectly healthy organism *without* any external morbific impulse, or even that morbid processes, started by external agents, may be intensified and rendered fatal to itself by the purely physiological reactions of such an organism.

The ideal of a perfectly healthy organism could not well be less than this, viz., that it is one in which, once arrived at its perfect stature, the waste of tissue consequent upon vital action would be so exactly replaced in kind, quantity, and distribution that its several parts and their relations to each other would remain unaltered, would not undergo the changes which mere lapse of time now brings with it. Such an organism would be proof against all outside injurious influences, short of actual chemical or mechanical violence, and would also be capable of accommodating itself to ranges of climate and of weather far more extensive than any to which our bodies in their present state could be exposed with impunity. Woe betide any pestilent micro-organism which ventured within reach of ideally *perfect* leucocytes. Now, of the existence of such ideal perfection in man or animal we have no knowledge; we call a living being perfect in its kind or perfectly healthy, when it comes up to the standard determined by anatomy and physiology as a matter of fact. Of organs and organisms, then, in their present known condition and in that alone I state that their very perfection, *i.e.*, their conformity to the highest ascertained anatomical and physiological standards, may prove injurious to themselves.

If any one is even yet disposed to look upon my thesis as absurd, his objection may be, in part at least, removed by an addition which I am now prepared to make to the title of my lecture, which would then stand thus: "On the Relation between Disease and the Regulating Nervous Centres as a Proof of the Imperfection of the Present Stage of Man's development."

I have limited myself to the consideration of some of the inconveniences resulting from the statutory perfection, if I may use such an expression, of the regulating nerve centres, because to attempt to enumerate and put in evidence all the instances of imperfect execution in the mechanism and dynamics of the

human body would require a wealth of knowledge, a keenness of observation, a power of reasoning, and a length of life for which I cannot hope.

Again, in these centres, probably the latest, and perhaps because they are the latest, additions to our framework, we find the most striking instances, the most telling illustrations, of Nature's waywardness, of "her prentice hand," indeed, just that class of facts essential to an argument which I am to-day compelled to treat by illustration rather than by strict induction.

Exception might be taken to the use of the term "nervous centres." It might be said that this involves at least two assumptions which are not yet proven, viz., that regulating mechanisms are "centres," and that they are "nervous." For thirty-five years ago Claude Bernard pointed out that in the case of excrementitious products such as urea, and even of substances foreign to the organism, such as iodide of potassium and yellow prussiate of potash, there is, as a rule, some one organ or other specially adapted for their elimination. So long as they are present in small quantities only they pass out through this channel alone, but if their percentage rises to a certain figure, as a consequence either of increased production or of a larger quantity being introduced from without, and especially if at the same time their natural exit be in any way interfered with, then with each successive rise in their percentage other organs, either of excretion or even of secretion, join in the task of removing them from the blood, and themselves suffer more or less severely in the process. Now all this might be done without any nearer approach to a nervous centre than is to be found in the common gas apparatus for maintaining fluids or an air chamber at a given temperature in spite of external variations. It cannot be denied that the regulation of temperature, or of intra-vascular pressure, or of the composition of the fluids of

the living body might be effected in some such automatic fashion; but in point of fact we now know that it is not so, at any rate in the majority of cases.

Granted, however, that this "overflow" theory were true, my thesis would undoubtedly be furnished with yet stronger proofs than it has at present, for judging from the result of the possible application of this method, *e.g.*, in the case of urea, its practical working would seem to be less satisfactory than even that of "nervous centres."

The difference between the rudest canoe of the lowest savage capable of making one at all and a modern war-ship is not so great as that between the lowest forms of life and ourselves. With each differentiation of function, with each advance in structural development, regulating centres become more and more necessary, and like the parts which they have to control, like the balance which they have to maintain, become more and more complicated.

Their action is required by the ever-multiplying needs of the organism in two directions, easy enough to distinguish in idea, but very difficult to separate by any hard and fast line. On the one hand they have to co-ordinate the action of highly complex groupings of muscles, so that each individual muscle may contribute its exact quota to the required result, *i.e.*, to a movement of given force, velocity, direction, and extent.

On the other hand, they have to maintain, and that in some respects within very narrow limits, the "internal climate," *i.e.*, the temperature, the pressure, the relations chemical and physical of gases, fluids, and solids, essential to the activity and even to the life of the sharply differentiated tissues. And this internal climate, be it remembered, is affected more or less by every act of the organism, and by every external impulse to which it is subjected.

The consequences of failure in this duty are sometimes directly

fatal, *e.g.*, the death, more or less sudden, which often follows upon shock to the nervous system. Its performance requires the harmonious co-operation of striped and unstriped muscles, and also of all processes of nutrition, secretion, and of excretion. Thus the connection of the regulating centres with the different parts of the organism through both afferent and efferent nerves must be most intimate, most complex; and to this very complexity we shall see that some of their chief imperfections are owing.

The scope of my present undertaking requires me to pass on one side all cases of disordered function which are clearly preceded by organic changes, due to disease in the nervous centres themselves, whatever the starting-point of these changes may be; *e.g*, defects in quality or quantity of blood supply, or processes of inflammation and degeneration, acute or chronic, or pressure by new growths or by effusions, etc. My argument must rest on those cases only where it is certain or at least highly probable that injury to the organism, more or less severe, begins in the normal action, within physiological limits, of central mechanisms.

From one point of view, which I have ventured to suggest, viz., that of incomplete evolution, it is interesting to observe the great comparative frequency with which defects occur in the central mechanism necessary for the production of articulate speech, one of the latest, if not the last, acquired of human faculties.

It would seem as if a sufficient number of years or of generations had not yet passed for its complete evolution, for its full establishment as a definite factor in our nervous system. In a large number of instances stammering is not even hereditary; it presents itself rather as a "reversion" on the part of individuals of the species than as a result of special acquired tendencies on the part of their parents. It has been compared to scriveners' palsy, but from my present point of view I venture to think unjustly so,

for the clinical history of the two affections is as a rule very different.

The latter is associated with overwork of certain groups of muscles and of certain co-ordinating nervous centres, with much greater frequency than is the case with stammering, at any rate when this begins early in life; and further, evidences of organic change in nerves, if not in muscles, such as pain and tenderness of nerve trunks, are common in the palsy, unknown or very rare in stammering. The term "functional impotence" may be loosely applied to both; but in stammering the impotence would seem to be often the result of insufficient development; in writers' cramp it follows upon over-fatigue.

Many of you will remember the short chapter in Sir James Paget's "Clinical Lectures and Essays" where he compares speech-stammering with functional discord of the muscles which take part in micturition, deglutition, and defæcation. In connection with all these, difficulties from time to time occur, apparently from imperfect co-ordination, without anything being present which can rightly be called disease, but the result of this imperfect co-ordination is sometimes death.

Again, the watchful irritability of the larynx and the ready action of the mechanism by which it is closed against the passage of foreign bodies is, beyond doubt, of the greatest importance to our well-being. There is no need before this audience to dilate upon the necessity for such a safeguard to the lungs. But this same apparatus is not unfrequently called into equally effective action under circumstances which render such action dangerous in the highest degree. None of you, I trust, will ever feel the very disagreeable series of sensations which attends the passage of a foreign body, even of moderate size, through the larynx. That experience happened to myself some three years ago, and I have not yet forgotten it. What struck me most at the

time and since was the intense spasm excited by the irritation below the glottis, such spasm being, of course, worse than useless, and serving only to render the removal of the cause of the irritation extremely difficult. Then and there I came to the conclusion that the controlling centre of the laryngeal movements was, in my own case at least, sadly wanting in discrimination, and that it would be greatly improved were its arrangements so far modified that irritation in the lower part of the larynx should lead to widening, and not to narrowing of the passage. It seemed to me that only by a great effort was I able to prevent the complete closure of the glottis, and that in doing this I was controlling, indeed reversing, the course which Nature, left to herself, would have followed—not to my advantage. In some cases of disease it is of great importance to recognise this misplaced irritability of the larynx. In young children suffering from bronchitis laryngeal spasm is sometimes almost as severe as in membranous laryngitis, and I have seen great relief follow the performance of tracheotomy. It may be said that in these cases there is acute laryngitis as well as bronchitis, and that the former is the cause of the spasm.

This may be true in some, but is certainly not true in all. Granted, however, that it were so, it seems to me that reflex spasmodic closure of a passage necessary to life, which has already been dangerously narrowed by the swollen state of its mucous membrane, is not an ideally perfect arrangement; and yet the more acute the sensibility of the parts, the nearer the nervous mechanism approaches the existing physiological standard, and the more readily it reacts to its natural stimulus, the more certainly is this brought about. I think it can scarcely be denied that if the sensory relations of the laryngeal mechanism were less extensive, if spasm of the glottis were not induced by irritation below as well as above the rima, we might still enjoy the benefits

of the present arrangement, and yet escape some of its inconveniences and dangers.

It might be objected that if this were the case we should not be able to cough; that, in fact, this irritability of the larynx below the glottis, and probably of the bronchi, and even of the air vesicles, does not prevent, but aids, the expulsion of foreign bodies or of harmful excretions, which may have found their way into them. But surely in this objection the fact is ignored that coughing can be performed, and most perfectly, by a simple exertion of the will, and without the stimulus of any local irritation whatever. For my own part, I have no objection to coughing being done away with altogether, but what happened to myself when that ginger lozenge went the wrong way was this: the larynx promptly took the first step necessary in coughing, namely, contraction of the rima glottidis, but showed no intention of taking the further and, as it seemed to me, still more necessary step of suddenly throwing it open.

My instinctive wish at the time was, not to cough, but to inspire, and that was made all but impossible by the persistent spasm. Success depended upon my overcoming the obstinate resistance of the larynx to the entry even of the air, without which coughing was quite out of the question. In the same way the difficulty with children suffering from bronchitis is primarily one, not of expiration, but of inspiration, for it is this latter which becomes stridulous, and during it the lower lateral regions and the soft parts of the thoracic walls recede, and cease to do so when the trachea has been opened. In point of fact, forcible and very effective expulsive efforts are quite possible without any preliminary closure of the glottis, that is, without any cough properly so-called; and of this every one can convince himself by making a sudden violent expiratory effort in the

course of an ordinary expiration. Minute observation of a few bronchitic patients will convince any one that this manœuvre is often resorted to by them, and succeeds in expelling mucus when ordinary cough has failed to do so.

Sir Benjamin Brodie, in his account of the famous case of Mr. Brunel (Works, vol. iii., p. 532) lays great stress upon the difficulty placed by the spasm of the larynx in the way of the expulsion of heavy foreign bodies from the trachea, and advises tracheotomy not only as providing an additional outlet, but also as a means of relaxing the spasmodic stricture of the rima glottidis It might almost seem as if this no longer takes place when it has been rendered harmless. To quote Sir Benjamin's own words, "We made an opening some few days afterwards below the thyroid gland, but the half-sovereign was not coughed up as a cherry-stone would have been, because it was too heavy. We made some attempts to use the forceps, but found it so dangerous that we desisted. When he had recovered from the effects of this operation—in the meantime passing a probe every now and then —we again placed him on a moveable platform, his back was struck with the hand, and the half-sovereign escaped from the bronchus. He could feel it rolling along the trachea, till it came to the glottis, and now, instead of sticking there, it passed through, just as you could roll it through the dead body, and came out of the mouth. There was no spasm of the glottis, and the absence of it was to be attributed to the opening in the trachea; for blood came out with the half-sovereign, which had evidently passed in from the external wound, and where blood went in you may be sure that the air went in also. I apprehend the rule to be this: In all cases where a foreign body has got into the trachea you must not trust to nature, but make an opening into the trachea; and then it is very likely that if the body be light it will be forced through the opening; or if, by its own weight, it

can be made to assume a certain position, it will pass out through the glottis." To this I would add once more that accumulations of mucus below the rima are also not unfrequently the cause of laryngeal spasm.

We are provided not only with the means, more or less satisfactory, of driving foreign bodies out through the larynx by a blast of air, but Nature has also enabled us in the case of minute particles of matter, according to their character, sometimes to dissolve, sometimes to wash them out by flushing the air-passages with a profuse secretion of thin watery mucus. Just as lachrymation is excited by chemical or mechanical irritation of the conjunctiva, so also similar causes acting upon the tracheal or the pulmonary mucous membrane produce a similar effect, viz., bronchorrhœa, and here, too, imperfect arrangements of the same kind as those which we have just been considering allow the mechanism to be set to work in such a way and under such conditions as to lead to results which, if less dangerous than spasm of the glottis, are yet highly inconvenient; *e.g.*, I have seen profuse bronchorrhœa kept up for two or three days by the lodgement of about two-thirds of the shell of a hazel nut in the right bronchus of a girl, thirteen years old, who did not even know that it had passed through the larynx. Here the offending body was insoluble, and could only have been washed out by an amount of liquid which would have rendered the patient's respiration, to say the least, difficult, as indeed it was. As soon as the shell was expelled through the larynx the watery secretion ceased. I do not wish to lay too much stress upon this case; the fluid may have aided in the removal of a foreign body so light as this one was, although, if it were so, the process was a clumsy one, took a long time to effect the object in view, and exposed the patient to dire discomfort and to no small danger. When, however, the flushing apparatus is set to work by irritation external to the air

passages, it is difficult to believe that it does not do more harm than good. Now, I have seen this happen in the case of small aneurisms pressing upon the root of the left lung, where the constant cough, and the restlessness produced by the consequent dyspnœa, materially, in my belief, shortened the patient's life.

Here, too, as in the case of the laryngeal movements, the imperfection of the action of the regulating centre, and its disagreeable results, are due to its afferent nerves being distributed more widely than its efferent nerves.

At any rate, one and the same physiological action, if not the sole, is far away the most prominent result of irritation conveyed from tissues so different from each other in site, structure, and function as is the mucous membrane of the bronchi from their outer wall and from the neighbouring parts. The development of the centre on the motor side has not kept pace with that on the sensory side. Impulses reach it, starting from widely separated points, and differing not less widely in meaning, yet to each and all of these it can give, and does give, but one and the same response. It might be roughly compared to an imperfectly organised postal service which collects more letters than it can deliver correctly.

The ground covered by my subject is so large that I ought not to occupy any more of the short time at our disposal by further details of imperfections in the working of the regulating centres connected with the great function of respiration. Nor shall I do so except by stating briefly and dogmatically certain points relating to spasmodic asthma. In an hereditary case there may be no history, no sign or symptom of disease other than the phenomena of the asthmatic attacks; and these are not, strictly speaking, pathological. The asthmatic paroxysm is a physiological act which, under certain conditions and within certain limits, is most salutary to the organism. The centre from which it pro-

ceeds supplements the office of the larynx in guarding the lungs from harmful influences. It commands an inner line of sentries, so to speak, by which noxious gases and perhaps minute foreign bodies which have passed the larynx may yet be prevented from reaching the air vesicles. Whether this be done by contraction of the muscular elements in the walls of the bronchi or by œdema of their mucous membrane makes no difference to my argument. Of course I do not assert that the nervous system of an asthmatic conforms in all respects to the normal type, but it often differs from that type, not in being the seat of pathological changes in the ordinary sense of the word, but in virtue of under, if not indeed of over, development. For the mechanism if looked at from the afferent side is too perfect, too sensitive, whilst on the efferent side it is deficient in the very necessary power of relaxing in due time the spasm which it has determined. The slightest stimuli, nay, even an idea, suffice to rouse it into strenuous action, action more injurious by its pertinacity than the danger, if it be a danger, against which it is directed, and the frequent repetition of which too often brings about at last fatal changes in the heart and lungs. Again, like the other centres we have mentioned, its sensory connections are too wide. It receives impressions from the stomach, from the pelvic organs, from the blood-vessels, indeed from almost every part of the body, and to all it gives but one answer, a fit of asthma.

My next illustration is taken from the operation of the thermo-taxic centre. What are rigors? How are they produced? Do they influence for good or for evil the course and issue of the many serious diseases in which they figure among the earliest and most prominent symptoms? I have put the last of these questions to several of my friends, and when an answer was given (I did not always succeed in getting an answer) it

rarely amounted to more than this, that the violence and duration of initial rigors are of great value in prognosis. This does not, however, carry us very far, and although perhaps from the *vis medicatrix naturæ* standpoint it is not the worst answer which might be given, still it is a curiosity in teleology which might well be bracketed with the ingenious suggestion that the development of certain species of tape-worm is the final cause of the existence of man. There is, indeed, another answer, a very old one, which it is necessary to discuss, if for no other reason, then for this, that it was endorsed by Dr. Hilton Fagge ("Principles and Practice of Medicine," vol. i., p. 40).

Given, it is said, a case of fever, then the high temperature which rigors aid in producing is of essential service to the patient, by removing in some way or other the cause of the fever, whatever it may be; burning it off, in fact. Dr. Fagge points out that the discovery of micro-organisms as the exciting and sustaining cause of many febrile diseases has made it easier to understand how this may be accomplished.

Briefly, the high temperature sterilises the blood and tissues just as it does the tube and its contents in the physiological laboratory. Now, I am quite ready to give full weight to this theory, because I know that "hyperpyrexia" when it occurs in rheumatic fever does seem to cut short that disease. Certainly in the cases which I have myself seen the patients who recovered from the hyperpyrexia were at its close entirely free from the well-marked rheumatic symptoms under which they had laboured when it began. Both the joint affection and the fever had disappeared, returning only slightly, if at all, and visceral inflammations rapidly subsided.

I am constrained to believe that in some way or other the disease was cured by the high temperature, or by something closely connected with it. But this single fact, and I know no

other like it, is a very slight foundation for the assertion that ordinary febrile temperatures, whether with the rigors or at any other period, have a beneficial, not to say curative, effect upon the patients. Clinical observers are all but unanimous in asserting the contrary.

Surely cases of ague, of relapsing, or of typhoid fever, which have the highest temperature during their first paroxysm, are not, as a rule, those least liable to relapses, or the most likely to come to an early and favourable termination. I know of no observations to prove that in the majority of infective febrile diseases, when once started, the parasites concerned in them can be destroyed by a degree of heat which is not at the same time all but fatal to their hosts. The advocates of antipyrin and of cold baths seem to think that micro-organisms and their effects are best combated and rendered harmless by a low temperature. They probably perish from the effects of their own activity, partly by using up the material necessary for their subsistence, partly by producing some poison fatal to themselves.

Now some recent observations of Brown-Sequard's (*Acad. des Scien. Compt. Rend.*, Nov. 28th, 1887, Jan. 9th, Jan. 16th, 1888) go to prove that the air expired by perfectly healthy men contains a most virulent poison (luckily for us in very small quantity), distinct from the hitherto recognised products of respiration. Thus I may be allowed to remark incidentally, it would seem that in the lowest organisms, as in the highest, normal physiological action may lead to death. What the effect of rigors may be upon the febrile disorders in connection with which they occur can be determined only by an appeal to facts. The typical form of rigors is that which follows exposure to cold. Here the contraction of the skin and of the superficial vessels checks the loss of heat which would otherwise take place, whilst the accumulation of blood in the deeper lying vessels, and in the viscera,

leads to increased production of heat. Thus, *e.g.*, the ultimate effect, upon a healthy subject, of a cold bath is not a fall but a slight rise of temperature. Under these conditions rigors are one of the means by which the thermotaxic centre meets an increased demand for heat, and does so successfully, thus rendering most valuable service to the organism.

But the conditions under which rigors occur in disease are totally different, and so, too, must be their effect. Instead of a slight fall, they are now preceded by a rise of temperature, which may be considerable. The body heat, already excessive, ought to be lowered, not raised, and yet, thanks to the thermotaxic centre, an attack of rigors supervenes, the tendency of which at such a time must be to do harm. It is sometimes urged that the sweating stage, which generally follows, lowers the temperature, and that it is a reaction from the rigors, which thus form, at any rate a part, perhaps a necessary part, of a process which, on the whole, is a beneficial one, whatever their effect might be if they stood alone. But sweating often takes place without any precedent rigors, and would surely be more efficacious for good if it did so here. It may well be doubted whether the part played by the rigors in bringing about the sweating stage does more than counterbalance the mischief they have previously wrought, if indeed it does so much.

Why rigors should occur with a rising temperature in disease and with a falling temperature in health is a puzzling question, which has hitherto been answered only on theoretical grounds. But it is clear that the stimulus which calls the centre into action is not always the same ; it may be that a difference of temperature between the superficial and the internal parts of the body, the former being the cooler of the two, and not any absolute temperature of either, is the stimulus, or rather one of the stimuli, to which it responds.

Or in infective disease it may be that some poison acts upon the centre, either directly or through commencing blood change, or even through local irritation in peripheral parts. Anyhow, remembering the many and various stimuli, such as external cold, abscesses in any region of the body, the use of a catheter, the passage of a gall stone, or thrombosis in a vein, to all and each of which an attack of rigors can scarcely be an equally suitable response, I hold that we have here yet another instance of a centre labouring under the same infirmity as those of respiration do, viz., that its afferent nerves are too many, or its efferent nerves are too few. In other words, it is as yet but imperfectly organised. The practical conclusion to be drawn from these facts is one which, in spite of the *vis medicatrix* theory, has always recommended itself to the feelings of the sick, and to the common sense of their attendants, viz., that rigors in disease are injurious, as well as extremely disagreeable, and, if they cannot be prevented, ought certainly to be cut short as speedily as possible.

The mechanism which adjusts to the wants of the organism the quantity of fluid contained in it, and which I venture to call briefly the hydro-taxic centre, furnishes an illustration that the very perfection, I mean of course the statutory perfection, of a physiological arrangement may lead to inconvenience and even danger. The centre attains its object by co-ordinating the functional activities, as inlets and as outlets, of the skin, lungs, kidneys, and alimentary canal. It receives sensory impressions of two kinds; of these the one arises from a deficiency of fluid in the body, and of this we become conscious and call it thirst; the other is connected with the presence of fluid in excess; of this we are not conscious, or only dimly so, but it serves as the stimulus to provoke the excretion of fluid by the skin, kidneys, and other sluices. It seems probable that both these sensations may

originate in any part of the body, so that the connections of this centre too are very wide.

Now the excellence of a mechanism working on these lines for such an object would consist, on the one hand, in its sensitiveness to any excess or deficiency of fluid, and on the other, in its readiness to restore the normal state of things by imbibition or by excretion as the case might require.

In 1887 Fr. Kraus published* the results of two sets of observations carried out with great care, and as far as possible under similar conditions—one upon a youth *æt.* 17, suffering from diabetes insipidus, or rather polyuria; the other, a control series, upon a healthy man. After being kept for some hours without any liquid, they each took the same quantity of water, and the amount of urine passed by each during several hours was ascertained.

In two of the observations they took three litres of fluid at once; in three observations they took half a litre every hour. In the first case, during the first few hours, the quantity of urine rose much more rapidly in the diabetic than in the healthy man; then, however, it fell rapidly, so that the quantity passed by each during the whole period of sixteen hours was about the same. Kraus's conclusions are that the diabetic passes a larger quantity of urine in a given time than the healthy man only when his system is saturated with liquid. He gets rid of the excess quicker, but if the quantity excreted is not at once replaced he does not on the whole pass more. He ought to be called "tachyuric," from the rapidity with which he excretes any excess, but he is not polyuric. If the fluid excreted is at once replaced by an equal quantity he may be said to be relatively polyuric; he becomes absolutely so if he indulges his thirst and drinks large quantities of fluid. It is true that the diabetes insipidus in the subject of Kraus's experi-

* Prag. Zeitschr. f. Heilk., H. 5 u 6, S. 431.

mental observations began after an epileptic fit, so that there was probably some antecedent organic change as its cause, and thus the case lies outside the limits which I have laid down for myself to-day, but it is difficult to believe that some pathological change exists in all polyurics from the very first. With the help of Kraus's experiments, it is easy to understand how a hydrotaxic centre, highly sensitive, and reacting readily to the impressions it receives, may produce a state of polydipsia and polyuria which, if not in itself dangerous, is yet extremely inconvenient, and frequently ends in serious disease. And this may happen although at first its functional activity does not exceed the mean physiological and anatomical standard more than is the case with the special senses and the general cerebral development in many individuals, who, so far from being pitied as the subjects of disease, are envied by ordinary mortals for their great powers.

It might be said that in this instance the disease clearly starts from the environment, that the quantity of liquid which the polyuric drinks, at first it may be unnecessarily, is the cause of his condition. But this is not the case, although it is true that if there were no liquid within reach there would be no polyuria. The true cause clearly exists, not in the environment, but in the centre itself, which by its sensitiveness and functional activity in certain individuals regulates the amount of fluid with such nicety that no margin is left for any extraordinary calls upon the activity or even for the ordinary needs of the organism, which is thus compelled to take in an extra quantity.

With reference to the nervous nature of the hydrotaxic mechanism, it is interesting to note that antipyrin has more influence over diabetes insipidus than, perhaps, any other drug. Its good effect was well shown in the case of an otherwise healthy girl of eleven years old, who was under my care at St. Bartholomew's Hospital a few months ago. After the disease

had been checked by restricting the amount of fluid as far as it could be done without disturbing the patient's general health, the use of antipyrin, in doses of 10 to 15 grains three times a day, was followed by a further diminution in the quantity of urine passed, with a rise in its specific gravity, and by great relief to the thirst; at the same time she gained weight.

I wish time had allowed me to enter into similar details as to the relationship of certain motor centres to chorea, and of the vaso-motor centres to the vascular troubles which form so large a part of hysteria. But I must not trespass on your patience longer than may suffice to formulate some conclusions suggested even by the imperfect statement just laid before you. If you cannot as yet accept these conclusions, I venture to submit to your candour that a case for inquiry has been made out, and I ask you to examine them without prejudice.

Looked at from the level of our human life, the regulating nerve centres present defects analogous to those which every one recognises in the outer world and in man's own works. Potent for good, they are scarcely less so for evil, and in order to fit them thoroughly for man's service they require to be in some sort "broken in"—if, indeed, that be possible.

These defects admit of being classified under different heads. Sometimes they seem to be caused by insufficient differentiation of structure, as when a large number of afferent nerves are in communication, doubtless through the medium of ganglionic cells, with a far smaller number of efferent nerves. And this is a state of things the existence of which seems to be established by the fact that, certainly in some centres, the most diverse impressions give rise to one and the same reflex act. Sometimes trouble results from the centre being too sensitive, being put in motion too readily by slight stimuli. And yet in both these cases there is often no such change of structure, no such devia-

tion from the normal type, from the anatomical and physiological standard, as can rightly be called disease. Indeed, what from its consequences we call over-sensitiveness, over-readiness, is, in itself, a degree of development above the average. And it is this which places the organism at variance with the environment, this which is the first step in the development of disease. Excess of zeal is a troublesome virtue, in both physical and social life. Whenever we recognise how largely ordinary physiological action enters into the processes of disease we cease to be surprised at the rapid development of therapeutics during the last twenty-five or thirty years. The ridicule attempted to be cast upon modern methods by those who ask what conclusions can be drawn from the action of a drug upon a healthy dog as to its effect upon a sick man is seen to have no better foundation than their own ignorance. In the treatment of the sick we have to deal, not with vague unknown conditions, but with physiological reactions often differing slightly, if at all, from those of the healthy, and at first in degree only. It is no wonder that the results of laboratory work are, if properly controlled, trustworthy and fruitful; that they have placed in our hands such remedies as nitrite of amyl, the salicylates, and strophanthus; that they have given fresh powers and uses to old and well-known drugs.

Without trenching on topics the discussion of which would be out of place here, I trust that you will allow me to repudiate beforehand a possible misinterpretation of the views which I have now submitted to your judgment. It might be said, from opposite sides of the question, and I might have no right to complain of any unfairness on the part of my critic if it is said, that I have brought an indictment against the wisdom and benevolence of the Power which has fashioned our bodies. If any one thinks that the facts support such an indictment he has a perfect right to hold that opinion; but for my own part I think he would be mis-

taken. And if the manner in which I have stated the facts with which we have been more immediately concerned this afternoon lends any colour to such a mistake I at once express my regret. It has been my intention and my endeavour to put forward, not a theological argument, but a statement of facts which it is of great importance to us as medical practitioners to acknowledge, and which, at present, seem to me to be in some danger of being overlooked or neglected. The exciting cause of man's progress, of the gradual widening of the gap which separates him from the lower animals, has been the necessity laid upon him of overcoming the difficulties placed by the seeming caprice of Nature in the way of his comfort and of his desires. I see no reason to doubt that imperfections in his physical organisation such as we have been considering have also had, and will have, a similar influence upon his development. To both sets of difficulties we may apply the language of the terse Greek proverb which I have placed at the head of this lecture, "Through suffering cometh wisdom."