

binocular vision and I have little doubt that the others have it too.

Many of the cases in my series are still in course of treatment. Some would have done better if the directions had been better carried out. The general result, however, is enough to show that treatment can be employed with benefit at a very early age, and if I may specially insist on certain points they are the importance of educating squinting eyes and the value of the corneal reflex of the ophthalmoscope as a test of fixation. To sum up, I would urge that the rational treatment of strabismus is, in many cases, a very early treatment; that in every case the child should be thoroughly examined soon after the strabismus begins; and that this principle should be urged by us upon the whole profession in order that it may reach the public.

THE LAW OF INCOMPATIBILITY IN TREATMENT.

By J. GORDON SHARP, M.D. EDIN.

It matters not how deep a man's knowledge of chemistry, physiology, and pharmacy may be; sooner or later he finds himself transgressing the fundamental canons of these sciences in his prescribing. Let him be ever so careful he finds on looking over his prescription book that he has broken the laws of compatibility times without number and has prescribed compounds which would shock the feelings of the pharmacist's youngest apprentice. These faults no doubt arise from the desire to attack the diseases of our patients at as many points as possible. This laudable desire more than ignorance accounts for our over-prescribing and multiple pharmacy. But there is the other side to be considered. If we are too strict in our observance of chemical compatibility and elegant pharmacy we may find we have imposed upon ourselves burdens grievous to be borne, while we are in danger of forgetting the patient by paying too much attention to the disease and the prescription. This leads up to the observation that the prescription is only a part, and often a small part, of the treatment. So far I have only spoken of chemical incompatibility. There is another and far more important form of incompatibility—namely, the physiological or pharmacological more properly so-called, hence the criticism of a prescription or method of treatment from the side of chemistry or pharmacy alone may be entirely erroneous. It thus goes without saying that the prescriber must take an all-round view of the patient and of his disease. I may now make a systematic division of incompatibles: (1) chemical; and (2) physiological, or more properly pharmacological. This second may be divided into (a) cases in which two or more drugs or chemicals are prescribed, the one having an action the very opposite of the other, as, for example, a drug increasing reflex irritability and one reducing the reflex irritability; and (b) cases in which we apparently prescribe drugs or chemicals at variance with the accepted pathology of the particular disease we are then treating. As an example of this class I might cite the giving of perchloride of iron in erysipelas, iron being till lately considered incompatible in febrile affections. We shall hereafter find an explanation of this apparent incongruity.

Having classified the incompatibles I may go on to criticise and seek for an explanation of the employment of some well-known mixtures. The examples shall be taken from every-day practice. It is not my intention to study the chemical and physiological apart from one another, for the one merges into the other. Such an arrangement only means the consideration of detached controversial points, and as prescribers our duty should be to take a comprehensive view of the whole subject. I take sodium salicylate as an example. The books tell us that we should not prescribe this salt with free ammonia or carbonate of ammonia, for if we do the mixture soon turns brown. Perhaps so; but we get out of this difficulty by prescribing mixtures which last the patient only 24 hours, and experience has taught us that patients often take salicylates better when it is given along with an ammonia stimulant. At the present time a popular compound is one made up of pepsin, a soluble salt of bismuth, prussic acid, nux

vomica, and opium. Such a mixture at first sight appears to transgress every law of chemical compatibility, and even allowing for clinical experience as to its efficacy I am not sure but what a simple mixture of prussic acid, nux vomica, and opium arranged by the prescriber himself would not accomplish all that the more elaborate preparation is supposed to do. Some incompatible mixtures are allowable, others are not allowable, and I believe this belongs to the latter sort. To go on ordering such compounds only turns the dispenser into the prescriber and the prescriber into the dispenser. Writing of bismuth reminds me that there is another preparation of this metal which is often prescribed. Subnitrate of bismuth and bicarbonate of sodium with prussic acid and peppermint-water is a favourite mixture with some of us. It is an example of a chemical but not of a physiological incompatibility. The subnitrate and the bicarbonate react on one another and produce carbonic acid gas in sufficient amount sometimes to break the bottle or discharge the cork. However, this happens rarely and the small quantity of carbonic acid gas which is generally generated has a salutary action on the patient's stomach. One could substitute the carbonate of bismuth for the subnitrate but then one does not get the carbonic acid gas.

As other examples we have Blaud's pills or capsules, in which case there is an intentional incompatibility, the sulphate of iron and the carbonate of the alkali reacting to form a ferrous carbonate. The same reaction results in the compound iron mixture of the Pharmacopœia. Some of the iron is, again, in the stomach changed into the chloride, and still further, when this reaches the small intestine an albuminate or peptonate of iron may be formed and finally the whole of the iron passes off by the bowel as a sulphuretted compound of the metal. None of it is absorbed and yet we know that it is our best remedy in a lack of iron in the blood commonly called anæmia. To digress further. The question may be asked, Why do we not prescribe the pure ferrous carbonate without the admixture of sodium sulphate present in Blaud's pills? The pure ferrous salt is difficult to keep, but even where it has been tried it has been found not to answer so well as the freshly prepared pill. To push the question, one might ask why we do not give the ferrous chloride. It, too, has been tried but does not act so well as the Blaud's compound. The fact probably is that the stomach forms the ferrous chloride in such amount as is suitable and compatible with the carrying on of the digestive process. Again we turn to iron. Perchloride of iron and sodium salicylate are incompatible from a chemical point of view, and yet in some throat affections we may, by prescribing them together in solution, obtain the advantages of both. The only objection is the colour, which is a dark purple. Perchloride of iron is sometimes prescribed with acetate of ammonium and from one point of view they are incompatible, but some prescribers like this compound and look upon it as an excellent tonic which does not disagree with the stomach as does the perchloride of iron in many instances. I have seen men prescribe tannin and perchloride of iron. These are assuredly incompatible. They form nothing more or less than ink and without the astringency of either the tannin or the iron, and it appears difficult to defend the prescribing of such a compound on any grounds, chemical or physiological.

I proceed to detail a somewhat different class of examples which deal more with the physiological than the chemical. One occasionally hears of men prescribing bromide of potassium along with solution of strychnine. From the chemical side such a prescription is incompatible, for the bromide may throw down the strychnine and the patient may receive the bulk of the alkaloid in the last dose. Still, this difficulty may be got over by prescribing small quantities and in dilute solution. From the physiological standpoint this compound too is to be criticised. Bromide of potassium lessens reflex irritability while strychnine has just the opposite action. Despite this declaration men go on prescribing the mixture and many have great faith in it for neuralgia, having proved its efficacy by experience. There must be some explanation for this and it may be found in the time of action of the two remedies. Although bromide of potassium and strychnine are within certain limits the physiological opposite of each other the one acts much more quickly than the other. The bromide being soluble soon passes into the circulation and is carried to all parts and acts as a calmate and analgesic to the sensory apparatus. Strychnine acts slowly in small doses and it only begins to

have effect after the main action of the bromide has passed off. Here, then, is a good reason for examining minutely into the physiological action of any remedy or set of remedies we employ.

Our forefathers in prescribing digitalis found that they got all the necessary dynamic action of the foxglove and obviated many of its untoward effects by combining the drug with sweet spirit of nitre. Experience taught them to prescribe what a limited knowledge of physiology might have told them to withhold. For are the two not physiological opposites within certain degrees? Digitalis constricts the blood-vessels and causes the heart to beat more slowly, and sweet nitre is more than the mere stimulant and diuretic which our forefathers thought it. The new pharmacology tells us that its main action is that of a dilator of vessels and an accelerator of the heart's action. We cannot gainsay this, for we can see this for ourselves in the laboratory; nevertheless, we prescribe the two together because we test the efficacy of the combination at the bedside. What is the reason of the apparent discrepancy? Again, it may be that we have to deal with a near and a remote action. Sweet nitre has a near action and this we examine for ourselves by exhibiting a dose of the drug and soon the finger detects the soft relaxed pulse. Digitalis acts slowly and it may be from 24 to 48 hours before we can perceive its presence in the circulation. But I hold that there is another explanation, although few may agree with me. I believe that sweet nitre and all the other nitrites and nitrates act only on the vessels, whilst digitalis acts entirely on the heart, and thus the equilibrium is maintained by prescribing the two together. Digitalis can still act on the heart and bring more blood to the parts, while the sweet nitre preserves the tonicity of the vessels and so the heart is protected from the effects of its own extra action. The value of this is apparent. The digitalis raises the blood-pressure (in what way I do not here stop to discuss) and there is a contraction of the vessels and the heart has to spend its own energy in overcoming this contraction of vessels. But if we give sweet nitre at the same time we overcome the contraction in great measure if not entirely.

The treatment of gout affords examples of physiological chemistry being wanting in clearing up obscure points. Sodium salts are said to be contra-indicated in gout and yet on looking up the analysis of many of the reputed spas to which the gouty resort we find sodium in some shape or other present and often is the predominating metal. In the recent treatment of a gouty patient with sodium, magnesium, and potassium salts the patient himself declared without prompting that the sodium mixture did him most good. Whilst on the subject of gout I am reminded that recent research has led to a modification of the prevailing views on the pathology and treatment of this historic disease. The relationship which uric acid has to gout in the acute and chronic manifestations is variously debated. The treatment of the malady is by some observers said to be best carried out by plenty of fluids to eliminate the poison. But might I not ask the question: Why not try to eliminate the poison of every disease? for is this not the basis of treatment in general? Colchicum is an old remedy in acute attacks and is admittedly a useful one in reducing the redness and exquisite tenderness of the affected joint or joints. It is the analogue of sodium salicylate in acute rheumatism. But in my opinion colchicum is not in the general sense of the term an eliminator of the poison of gout. It paralyses the sensory nerves and soothes the patient and places him on the high road towards recovery. To complete the cure the colchicum must be combined with, or be followed up by, more powerful eliminants. Pharmacology has not yet decided the exact action of colchicum. Some authorities say that it increases the excretion of uric acid, others say the urea, and some, again, that it increases neither. I may, however, say with some degree of certainty that it has little or no action on the higher centres and therefore does not affect the chief vaso-motor area; but it does act on the cord and first stimulates and then paralyses the sensory nerves, leaving the motor nerves unaffected. I speak of moderate doses, of course. But here the laboratory stops and the remainder of the pharmacology is best understood by watching the action of the drug at the bedside of the patient. To begin with, colchicum is a poison and even in small doses its poisonous action is evident; and to go further, it is one of those which is eliminated by many channels and in its elimination it stimulates the secreting

organs. It stimulates the kidneys, the alimentary tract, the skin, and the liver. This points to its action on the circulation being reflex. The same may be said of its action on urea and uric acid. One wonders, after all, if there is any better combination for the general treatment of gout than the mixture made up of medium doses of colchicum wine, large doses of magnesium carbonate, and medium doses of bicarbonate of potassium given in peppermint water. For another example I turn to the theoretical and the practical treatment of lead poisoning. Physiological experiment teaches that iodide of potassium is rapidly eliminated by many channels, and chemistry proves that iodide of lead is comparatively soluble at the body temperature. What more natural conclusion, then, that for the elimination of the lead poison we should employ the iodide? During 12 months' experience of an epidemic of chronic lead poisoning due to the using of soft water I tried this remedy extensively, but had to give up its use because of the frequency with which it aroused all the old symptoms of colic and muscular and joint pains. This shows us that the apparent dictates of science must be studied in the broad light of practical experience. Science does not err, but we err in the interpretation of her teaching, and in the present instance we err in taking too limited a view of the laws governing the elimination of lead poison. A short review of the progress of lead poisoning helps us to understand this. When lead is introduced into the body in dilute solution, as in drinking water, for a time no symptoms supervene because the alimentary tract casts the poison nearly all off as an insoluble organic compound. But it is not all passed out: a little is absorbed in the form of a soluble albuminate of lead which circulates in the tissues and in turn is passed off by the kidneys and largely by the bowels. In time the tissues become exhausted and instead of a soluble albuminate we find an insoluble albuminate which is stored up in the tissues. The intestinal tissues suffer especially and now the symptoms become severe. If no more of the poison is injected the tissues regain their power and particle by particle the insoluble lead albuminate is changed into a soluble albuminate which passes off by the kidney and in great part by the bowels. When the poison reaches the bowel it is changed into an insoluble sulphur compound. Now if the bowels be kept open, preferably by a sulphate aperient, elimination proceeds at a rate which does not disturb the equilibrium. However, if, instead of watching nature, we step in and try to take her place, as in exhibiting iodide of potassium, we run the risk of causing a too rapid elimination and the poison reaches the bowel in larger amount than that organ is able to cope with, and the result is a re-absorption of the lead and a second deposition in the tissues with the former distressing symptoms. Iodide of potassium then must be employed with caution. The treatment found most useful consisted in giving a mixture of Epsom salts with tincture of opium, tincture of ginger, and chloroform water till the acute symptoms passed off, when the patient was instructed to take a dose of Epsom salts twice a week and to suck an orange or lemon every day in addition to the preventive measures. Magnesium sulphate acts beneficially in lead-poisoning in two ways: (1) by clearing the bowels and so aiding elimination; and (2) by supplying the sulphur element necessary for the formation of the insoluble lead salt. The employment of a calomel purge or the old blue pill and black draught in biliousness furnishes us with another example of the apparent discrepancy between pathology and pharmacology. Calomel and blue pill and black draught were the stock remedies of our forefathers in bilious troubles so-called and they even received the sanction of poets and philosophers. Yet how rudely did Hughes Bennett and Rutherford in their extensive and accurate experiments on the secretion of the bile trample all the old traditions under foot and declare that these remedies had no action in bile secretion. But the fault lies with the pathologist, for biliousness has nothing to do with the bile. Still, the remedies I speak of are of the highest service in the treatment of the condition designated by the name "biliousness," and, curiously enough, the resinoid principles known as hydrastin, podophyllin, leptandrin, iridin, and euonymin, which Rutherford proved to be biliary stimulants, have not been found of especial benefit in this distressing affection. The beneficial action of the mercurials is explained by the reflex and actual stimulation of the kidneys and the alimentary tract whereby the products of auto-intoxication are rapidly expelled. We still go on prescribing the old remedies and we still find they do good.

The exact pathology, we may take it, is unknown, for Sir William Gairdner with his vast experience has recently asked, What is a bilious attack?

Mention has already been made of perchloride of iron as a remedy in erysipelas and poisoned wounds. The treatment was introduced by the Bells nearly 100 years ago and was, and is still, prescribed in the two named conditions by a large section of the Edinburgh school. And these very men would scruple about giving iron in maladies closely related to erysipelas and accompanied by a chain of symptoms which are spoken of as inflammatory. The teaching is that we should not exhibit perchloride of iron in cases of loaded tongue and disordered alimentary tract, conditions which we often find in erysipelas and poisoned wounds, and still we find the iron highly useful. Till recently pathology and treatment appeared to be directly opposed to each other on this point. The dark points have now been made light and erysipelas and similar affections we know are not to be feared because of the inflammation which they set up but because of the poisons which circulate in the patient's tissues; and we further know that perchloride of iron is within certain limits a direct or indirect antidote to these poisons. I may be pardoned if I point out that for once pathology has lagged a long way behind therapeutics.

On almost parallel lines run the pathology and therapeutics of peritonitis. At the beginning of the nineteenth century practitioners looked upon peritonitis as an inflammatory affection pure and simple and one that was to be treated by purging. So far so good; but as the century advanced the treatment was changed while the general teaching as to the exact pathology remained the same as when purging was advocated. Instead of Epsom salts opium was administered in large and continued doses, the object being to quieten the movements of the bowels and appendages that the diseased parts might have a chance to recover. One wonders if John Hilton's "Rest and Pain" had anything to do with the universal adoption of opium and the same widespread banishment of purging. If peritonitis is, then, a highly inflammatory disease we may take it that purging is useful and, to put it generally, opium in the large doses advocated is a bad line of treatment—that is, judged by our known therapeutic standards. Such was the treatment employed till Lawson Tait, brushing aside all the details which so often bewilder us in our treatment, boldly said that if patients are subjected to the purgative treatment *threatened* peritonitis (from whatever cause) stands the best chance of being prevented. We must bear in mind the words "threatened peritonitis," for they not only clearly define the position which Tait took up but they are invaluable in impressing upon us the necessity of trying to avert the onset of the dread disease. I can well remember the shock which I received when I went to assist an old practitioner. We had some severe cases of operative midwifery and on the day after when I reported the heightened temperature, the altered tongue, and the tumid abdomen, my principal at once prescribed a mixture of Epsom salts, bicarbonate of sodium, and nitrate of potassium in peppermint water. This was to be taken till the bowels had operated freely. I looked upon this line of action as rank heresy, but next day on visiting my patients I found them comfortable and the alarming symptoms either gone or subsiding. The same treatment was employed in threatened peritonitis from other causes and often with the same happy result. Opium was not employed till after the bowels had been moved and then only to procure a sound sleep or give comfort to a restless patient. One could not help being a convert.

We may here pause and ask ourselves the question, Why does a saline purge act so beneficially in threatened peritonitis? We shall be the better able to answer this question if we turn to Treves's Lettsomian Lectures for the year 1894.¹ Treves says: "It may almost be said that peritonitis, clinically as well as pathologically, has comparatively little to do with inflammation of the peritoneum. There is about the patient who is dying from peritonitis every suggestion of a poisoned man. So far as the aspect of the patient goes he might be dying from snake-bite or from the poison of cholera." Here we have the pathology in a nutshell and if Treves has not been the first to recognise the exact pathology he has certainly been the first to put it into language which we all can understand. Our forefathers

then who purged in peritonitis because they believed they had an inflammation to deal with were wrong in their pathology but right in their therapeutics. The saline purge by stimulating the intestinal glands and neighbouring parts and by clearing off noxious materials might save the patient from being poisoned. A purge is another method of flushing or cleansing the peritoneum and adjacent parts. How does opium stand in the light of the new pathology? It quietens the nervous system and we must allow that that is something, but if pushed there is the greater risk of the patient absorbing the poisons of his own body in sufficient amount to cause death. Opium must not be looked upon as a curative agent. It relieves the pain as no other drug does, but here its mission ends. We must bear in mind that we have a poison to get rid of and a purge at the onset may effect this, but not always.

In medicine, as in everything else human, there is the tendency to extremes and of late there has been the extreme avoidance of opium in abdominal affections accompanied by pain. Surgeons especially sin in this instance and say that "opium masks symptoms." I may safely say that this is a fine point, for if there be any serious organic mischief causing the pain neither opium nor any other drug will for long keep pain in subjection. While I am on the subject of elimination, another class of diseases or symptoms arises before my mind. These are puerperal convulsions, uræmic convulsions, and tuberculous meningitis. In them there is the tendency to serious or fatal coma and opium or morphine have for long been considered incompatible with the sound treatment of these affections. Looked upon as a general rule this is right, for morphine, as we are aware, checks waste and hinders the elimination of the poison or poisons causing the convulsions. But the man who adheres too strictly to this law may find when too late that the treatment of the immediate symptoms is of far more importance than the treatment of the remote cause, for the convulsions attending the pregnant woman or the kidney disease and the sleeplessness and irritation in the tuberculous meningitis may be of far more immediate danger than the coma we fear so much. The nervous and muscular waste dependent on the convulsions and restlessness throws other poisons into the economy, and hence a single or a second full dose of morphine may obviate this danger and give us time to consider how best we can effect the primary object we had in view—namely, getting rid of the cause of the symptom or symptoms. A study of the laws of compatibility and incompatibility teaches us that in the practice of medicine we may often have apparently to break through all law and order. But the breach is only apparent, for on looking at the subject in all its outs and ins we may find that we are doing the best for our patients and this is what the wise man and the honest man always tries to do.

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TUMOURS OF GIGANTIC SIZE.

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MUCH interest attaches to the study of extreme types of pathological variation. We naturally desire to know the limits within which such variations are possible and the special features they present. In this communication I propose briefly to notice some examples of the largest tumours known.

When we consider the minuteness of the germs whence these big tumours arise and the high degree of organisation they attain it seems not unreasonable to regard the force which originates them as analogous to that which determines the development *ab ovo*. It accords with this that the largest tumours almost invariably spring from those parts of the body where post-embryonic developmental changes are most active—such as the uterus, the ovaries, and the mammae. Tumours of this kind are nearly always of slow growth and of the non-malignant variety; malignant tumours, being for the most part poorly nourished and of rapid growth, seldom attain the largest size, owing to the supervention of degenerative changes; hence it is among the slow-growing sarcomata that the largest malignant tumours are found. Those who bear these very large tumours—even

¹ THE LANCET, Feb. 3rd, 1894, p. 263; Feb. 17th, p. 405; and March 3rd, p. 541.