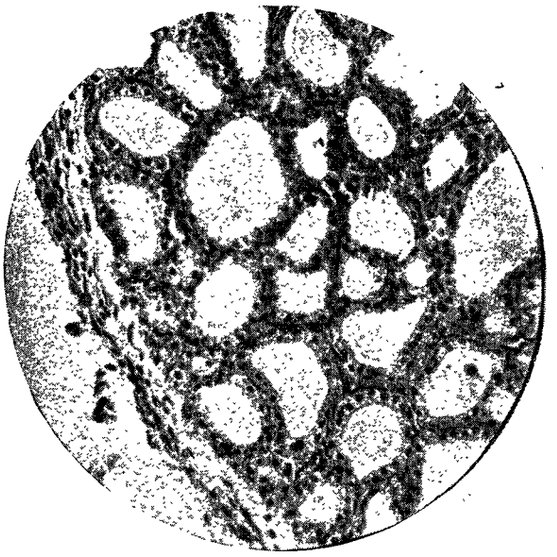
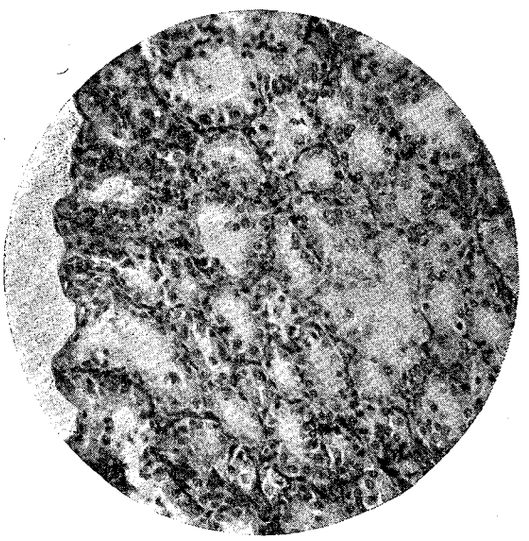
diminution in colloid material; (*b*) proliferation of the epithelial cells and also of the connective tissue; (*c*) evidence of rapid degeneration of the colloid into a mucinoid material; and (*d*) congestion of blood-vessels. Professor W. S. Greenfield kindly examined some of these specimens and pointed out to me that in the more marked cases

FIG. 3.



Thyroid gland of rat fed on bread and milk. (× 200.) Observe (1) the size of vesicles and regularity of outline; (2) the colloid material in the vesicles. Cf. Fig. 4.

FIG. 4.



Thyroid gland of rat fed on raw meat and water. (× 200.) Observe (1) catarrhal changes in the epithelium; (2) diminution of the colloid material.

the appearances bore a striking resemblance to those seen in exophthalmic goitre in the human subject. In the case of the one *adult* meat-fed rat, which succumbed after three weeks of the diet, the appearances of the gland were those of an advanced atrophic catarrh with complete absence of colloid. In the great majority of cases the parathyroid glands were normal. So far as I am aware, this is also the first occasion on which it has been directly shown that a particular diet induces distinct histological changes in the thyroid gland of an omnivorous animal (rat), and, further, that these changes are of a nature similar to those seen in the gland in cases of exophthalmic goitre in the human subject. It should be stated that the animals showed no other signs or symptoms of this disease.

Remarks.—The results obtained from the two investigations agree in showing that a diet of meat and water profoundly influences the thyroid gland. In poultry the diet induced a striking hypertrophy of the gland with great increase of colloid material which appeared for the most part normal. In the case of rats the striking change was the alteration in the character of the secretion with catarrh of the epithelial lining of the vesicles, the general appearance of the gland indicating exhaustion of its functions. Further investigations are necessary before the difference in the results obtained in the two classes of animal can be explained. In the meantime it appears to me that these new facts have some practical interest and importance. There are figures in the Blue-book which conclusively prove that there has been a great increase in the consumption of meat in this country in the past 30 years. Evidence is also accumulating to show that thyroid medication is of value in a number of diseased conditions which have no known relationship to the thyroid gland—e.g., skin diseases, mental affections, eclampsia, and other disorders. May not the new facts recorded in the present paper explain the value of thyroid medication in those cases? It is, I believe, possible that as a result of the excessive use of meat there has been established in many subjects an alteration in the character of the thyroid secretion, which defect is remedied in the cases in question by the administration of thyroid gland. The adoption of this view has led me in the past year to try the effect of the administration of small doses of thyroid extract in two inveterate cases of chronic gout which had not been amenable to dietetic measures aided by skilled balneological methods. In both cases the symptoms were relieved to a striking degree, this relief having been so far of a fairly permanent nature.

Edinburgh.

CARBONIC ACID AS A FACTOR IN THE GENESIS OF THE GOUTY STATE.

BY DONALD F. SHEARER, M.B. OXON., F.R.C.S. ENG.

THE origin of the gouty state, in which it is usual to group together clinically gout, arterio-sclerosis, and chronic interstitial nephritis, is commonly attributed to the over-production or the retention of uric acid or its salts within the body; and a bewildering wealth of chemical experiment, of pathological record, of physiological research, of clinical observation, and of polemical argument awaits him who seeks for further enlightenment. So overwhelming is the mass of literature on the subject that one is justified in putting it all aside in order to consider the question *de novo* and in avoiding the narrow purview of the test-tube or the microscope in order to seek a solution in a less restricted field of vision. We have learnt empirically that these pathological conditions are wont to follow long-continued excesses in diet and also upon deficient muscular activity and we also know that lead poisoning has a definite etiological relationship to them. On the first two we have built our prophylactic and our curative treatments and from them it is possible to trace the genesis of the diathesis. It is interesting to note that notwithstanding all our investigations the modern treatment follows exactly the lines laid down in the days when uric acid was unheard of or had not been causally related to gout. This fact, moreover, which can be verified by a reference to Sir T. Watson's lectures, indicating as it does that uric acid has led us into a blind alley barring further progress, is an additional reason for a wider review.

Now when we have to deal with a common phenomenon following upon diverse antecedents so various as undue indulgence in alcoholic drinks, excessive consumption of nitrogenous food, excess of carbohydrate diet, and insufficient exercise, when we find a mitigation of the symptoms succeeding to an alteration of each separate antecedent as well as of all combined, we may rightly seek for a causal factor common to all the antecedents rather than make the assumption that the cause is other than the known antecedents. A reference to any text-book of physiology tells us that the one factor common to all the antecedents of gout is the tendency to the production of an excess of carbonic acid in the blood. The cardinal feature of muscular exertion is the large increase in the output of carbonic acid without affecting the nitrogenous excreta. Alcohol and carbohydrates can only produce as the end products of their combustion water and carbonic acid. Nitrogenous diet increases metabolism not only of proteid but of carbohydrate and hydrocarbons and thus leads to an increased amount of carbonic acid. And just as the action of the antecedents tends towards an excessive manufacture

of carbonic acid, so the treatment we prescribe, whatever object we have in view and whatever may be our preconceived theory, is actually directed to the diminution or the elimination of this waste product.

There is further an *a priori* probability, derived from a consideration of the anatomical distribution of the lesions, that if there be any toxin circulating in the blood to which the lesions may be attributed that toxin will be one that should normally be eliminated by the lungs in respiration. For the brunt of the disease is borne not by the joints in articular gout but by the arterial system and the kidneys to which are assigned the work of conveying the purified blood and of further purifying it, and when we remember that the chief, if not the sole, portal of exit for uric acid is through the kidneys we have good ground for concluding that all the organic phenomena associated with gout may well owe their genesis to a toxin that has escaped its normal excretion through the agency of the lungs. It is not hard to conceive that such a toxic blood should have the power to inhibit the excretion of uric acid and lead to an accumulation in the tissues such as precedes the gouty paroxysm, while the actual paroxysm itself may be dependent on local deposition initiated by local causes. There is then a natural likelihood that the toxin of gout is, or ought to be, an excretion of the respiratory function and there is an actual factor common to all the antecedents—the excess of carbonic acid. If carbonic acid is to be considered the *fons et origo mali*, if not the *materies morbi*, it must be shown that the excess is sufficient to be appreciable and to alter the composition of arterial blood deleteriously, but it is not necessary that the excess should be large, for, to use a mathematical figure, the integration of an infinite number of infinitesimal divergencies from the normal yields a finite result, and in the second place the toxic action of carbonic acid must be such that the sum of a large number of such intoxications would produce the organic and functional lesions characteristic of the gouty state.

The normal daily excretion of carbonic acid is 800 grammes, corresponding closely to the amount which the oxidation of typical normal diets would yield. A man doing hard work will excrete much more largely—say, 1200 grammes—and in order to maintain his weight would have to consume food of corresponding weight and quality. If now we supply such a quantity of food without permitting the muscular activity necessary to excrete it the man will either not assimilate it, or he will convert it into fat, or he will metabolise it and excrete it as carbonic acid. We know that he does assimilate it, we know that only a very small part is converted into fat, and we are compelled to the conclusion that he does excrete it as carbonic acid. In the absence of the muscular activity, which would naturally increase the rapidity of the pulse and the frequency and depth of respiration, and therefore the quantity of blood exposed to aeration, the exchange of carbonic acid with the air must be greater than normal. Under normal conditions of feeding and blood tension six out of 48 volumes of carbonic acid escape; in the altered circumstances nine must be evolved, other conditions being equal, and in order that nine may be evolved the carbon dioxide tension of the blood must be increased; that is, it must contain something like 72 volumes per cent., since the exchange of gases is proportionate and not a mere overflow. If that be so the arterial blood in such a case will contain over 60 volumes of carbonic acid per cent., and making every allowance for the increased respiration from other automatic agencies there is obviously a large balance of carbonic acid which can only be accounted for on the supposition that during a portion of the day at any rate the carbonic acid tension is such as to allow an extra excretion and in consequence an excessive accumulation of it in the arterial blood with such deleterious consequences as its toxicity may give rise to. The important fact in this connexion is that whereas the normal and healthy man regulates to some extent his diet by his activity, the man who is to become gouty fails to keep the necessary balance and continually and continuously soaks his arterial system and his kidneys with blood overcharged with carbonic acid. All the modes of computing the discharge of carbonic acid point to the same result, whether we estimate it directly or by the oxygen inhaled or by the carbon ingested. In all cases we find that muscular activity, excessive discharge of carbonic acid, and increased diet go together, and we are forced to the conclusion that the gouty individual who on an excessive diet produces, by virtue of the increased metabolism consequent on a nitrogenous diet or by an excessive consumption of carbon compounds, an increased quantity of carbonic acid which is not removed by the direct cardiac and pulmonary effects of exercise must rid himself of it by means of an increased carbonic acid tension of the blood.

As corroborative evidence let me adduce the well-known gout producers—ale and port. A pint of ale contains an ounce of alcohol and an ounce of saccharine matter. A pint of port contains also an ounce of sugar and some five ounces of alcohol. The former will produce by combustion 100 grammes of carbonic acid and the latter 340, so that a pint of ale or a quarter bottle of port are approximately equivalent gout producers and raise the total carbonic acid to be excreted by 12 per cent. It remains to ascertain what, if any, is the effect of an excess of carbonic acid in the blood. It appears that it augments the activity of the vaso-constrictor centre, thus leading to a general contraction of the small arteries. The heightened blood pressure thus produced is increased by the direct irritative action of venous blood on the muscular coats of the arterioles and by the increased peripheral resistance which occurs within the capillary area. One cannot but be struck by the correspondence between this description of the action of venous blood and that which obtains in the gouty condition under consideration and it is obvious that a frequent repetition of such a state would inevitably induce hypertrophy of the muscular coat. And the analogy of lead, a marked vaso-constrictor, which is admittedly a cause of gout, and of adrenalin, which has recently been adduced to account for arterio-sclerosis, shows that there is no need to labour this point. We may conclude, then, that the sum of the small additions to the blood pressure which are consequent upon the excessive presence of carbonic acid is sufficient to account for the muscular hypertrophy. But we have also to account for the fibrosis, for the hyperplasia of connective tissue which exists both in the outer coat of the arteries and in the stroma of the kidney. If we assume that carbonic acid in excess in arterial blood is an irritative toxin, as the cause evidently must be, we can see by analogy how these tissues, which are the first directly subject to the action of arterial blood and are therefore the first to suffer, would develop an excess of fibrous tissue. The action of alcohol on the liver is quite analogous; there we find its irritative effect is expended not on the cellular elements but on the supporting structure in which the venous channels run. So, too, with the irritation of the secretion from carcinomatous cells; the effect is also to produce hyperplasia of connective tissue with subsequent shrinking, and we may therefore easily believe that the effect of the chronic irritation of blood overcharged with carbonic acid would be increased connective tissue.

From the nature of the case it is not possible to show by direct experiment that either fibrosis or muscular hypertrophy follows upon excess of carbonic acid; nor is it any more possible to show that carbonic acid possesses an inhibitory function upon the renal secretion but there are examples which go to show that this is so in general and in particular with regard to uric acid. We can show from the experience of many patients that excess of carbonic acid will produce a high tension pulse followed by certain well-marked symptoms of intoxication, headache, vomiting, and partial suppression of urine and that as recovery takes place we get a soft pulse and a return of cutaneous heat—i.e., vaso-dilatation instead of constriction—accompanied by profuse diuresis, the urine laden with urates. And this form of migraine is attributable either to over consumption of food, especially alcohol, with insufficient exercise, or to exposure to a vitiated atmosphere charged with excess of carbonic acid. In addition to such cases of the temporary toxic action of excess of carbonic acid there are cases where persistent excess leads to chronic nephritis and arterio-sclerosis. An example of this occurred in a patient in whom one lung had been collapsed entirely for many years. In her case any symptoms of uric acid, if they existed, escaped notice and must have been of the slightest, for she was practically an abstainer from meat. Her difficulty in getting rid of the carbonic acid, made greater by the little exercise she took, led in the aggregate to the organic lesions. Many other such cases could be adduced, as well as others of different nature, to show that all the three classes—gout, arterial sclerosis, and chronic interstitial nephritis—and in general all so-called uric acid conditions are inseparably bound up with antecedent conditions, of which the main factor and the common

factor is the excess of carbonic acid in the arterial blood. One would argue, of course, from such cases that carbonic acid is the determining factor which decides whether or no uric acid shall be eliminated or retained. It is worth noting also that its power to limit the water secreted by the kidneys is not absolute, for it may be, and is in the later stages, entirely overborne by the high tension in the glomeruli while still retaining its controlling influence over uric acid. This latter, then, in this view, occupies a secondary place, it remains no longer an etiological factor but becomes merely a retained normal secretion which under certain conditions obtains a pathological importance by being deposited in the neighbourhood of a joint and becoming the active cause of a local inflammation. The primary place must be assigned to the unnatural excess of carbonic acid in arterial blood as the most potent factor in bringing about those changes which go to make up the gouty state.

Putney, S.W.

THE RATIONAL TREATMENT OF FRACTURES.

BY J. STAFFORD MELLISH, M.R.C.S. ENG., L.R.C.P. LOND.,
SURGEON TO TETBURY COTTAGE HOSPITAL.

RECENTLY I wrote a rough draft of a letter on the rational treatment of fractures which I intended to forward to THE LANCET when I had had time to elaborate it. The leading article on the subject which appeared in THE LANCET of Jan. 21st last, p. 172, at once confirms my opinion that there is much room for improvement in this branch of surgery and emboldens me to send for publication what I had written. The leading article in question says:—

> The lack of completeness in many of our results opens a way, and is responsible, for much of the bone-setting which abounds in this country to-day and it is necessary to consider closely the situation which presents itself. We can all treat with success an uncomplicated fracture, say, of the tibia. The fragments of the broken bone are carefully replaced, splints are bandaged on, and a few weeks' rest in bed produces a firm osseous union of the two portions of the bone. Hardly any deformity can be detected on rigorous examination or even with the aid of a skiagram. Yet when we regard the case from another aspect we see that the result leaves much to be desired. Anatomically there may be little fault to be found with the limb but physiologically it is far from being a perfect member. The patient cannot use it as he could before his accident. The knee-joint and the ankle-joint are stiff; the long confinement between splints has resulted in the formation of numerous bands of adhesions, whether within the joints themselves or in their neighbourhood; muscles and tendons may have shortened from the enforced rest and the pain and tenderness combine with the adhesions in limiting movement. The patient can hardly after six or eight weeks of rest do more than get about feebly with the aid of crutches After some months an increased mobility of the limb may be obtained and work may be resumed.

I am convinced that this state of things can, and ought to, be prevented in the vast majority of cases of fracture and would be if the methods which I follow and try to describe were commonly adopted. These methods include rubbing and as much freedom and movement as can be permitted in each individual case. Having been dissatisfied with the results of fractures which I have seen treated both in hospitals and in private practice by the ordinary methods of splints and so-called passive movement "administered by the surgeon" I have been at some trouble to apply any hints on the treatment of injuries which might tend to avoid the subsequent stiffness of joints and the muscular wasting which invariably follow the continued use of splints, plaster-of-Paris, and other rigid apparatus, and from a treatise on bone-setting by Dr. Wharton P. Hood, as well as from a later work by the same author on the treatment of recent injuries, I have learnt much which has been of the greatest practical use and which varies widely from the general tenor of the usual text-books.

We have all seen stiff and wasted limbs "go on strike" and become œdematous and painful on being called upon to perform their wonted movements, often taking a longer time to get into a healthy working condition physiologically after the bone was firm than the bone itself had taken to unite. For my part I have come to look upon the bone as being quite able to take care of itself if the surgeon, after having approximated the fractured ends, will give his chief attention to keeping the circulation of the limb in a healthy condition. For this purpose I find that the less splinting one can do with the better and dependence must be placed upon rubbing and movement of a voluntary kind. Where a splint has to be used as in fracture of the humerus, of the femur, or of both bones of the leg, rubbing must be practised and the patient be induced to move his joints voluntarily every day, the splints being taken off for this purpose and then being replaced. The rubbing must commence at the proximal end of the swelling in the region of the fracture and be directed towards the body—i.e., in the direction of the venous circulation, gradually working down to the distal portion of the swelling. As a student I was always taught that the joints above and below a fracture were to be secured and kept rigid, but this course invariably produces stiffness which has to be got rid of after the bone is united. For some time past I have followed the recommendations of the author of the works mentioned above and it is now my practice to endeavour to give the joints free play where possible and in this manner to prevent both wasting and stiffness, by encouraging the patient to move the joints, merely supporting the bone. The patient must be persuaded to flex, to extend, to rotate, and, in short, to execute all the movements that the joints are in the habit of performing voluntarily. This is a much more efficacious and to my mind a more rational proceeding than waiting a stipulated time from the occurrence of the accident, as is generally done, and then beginning so-called passive movement to be performed by the surgeon, for in the voluntary movement the nervous stimuli are called into use, while in the passive they are not and, in fact, there is generally more or less antagonism on the part of the patient. I will describe two cases which have recently come under my care, in one of which I saw the patient two hours after the accident and treated the case according to the plan already enunciated. The other patient had been treated in the more classical manner and I was called in eight months after the accident, when I found her suffering from a stiff knee and ankle, muscular wasting, and pain on attempting to walk.

CASE 1.—The patient, a man, aged 42 years, and weighing 15 stones, had fallen down and broken his leg. On seeing him some two hours after the accident I found the tibia fractured at the junction of the middle and lower thirds, the fibula being fractured somewhat higher up. There was a good deal of swelling. I first flexed the knee and rotated the thigh outwards, resting the knee on a pillow to check muscular spasm, and gently rubbed at the swelling for an hour, beginning at the upper end and gradually working downwards, but always rubbing in an upward direction, in this manner squeezing out of the tissues and passing on the effusion which had gathered there. One who has not tried this would be surprised to find the reduction in size that he will produce and the comfort that it gives to the patient. It is as well during rubbing to take advantage of gravity by elevating the limb when able to do so. I then, as I always do in cases of simple fracture, strapped the leg. To do this I used pieces of strapping about two inches wide, and having placed the broken bones in as good a position as possible I applied the plaster to the leg *from above the break downwards* to the ankle, not tightly, but just so as to support the limb, letting each succeeding piece of strapping overlap its predecessor by about one half. It will be noticed that the limb was strapped from above downwards. This is done in order that in the daily upward rubbing of the limb afterwards the strapping may lie the right way and its edges may not become displaced by the hand of the rubber. In some cases where it is difficult to apply the strapping with equal pressure on account of the shape of the limb, advantage may be taken of the American method of bandaging the legs of racehorses—i.e., by surrounding the limb with a layer of cotton wool or Gamgee tissue, filling up cavities with the wool and strapping over it, thereby producing equal pressure. Having strapped the injured part I applied a pair of Cline's splints and rested the leg on a pillow with the knee flexed in the ordinary way. The splints were removed twice daily and the limb was rubbed for half an hour, morning and evening, the leg being supported and the patient being persuaded to flex and to extend his knee and ankle. On the evening of the fourth day the plaster, being loosened by diminution of the swelling, was taken off and replaced, this being done at intervals as the case demanded. The splints after a week were kept in position merely by two webbing straps and the patient's wife (an intelligent woman) was instructed to undo the straps and to remove the top or