which the student of medical geography has occasionally to encounter. It is only one of many which have met me in my investigations as to leprosy.

CASE VIII.—A colonel in the army, aged 53, who had been born in England, but had lived twenty-seven years in different parts of India, Burmah, etc., became leprosy. The beginning of his disease was three years before I saw him, and occurred in the left foot. He was a man of splendid physique, of most temperate habits, and in excellent general health. Although both feet were numb, he had only about a year before I saw him engaged in athletic sports, and won a race. Both his ulnar nerves were affected, but on the right side the paralysis was only commencing. This gentleman had been exposed to the ordinary dietetic and climatic influences of India and Burmah, but had never suffered any hardship. He had eaten fish, etc., when he could get it.

CASE IX.—Colonel B. F., aged 45, consulted me first in May, 1879, having been then the subject of leprosy for about six years. He was of English parentage, but had been engaged in service in India for twenty-four years. He had been stationed chiefly on or near to the sea-coast, and he said that he thought he had rarely been a day without taking fish at dinner. He had been very fond of prawns and of prawn curry.

CASE X.—A gentleman, Mr. P., aged 48, had resided twenty-seven years in India. He had been born in England, and of English parents. He had lived in different parts of India, having been engaged for six years on the Ganges, and subsequently at Allahabad, Oude, and Scinde. He stated that he had been accustomed to eat fish whenever he could get it, and had been fond of prawns. His leprosy, which was very severe when I saw him in 1883, had commenced six or seven years prior to that date. There was a very interesting fact in this gentleman's family history. His wife, an English lady, had never suffered in any way, but one of his children, who had lived with him in India and was, I believe, born there, showed the disease at the age of 9. This child had returned to England a little before the symptoms had shown themselves. He was seen and the disease diagnosed by Sir Joseph Fayrer and Mr. Balmanno Squire. He subsequently returned to India, where he died of heat apoplexy. Having regard to the dates at which the disease appeared in father and son, and to the entire immunity of the mother, it would appear improbable that the child acquired the disease by inheritance. It would seem more likely that he and his father got it at the same time from one common source. This supposition is also supported by the fact—one to which I shall have to draw attention shortly—that it is not very uncommon for the children of English parents born in leprosy districts to acquire the disease while their parents remain free. It would seem that the bacillus develops with facility in the young.

Both the portraits which are given in the New Sydenham Society's *Atlas*—one showing the anæsthetic and the other the tubercular form of leprosy—are from patients with English parents who had acquired the disease in foreign parts. One of these (Case XI) a Scotch sea-captain, in vigorous health, had traded for many years to and from Barbadoes. He had usually stayed in the island about six weeks at a time. He had never suffered from any kind of hardship, and, on the contrary, had led what would seem to have been a most healthy kind of life. At about the age of 45 he became a leper. In the other case (No. XII) a woman who had been born in Ireland went to India as the wife of a soldier. She resided there for many years and in various parts, being employed chiefly, I believe, as a washerwoman. She eventually became the subject of leprosy in a severe form.

The twelve cases which I have quoted do not, I believe, comprise by any means all the examples of leprosy beginning in patients of British birth and descent which have come under my observation. They are all, however, of which I am able at present to find record in my notebooks.² One and the same criticism may be said to apply to all. They are examples of the acquisition of a specific disease by healthy persons who had no inherited predisposition. In no single instance had the person so acquiring it been exposed to any degree of hardship, or deviated in any definite manner from the ordinary conditions of a cleanly and well-regulated life. In every case the acquisition of the disease had occurred in some country where it was known to be prevalent, the East and the West Indies being the chief localities. I submit—as, indeed, I have already suggested—that there are

² In particular I well remember to have seen two or three soldiers who had become lepers in the Indian service, but of whose cases I cannot find any record.

only two suppositions open to us by which to explain the *de novo* acquisition of such a disease in cases such as these. The patients must either have received the specific contagium of leprosy on some part of the skin or mucous membrane, or they must have swallowed it in connection with food. Both these suppositions are possible. I may confess, however, that to my own mind one of them seems far more probable than the other. In no single instance had there been any known exposure to contagion. In no case had the patient associated with anyone suffering from leprosy, and in most instances the statement given was that they had but rarely seen lepers, and had certainly never come near them. All had, however, eaten the food common in leprosy districts; and if we incline to suspect that fish, and especially potted fish, is an ordinary vehicle for the contagion, all had undoubtedly been exposed to this risk.

Another and perhaps larger group of cases, very similar to those I have just quoted, consists of examples of leprosy beginning in persons of European blood, but born in leprosy districts. The evidence which these cases give is somewhat less conclusive than that of the group which we have been considering. Thus it is obvious that in some instances the parentage may have been mixed, and thus the disease may have been inherited. Where the admixture of native blood is but slight, and its evidences not very obvious, our patients are not always eager to divulge the truth, and may be willing to pass as of pure English descent when not really so. Again, it is possible that a child born in India may inherit something which has never as yet made itself manifest in his parents; there are also the perils of vaccination; and lastly, we have the fact that a child born in India, of English parents, may have been suckled by a native woman, and possibly by one having a taint of leprosy. I do not myself attach much importance to any one of those sources of fallacy, but it is right that they should be named. My belief is that the cases which will form the subject of my next series may most of them be placed side by side with those already quoted as being examples of leprosy acquired by Europeans as the result of residence in affected districts.

THE CROONIAN LECTURES

ON THE RELATIONSHIP BETWEEN

CHEMICAL STRUCTURE

AND

PHYSIOLOGICAL ACTION.

Delivered before the Royal College of Physicians of London.

By T. LAUDER BRUNTON, M.D., D.Sc. EDIN., LL.D. ABER., F.R.S.,

Fellow of the Royal College of Physicians; Assistant-Physician and Lecturer on Materia Medica at St. Bartholomew's Hospital.

LECTURE IV.

ANALGESICS.

Non-reception and Non-perception of Painful Stimuli.—The two classes of drugs which we have already considered, general anæsthetics and local anæsthetics, both abolish pain: the latter by acting upon the peripheral terminations of sensory nerves, so that they do not receive the painful stimuli; and the former upon the nerve centres, so that they do not perceive them.

Non-transmission of Painful Stimuli.—But pain will also be relieved if the conducting power of the sensory nerve trunks or of the sensory paths in the spinal cord be so altered that painful impressions can be no longer transmitted.

Action of Cocaine on Nerve Trunks.—Cocaine has this effect upon nerve trunks when locally applied, for, when injected subcutaneously near a nerve, it may produce anæsthesia in all the district to which that nerve is distributed.¹

Action of Cocaine on the Spinal Cord.—It has a similar action on the sensory tracts of the spinal cord, for Hughes Bennett² found that it rendered these tracts insusceptible to stimulation; and Mosso³ found that both conductivity and reflex excitability in the cord are destroyed by it before the nerve trunks, either sensory or motor, are paralysed.

Action of Cocaine on the Cerebral Cortex.—It lessens the irritability of the cerebral cortex when directly applied, for if a 4 per

¹ Hall and Halsted, *New York Medical Journ.*, Dec. 6th, 1884.

² Hughes Bennett, *Edin. Med. Journ.*, Oct., 1873.

³ Ugolino Mosso, *Arch. f. exp. Path. u. Pharm.*, vol. xxiii, p. 153.

cent solution be applied to the motor areas, no convulsions can be produced by irritation by a faradic current.⁴

Excitability and Conductivity.—We must distinguish between excitability and conductivity both in nerve trunks and in the spinal cord. For these two functions of nerve fibres are to a certain extent independent of each other, and a nerve fibre may still be able to conduct stimuli from the peripheral terminations to the nerve centres, and *vice versa*, when irritation applied to the nerve trunk produces no apparent effect. This condition may occur after exposure to great cold, and also in some pathological conditions.

Action of Drugs on the Conducting Power of Nerve Fibres.—Loss of conductivity may also be produced by the application of various substances to the nerve trunks, and a knowledge of the effect of drugs on the conducting power of nerve fibres appears to me absolutely necessary in order to understand the action of drugs on the spinal cord or on the higher nerve centres. For in the cord and brain the nerve cells and nerve fibres are so closely associated, that it is very difficult, if not impossible, to separate the action of a drug on the one from its action on the other. But in the nerve trunks we can apply the drug to nerve fibres alone. Having thus ascertained its action upon them, we may be able to judge with greater certainty what part of the drug's effect on the spinal cord is due to its action on the fibres, and what to its action on the cells.

For this reason I thought it necessary to begin a research on this subject along with my assistants, Dr. Batten and Mr. Bokenham.

The method employed was to take the sciatic nerve of a frog, with the gastrocnemius muscle attached, so that its contraction or non-contraction when the nerve was stimulated might serve as an index for the presence or absence of functional activity in the nerve.

The nerve could be stimulated by a faradic current, either at the end A, farthest from the muscle M, or at a point B nearer the muscle. A large portion of the nerve was placed in a small glass chamber C, into which various vapours or liquids could be introduced at will, so as to act on the nerve trunk. When the nerve was in its normal condition, the muscle M contracted on stimulation of the nerve either at A or B. But if carbonic acid was introduced into the chamber, it abolished the irritability of that part of the nerve on which it acted, so that stimulation at B no longer caused any contraction of the muscle. But it did not destroy the conductivity nearly so quickly, for a stimulus applied at A would be conducted to the muscle, and cause contraction, when one applied at B had ceased to have any effect. Alcohol and ether had just the opposite effect, for they destroyed conductivity before irritability, so that stimulation at A had no effect, while it caused contraction if applied at B. Phenol acted like carbonic acid, and destroyed irritability before conductivity. The action of dimethylbenzene differed according to the position of the methyl groups. Orthodimethyl, benzene, or orthoxylene had almost no action; paraxylene increased the irritability of the nerve, so that a single stimulation caused tetanus, and metaxylene did the same to a still greater extent. The number of substances experimented with has been considerable, but it would occupy too much time to discuss the results now. I would merely draw attention to the action of xylenes as having a possible bearing on the action of analgesics.

Mode of Action of Analgesics.—But our knowledge of the conduction of impressions in nerve trunks and the spinal cord is insufficient as yet to explain either the physiology of pain or the action of analgesics. We frequently notice that a very small dose of laudanum, such as 3 or 5 minims, will relieve abdominal pain without producing the least drowsiness, or, indeed, without exerting any other apparent effect upon the organism; and a similar result

may be observed in severe headache from the administration of 5 or 10 grains of antipyrin. In trying to explain such phenomena we are obliged to have recourse to hypotheses. A hypothesis in itself has no value, and is worse than useless if it leads people away from facts, but it is extremely useful when limited to its proper function, namely, to help us to string together facts which are already known, and to indicate the direction in which to look for new ones. Thus Dalton's atomic theory has been of the utmost value to chemistry, and the hypothesis that the carbon atoms are united into a ring has not only rendered the classification of aromatic compounds much easier, but it has aided in the discovery of new ones.

Facts regarding the Transmission of Painful Impressions.—As the first function of the hypothesis is to link facts together, let us first see what facts we have got in relation to pain. Painful impressions are conveyed by the grey substance in the spinal cord. This seems to be shown both by physiological experiments and by clinical observations. Tactile impressions are conveyed by the white matter, probably in the lateral columns. Tactile impressions are conducted more quickly to the brain than painful ones, and a more powerful stimulus is required to produce a painful impression than a tactile one.

Fibres and Cells as Conductors.—This is exactly what one would expect from the different nature of the conducting paths of the two instances; for the nerve fibres which conduct the tactile impression have an almost direct course, and afford little opportunity for any weakening of the stimulus by diffusion. The branching cells of the grey substance, on the contrary, form a zigzag path which must be longer than the other; it probably presents greater resistance, and it affords more opportunity for entire loss of the stimulus by diffusion to other cells in the cord. Thus, unless the stimulus is tolerably powerful, none of it may pass upwards to the brain, and therefore no painful sensation will be perceived.

Summation in Cells.—But, on the other hand, it would appear that the cells of the grey substance in the spinal cord or the sensory ganglia of the brain may be so excited by a succession of very feeble stimuli, each reinforcing the other, that the extremest agony may be produced. Thus we have all heard that one of the most dreadful tortures of the Spanish Inquisition consisted in allowing a single drop of water to fall at regular intervals; and Naunyn⁵ has found that in some cases of spinal disease intense pain may be caused by gently touching the foot with the point of a camel's-hair pencil at regular intervals. A summation of the stimuli appears to go on in the cells, each stimulus increasing the effect of the preceding, just as a slight touch upon a swing, repeated at the proper moment, will send it higher and higher until it oscillates to the fullest extent of which it is capable.

Effect of Stimuli depends on Time of Application.—But if similar touches be applied to the swing so as to interfere instead of to assist its oscillation, they will soon bring it to rest. Similar touches will thus produce opposite effects from a change in their relations to the oscillation of the swing. Translating this into physiological language, we should say that in the first instance we had a case of summation, in the latter of inhibition. Let us follow this familiar illustration one step further. We all know that when we start a swing we stand close to it at the spot where it hangs when it rests, and as its oscillations get longer and longer we move further back. If we move a little way back our pushes will first have the effect of summation, but if we remain in that position and do not adapt our pushes to the increasing oscillation of the swing, they will lessen instead of increase its movements, or, in other words, they will have an inhibitory action. Thus we will have stimuli producing alternately an increase and a diminution in the oscillations in the swing, though the increase and diminution will not be very great.

Alternate Stimulation and Inhibition in Health.—We seem to have a somewhat similar condition in the nervous system. Some time ago I was making some experiments with one of Mr. Francis Galton's whistles, which he kindly lent me. I adjusted it so that the sound produced was almost at the upper limit of my sense of hearing. On then sounding it continuously I was struck by the fact that the sound was alternately audible and inaudible, although I ascertained that no corresponding change occurred in the strength with which the whistle was blown.

In Disease.—A similar observation was made by the younger Remak⁶ in relation to pain in a case of tabes dorsalis. He found

⁴ Tumass, *Arch. f. exp. Path. u. Pharm.*, vol. xxii, p. 107.

⁵ Naunyn, *Arch. f. exp. Path. u. Pharm.*, vol. xxv, p. 301.

⁶ Remak, *Arch. f. Psych. u. Neurokrankh.*, vol. vii, p. 506.

that when a faradic current was applied by a brush the sensation it produced gradually increased, then diminished, and increased again, although the strength of the current remained perfectly the same. With a weak current, the increase each time became less, and the pauses between became greater, until at last no sensation was felt. With a stronger current the sensation gradually increased until it became so painful as to be unendurable.

Possible Effect of the Blood.—In my own case I was unable to satisfy myself that the alternate appearance and disappearance of the sound of Galton's whistle might not be due to an alternate increase in the sensibility of my auditory centres from altered supply of blood, for I observed some years ago a capillary pulsation in man which usually occurs about once in twenty seconds, and this appeared to be nearly the time of each wave of hearing. In Remak's case the waves of sensation were from twenty to fifty seconds, and the alteration in the length of interval between them renders it probable that they were due to summation in the nervous system itself rather than to its vascular supply.

ANALOGY BETWEEN SENSATION AND MOTION.

Summation of Motor Stimuli.—A marked analogy seems to exist between sensory and motor processes in the spinal cord. In a research which Stirling made under Ludwig's direction, he showed that reflex contractions only occur from repeated shocks to the nerve centres—that is, through summation of successive stimuli.

Summation of Sensory Stimuli.—According to Naunyn the same rule holds good for pain, which he regards as also a consequence of summation. For this reason it can only occur when conduction through the grey substance is not too much disturbed, because it is only in the grey substance that summation can take place, the structures of the white columns not being adapted for it.

Summation in Peripheral Nerves.—But if the analogy between sensory and motor processes be true in the spinal cord, we should expect to find something similar in the peripheral ends of nerves.

Tickled to Death.—There is no phenomenon in physiology which strikes me as more wonderful than the extraordinary motor effects which can be produced by the application of extremely slight stimuli to the skin, phenomena which seem utterly disproportioned in their extent to the slightness of their cause. I well remember, as one of the most frightful moments of my life, being nearly tickled to death by a nurse. I do not think I could have been more than 5 years of age, but the agony of that moment is deeply imprinted in my memory, and I can well believe the truth of the statement that Simon de Montfort, during the persecution of the Albigenses, put some of them to death by tickling the soles of their feet with a feather. Yet of all parts of the body the skin of the soles of the feet is liable to the most constant and severe stimulation in walking, running, and leaping. It has sometimes occurred to me that possibly the different effect of a slight stimulus like the touch of a feather, which causes intense reflex action, and of a gentle but steady pressure of the finger, which gives rise to no reflex action at all, may be due to the stimulation by the latter of two sets of nerves which counteract or inhibit each other. The prolonged course of the nerve fibres in some of the tactile corpuscles may possibly have something to do with this. A similar phenomenon to the effect of steady pressure in lessening reflex action may be observed in the relief afforded by rubbing or stroking a part which has been pinched or bruised, or by scratching an itching spot.

Transference of Hysterical Hemi-Anæsthesia.—But this is much less in degree and is by no means striking, while the transference of hemi-anæsthesia to the other side of the body in hysterical patients by the simple application of a piece of metal or even a wooden button is comparable to death from tickling, both in the extraordinary character of the result and the slightness of the cause.

MODE OF ACTION OF ANALGESICS.

In considering the action of analgesics we must take into account their possible effect on nerve endings, peripheral and central, as well as their action upon nerve trunks and nerve cells. It is *a priori* probable that when the blood contains any drug having the power to lower the activity of nerve fibres its action will be exerted upon the peripheral ends before they have received a medullary sheath, and at the central ends where they have lost it, at their junction with nerve cells, before it can act on the

nerve trunks. For not only is a nerve trunk sparingly supplied with blood, but the medullary sheath will oppose a certain obstacle to the action of drugs upon the axis cylinder. This appears to be the case with cocaine; for, at a certain stage of poisoning, irritation of the nerve trunks will produce reflex action, although irritation of the skin is no longer followed by any response, a fact which indicates that the peripheral terminations of the nerves have been paralysed before the fibres in the trunk.

Explanations.—Dealing with hypotheses, as we must do in relation to the action of analgesics, one of the first explanations that occurs to us as probable is that the sensory impulses which in the normal condition would give rise to summation in the cord or sensory ganglia, and, being transmitted to the brain, give rise to pain, may be diffused from one cell to another, and the impulses, instead of causing summation, may even produce inhibition.

Possible Failure of Analgesics to Relieve Pain.—It is evident that if the relief of pain by analgesics is due to the diffusion of a sensory stimulus, so that it does not reach the brain, it is quite possible for a very powerful stimulus to pass to the sensory centre in spite of loss by diffusion. In such a case the pain might actually undergo a process of summation in the cord and be rendered more excruciating instead of being relieved by the remedy.

Irradiation of Motor Impulses Produced by Analgesics.—There appears to be, as I have said, a resemblance between the sensory and motor processes in the cord, and most of the analgesics, as distinguished from the anæsthetics, tend to cause irradiation of motor impulses. While anæsthetics lessen the activity of all the nervous tissues and thus produce drowsiness, loss of sensation, and abolition of motor power and reflex action, many of the analgesics, when pushed to excess, tend to produce excitement of reflex action with diffusion of movement. Thus, when the toes of a frog are slightly pressed it only draws the foot away, but in a frog poisoned by an overdose of some of the analgesics the stimulus, instead of being localised in the cord and producing a reflex action limited to one limb, appears to be diffused through the nervous system generally, giving rise to tremor over the whole body or even to convulsions and tetanus. This condition is observed when frogs are poisoned by the most powerful of all analgesics, namely, morphine, and it is common to most of the others—cocaine, anti-pyrin, antifebrin, phenacetine, and exalgine.

CHEMICAL STRUCTURES OF ANALGESICS.

All those substances belong to the aromatic group of bodies, and it is in this group that we are likely to find the most powerful drugs to relieve pain as well as to reduce temperature. The constitution of morphine is very complicated, and we do not yet know what it is; all that can be said about it is, that it is probably a quinoline of phenanthrene. Antifebrin, or as it is scientifically called, acetanilid, or phenylacetamide, has the simplest constitution of any of the bodies that I have mentioned, for it merely consists of aniline in which one atom of hydrogen is replaced by

Ammonia.

Phenylacetamide.

Acetanilid.

acetyl. You will see from its formula that it may be regarded as ammonia, in which one atom of hydrogen is replaced by phenyl, and another by acetyl. When regarded from this point of view it is called phenylacetamide. But it may be regarded also as benzene in which one atom of hydrogen has been replaced by NH_2 , and thus converted into aniline, and then an atom of H in the NH_2 has been replaced by acetyl CO_2CH_3 . When regarded from this point of view it is called acetanilid. In two long researches on which Dr. Cash and I have been engaged for more than six years, as well as in some experiments in aid of which I obtained a grant from the Royal Society, fifteen years ago, we have been trying to ascertain the effect of ammonia and its various compounds on the one hand, and of substances belonging to the aromatic or benzene series on the other, upon muscle, nerve, and nerve centres.

Action of Ammoniacal Compounds.—In the course of the research we found that ammonia and its salts stimulate and afterwards paralyse the spinal cord. The stimulant action was marked in

¹ Lauder Brunton, *Journal of Physiology*, vol. v, p. 14.

ammonia, ammonium bromide, and ammonium chloride. The paralyzing action was more marked in the case of the iodide. The compound ammonias have a much more powerful paralyzing action both on the spinal cord and on the motor nerves, especially on the latter, and here again the paralyzing action is most marked in the case of the iodides.

Action of Aromatic Compounds.—The aromatic compounds all tend to produce increased sensibility, inco-ordination, and tremor, but they do not all seem to affect the spinal cord alike, for while benzene and its haloid compounds, mono-chlor-, mono-brom-, and mono-iodo-benzene produce in frogs tremors which remind one of disseminated sclerosis in man, with ethyl benzene the movements of the frog's legs were short, clapping, and ineffective, reminding one of locomotor ataxy in man. Aniline may be regarded either as amido-benzene, that is, benzene, C_6H_6 , in which one atom of hydrogen is replaced by amidogen, NH_2 , or as phenylamine, that is, ammonia, in which one atom of hydrogen has been replaced by phenyl, C_6H_5 .

Action of Aniline.—In accordance with this constitution we found that the symptoms produced by it were different both from those of benzene and those of ammonia. They differ from those of benzene, and resemble those of ammonia in the tendency to more violent spasm and to greater paralysis of muscle and nerve.

They differ from those of ammonia, inasmuch as the convulsion never assumes the form of true tetanus, the tetanic spasm which the ammonia atom would produce being broken up, so to speak, by the action of the benzene.

Tetanus Agents ought to be Analgesics.—If the hypothesis be correct that a relationship exists between the power of a drug to cause diffusion of sensory and of motor stimuli in the cord, one would expect that substances which cause tetanus like ammonia, chloride of ammonia, and strychnine ought to act in some measure as analgesics. Indeed, this seems to be the case, for ammonium chloride is sometimes a very successful remedy in the treatment of neuralgia, and strychnine is sometimes useful in the lightning pains of locomotor ataxy. But the fact that ammonia, benzene, and ethyl benzene, while all tending to produce spasm, cause movements of such different kinds, indicates that they affect the motor parts of the spinal cord in different ways. We might, therefore, expect that similar differences would exist in the sensory parts of the cord, and thus one drug might have a special tendency not only to relieve pain in general, but to relieve a particular sort of pain more than another.

According to Dujardin-Beaumetz,⁸ the power to relieve pain is most marked in those amidogen derivatives of the aromatic group in which an atom of hydrogen is replaced by an alkyl and especially by methyl, while the amidogen derivatives, where no such substitution has taken place, have their antipyretic action most marked. Thus acetanilid, which is an amidogen derivative of benzene, is a powerful antipyretic. It has also an analgesic action,⁹ but when it is combined with methyl its analgesic power is increased.

Constitution of Acetanilids in Relation to their Action.—It is a matter of considerable importance where the methyl is placed. There are three positions in relation to the amidogen group where it can be placed in the benzene nucleus,

According to Jaffe and Hilbert, the meta-methyl-acetanilide or meta-aceto-toluide is the only one which retains the antipyretic

action, the compound in which the methyl is in the para position being inactive and the ortho compound being toxic but not antipyretic.

Exalgine.—These compounds have again been investigated by Dujardin-Beaumetz and Bardet, and they have found what the previous investigators missed, that the ortho-aceto-toluide has a marked analgesic power, so great that they think it deserves the name of exalgine. According to them, its power to relieve pain is very marked in all kinds of neuralgia, and is greater than that of antipyrin.¹⁰

Effect of Alkyls on Aromatic Compounds.—Another most interesting research on the effect of introducing alkyls into aromatic compounds has been made by Baldi under Schmiedeberg's direction. Curiously enough though phenol and aniline are both poisonous, yet ortho-amido-phenol is not poisonous. If the two hydrogen atoms in the amidogen group in this body are replaced

weak narcotic substance is produced, and curiously enough the narcotic action is still weaker if the hydrogen in the hydroxyl is

stance has a distinct narcotic action, and the body,

has a powerful analgesic action.

Prospect of Numerous Analgesics.—As the ways in which methyl may be combined with aromatic bodies are almost numberless, we may expect before long a great increase in the number of analgesics, and not improbably some new ones may far surpass in their power to relieve pain anything that we as yet possess. Before passing from this subject, however, I must indicate a possible source of danger from the continued employment of such analgesics.

Dangers from Analgesics.—We know that the continuous employment of narcotics, such as morphine or chloral, is apt to grow into a habit, and the consequences may be very deleterious to the mental functions. A similar habit, we know, may be established by the use of cocaine, and it is possible that something similar may occur in the case of other analgesics. But there is another possibility which I wish to indicate in addition to this, namely, that just as the brain may become deteriorated by the use of chloral or morphine, so the cord may possibly be injured by the use of analgesics. I have already mentioned that Dr. Cash and I observed in frogs symptoms resembling those of disseminated sclerosis, or of locomotor ataxy in man, and Batten and Bokenham have noticed that antipyrin may produce in frogs a condition like that of spastic paralysis. Cash and I tried to produce symptoms of permanent disease of the spinal cord in frogs by keep-

⁸ Dujardin-Beaumetz and Bardet, *Compt. rend.*, cviii., p. 571.

⁹ Lépine, *Rev. de Méd.*, 1887, pp. 306, 520.

¹⁰ My own experience of this drug has been somewhat disappointing, but it is much too limited to enable me to express any definite opinion.

ing up the poisoning for some time. We were unsuccessful in the attempt, as the symptoms always passed off when the poison was eliminated, but still the conditions in our experiment were very different from those which would occur from the prolonged use of analgesics by a patient, inasmuch as the treatment of the latter might continue for weeks, months, or years, whereas in our experiment time could be counted by days. A circumstance that renders circumspection in the use of analgesics all the more necessary is that various nervous disorders in which the symptoms appear to depend either upon peripheral neuritis or an affection of the spinal cord have lately been described as arising from the use of some of the new explosives, whose chemical constitution approximates somewhat to that of the analgesics. Another action of analgesics which renders caution desirable in their use is their effect upon the blood. Thus exalgine may render the blood incapable of performing its respiratory functions, and thus induce marked lividity, with tendency to collapse, and thus endanger life, while others may destroy the blood corpuscles and produce marked anaemia.

Possible Relation of Leucomaines or Ptomaines to Spinal Disease.—In relation to this, another question suggests itself: whether diseases of the spinal cord may not owe their origin, at least in part, to poisons of the aromatic series, generated either in the intestinal canal or in the tissues of the cord itself.

Use of Suspension.—The remarkable benefit obtained from suspension in cases of locomotor ataxy is one of the most striking discoveries that have been made in therapeutics of recent years. It is very difficult to explain, but I should be inclined to think that suspension merely acted upon the cord in the same way that massage does upon the muscles, by removing the lymph and with it the products of nerve waste; while, at the same time, it may increase the processes of oxidation and repair by promoting a free circulation of the blood.

SUMMARY OF THREE LECTURES

ON

SOME AFFECTIONS OF THE GENITO-URINARY ORGANS.

Delivered at the Royal College of Surgeons of England.

By MATTHEW BERKELEY HILL, F.R.C.S.,

Senior Surgeon to University College Hospital.

LECTURE III. PROSTATITIS.

Symptoms.—In inflammation of the substance of the prostate besides the symptoms of granular prostatitis, there are aching or stabbing pains in the anus, sacrum, or perineum; pain at the suprapubic region is a common sign. There are also radiating lumbar or femoral pains after exercise or long journeys, general languor, *malaise*, or depressed spirits. Increased frequency of micturition is often absent; when present, it is felt by day, not by night. The flow of urine is altered by delay at the beginning, which may amount to retention. Dull pain after micturition, sometimes spasm at the end of the flow, with a sense of more to come are complained of. In cases of long standing, micturition during sleep is a symptom,—constipation is almost invariable. When the congestion is great, there is pain during defaecation and between the acts a sense of weight at the anus or in the perineum. Pain in the testes when it occurs is simply a neuralgia. There is constantly hypersecretion of mucus.

In some patients, the organ recovers its natural condition in a few weeks; but usually the disease drags on a course more or less wearisome; thus the termination is very uncertain. Relapses are almost sure to follow if the patient exceed in his diet or *régime*. In relapses small abscesses often collect in obstructed ducts, which usually empty themselves through a duct before accumulating much. Sometimes the inflammation spreads to the parenchyma, and the prostate then becomes unyielding to the touch, hard, and sensitive. The enlargement of the organ may last long. The increase in size may be symmetrical, or only affect one part, giving the sensation of irregularity or lobular form when felt by the finger. In course of time, the nodules may disappear, and the organ regain its natural size, or even shrink below it, and feel quite firm and smooth.

Treatment of Chronic Prostatitis: General.—The treatment of chronic prostatitis is very tedious. Of the many remedies in use, but few are trustworthy. General treatment only assists local remedies. In the first place, the dyspepsia must be cured. The tonics most beneficial are iron in non-astringent forms; nuxvomica or strychnine are usefully added to the iron. Belladonna also may be added to the tonics if micturition during sleep be a symptom. Ergotine is especially useful when the organ is large, and aching is caused by walking, or standing, or railway journeys.

Local Treatment.—When the organ is enlarged, soft, and not tender, a very good remedy is the cold sitz bath, taken at first for one or two minutes, once or twice daily, at a temperature of 50° F., gradually prolonged to ten minutes, and lowered to 35°. The cold douche on the perineum or anus is also useful. Cold enemata are more generally beneficial than baths, two to four ounces of cold water thrown into the rectum daily, and retained there; beginning at 45° F., and gradually lowered to 35°. Among recognised remedies is blistering the perineum, but the lecturer has no faith in its efficacy. Caustic injections are valuable if used after other means. The solution of 20 to 30 grains of nitrate of silver to the ounce, and ten minims injected at a time, is a good preparation. This has to be repeated several times.

Prostatitis from Masturbation or Excessive Venery.—Masturbation is a frequent provocator of prostatitis, sometimes in the acute form, more often in the subacute or chronic forms. In the mildest form of prostatitis through masturbation, the prostate bleeds easily, the urine is often tinged with blood, smoky, or even coffee-coloured. If felt per rectum, the organ is found little changed from the natural condition. General *malaise*, inappetency, and slight elevation of temperature usually accompany the bleeding. Bleeding from the congested prostate may be copious in young men when it follows prolonged venereal excitement and excessive copulation. Commonly very copious when thus originated, it may be profuse for an hour or two, and exhausting.

Treatment.—In these affections the liquid extract of salix nigra, a drachm three times daily, has often a marked effect in checking involuntary emissions, and thereby preventing the irritation and exhaustion and neuralgia which some persons feel after these attacks.

Sequela of Prostatitis.—Persons who have suffered from a congested prostate are liable to too speedy ejaculation during copulation. This may be so rapid, and erection so fugitive, that effective coitus is impossible. For such cases the liquid extract of damiana has sometimes a powerful effect. But cure is almost hopeless if continence is neglected. Some persons give way to the sexual appetite without limit. Then follows a condition of great helplessness. The intense neuralgia of the lower extremities which follows the shortest walk renders exercise impossible. Pain is rarely absent, even when at rest; it extends from the sacrum along the spinal column to the occiput. The digestion is deteriorated. Topical treatment, after the mucous catarrh and chronic inflammation of the prostate is quelled, must be laid aside. The best remedy is a life of quiet, absence of exertion of any kind; a long sea-voyage is one of the best remedies. In rare cases chronic parenchymatous prostatitis excites temporary mania, which has erotic irritation for an early or leading symptom. It disappears if the patient recovers from the physical affection.

TUBERCULOUS DISEASE OF THE PROSTATE.

Etiology.—This frequently follows gonorrhoea. In the early stages the symptoms, being those of catarrh, escape notice, and the tubercle in the prostate cannot be detected by the finger until it has become considerably developed.

Early Symptoms.—This catarrhal condition of the prostate, with slight irritation of the bladder, lasts an indefinite time; eventually attention is directed to the prostate by the occurrence of other symptoms, such as frequent seminal emissions or by weight in the perineum and pain in the sacrum. In other cases, the patient notices increased frequency of call to micturate, but a slowness in starting the stream of urine; then he feels a burning or cutting pain during the flow.

Later Symptoms.—As soon as the shape and consistence of the prostate are altered, the finger in the rectum finds the prostate irregular, perhaps larger than natural, tender, particularly at the posterior part near the trigone. The disposition of these irregular thickenings is variable. When cystitis is developed, copious viscid pus mixed with shreds and blood clot form the urinary sediment, and the urine contains albumen in considerable quantity. The