The Relationship between General Paralysis and Chronic Renal Disease. Illustrated. By HUBERT C. BRISTOWE, M.D., Assistant Medical Officer, Somerset and Bath Asylum, Wells. (Read at the S.W. Division, Dec. 13th, 1894).

Whilst studying the pathological changes met with among those dying insane, I was much struck by the large number of cases in which chronic renal disease of a more or less advanced state was present. This led me to work out, from the post-mortem records of the Somerset and Bath Asylum, the percentage of chronic renal disease noted in such cases. But whilst engaged in these inquiries my attention was especially called to the number of general paralytics presenting this condition, and I proceeded, therefore, to collect all the cases of general paralysis of which the records were sufficiently trustworthy. In this way I collected 75 cases, and of these only nine were free, or apparently free, from renal disease. Of the 66 cases remaining 51 had what must be considered well-marked granular kidneys, and the other 15 had diseased kidneys which were most probably granular, though in a less advanced degree. One of these latter cases had renal calculus. In other words, only in 12 per cent. of the cases were the kidneys apparently healthy, and we may, I think, take it that almost all the remainder (88 per cent.) had granular disease of the kidney. I do not suggest that this is the usual percentage, but among the cases of one asylum it is sufficiently remarkable.

I then proceeded to work out the frequency of chronic renal disease in persons dying of other forms of insanity, and found that out of 688 cases 380 (or 55·872 per cent.) presented this condition, making a difference in this respect between them and general paralytics of nearly 33 per cent. These figures are of extreme interest. But it is now only my intention to discuss the relationship between chronic renal disease and general paralysis of the insane. The other point must be left for some future occasion.

The extreme frequency of contracted granular kidney in general paralysis puts out of court entirely a mere accidental relationship, and shows that there must be some pathological connection between the two. I do not pretend to be able to state definitely what that relationship is, but I shall attempt to show in what direction my own observations have led me.

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For the accurate study of this matter I have first examined the vessels of the pia mater and cerebral cortex in patients who have died of well-marked granular kidneys. Then I have examined vessels from those dying of general paralysis with chronic kidney disease, and finally I have been able to investigate similar vessels in two patients who died of general paralysis without apparent renal lesions. The rareness of this occurrence has rather hampered my observations. I regret that no portion of the kidneys from these cases were kept for microscopic examination. But although desirable from the point of view of accuracy, the omission of such examination makes but small difference to my general conclusions.

I shall not devote much time to the changes that take place in the vessels of the kidney, but briefly state that in contracted granular disease the vessels become thickened, especially their inner and middle coats, and that there is a tendency to the occlusion of some of them, due to the progress of endarteritis obliterans.

The changes which take place in the heart and systemic arteries are of exceeding interest. There is a rise of tension in the arterial system generally. The arteries become thickened, more especially in their middle and outer coats, though as a rule the middle coat suffers most. As a result of this thickening and increase of tension the heart has more work thrown upon it, and an extra impediment to overcome. If the condition of the patient is sufficiently good—and mark those words "sufficiently good"—hypertrophy of the left ventricle takes place.

The next thing to be considered is the change which takes place in the smaller arteries, and for this purpose I have chosen the vessels of the pia mater. They are easy of examination, and can be got at in all cases. There is a marked thickening of the middle coat, and to a less extent of the adventitial. But in all the thickening is well marked (Fig. 1).

Before passing on to the vessels of the cerebrum it would be as well to investigate the changes in the heart and arteries in general paralysis. As a rule, in this disease there is no hypertrophy of the left ventricle. But we know that clinically there is to be found a marked rise in the arterial tension. Before the days of the sphygmograph Milner Fothergill spoke of "the hard pulse of increased arterial tension" in general paralysis "such as characterizes

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chronic Bright's disease." But far more recently than this the whole subject has been investigated by Bevan Lewis with the aid of the sphygmograph. I cannot do better than quote his own words:—"It requires but a slight familiarity with the pulse tracing of chronic Bright's disease to recognize in the sphygmogram of general paralysis a miniature reproduction of the same curves. I say a miniature copy advisedly, for if *cet. par.* a high percussion stroke be given to these, we should get a tracing very similar, if not identical with that characteristic of arterio-capillary fibrosis. And it is herein that the distinction between the two tracings becomes apparent. The tracing in chronic Bright's disease gives evidence of very high arterial tension, the percussion impulse indicating compensatory hypertrophy of the ventricle."* From this it is clear that in all respects except the results of the hypertrophy of the left ventricle the condition of the arterial beat is much the same in general paralysis as in chronic Bright's disease. It is now clear why I laid stress a short space back on the words "sufficiently good." Hypertrophy of the left ventricle does not take place if the nutrition is poor, and in general paralysis, at all events after the earlier stages, there is marked impairment of nutrition. Again I may ask, why do we not find hypertrophy of the left ventricle in cases of general paralysis where chronic renal disease is well marked? As regards the arterial system, thickening of the vessels and increase of tension are generally admitted. I have examined the vessels of the pia mater in health (Fig. 2), in general paralysis where contracted granular kidney was present (Fig. 4), and in general paralysis where it was apparently absent (Fig. 3). The latter two, as may be seen, are not only much alike, but present a marked similarity to the vessels in simple chronic renal disease. Nor would it be possible, from looking at the vessels, to say which belonged to which. In all there is marked thickening of the middle and, to some extent, of the adventitial coat.

The smaller cerebral vessels in health present a regular appearance equally stained by reagents and scattered at comparatively rare intervals, the nuclei of the cells of which the blood-vessel, or, in fact, here it might be called the capillary, is composed. The nuclei in these vessels are, as a general rule, spindle-shaped, with their long axis in the

* "Teachings of the Sphygmograph," "Journal of Mental Science," Vol. xxvii., pp. 3 and 4.

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direction of the vessel. In contracted granular kidney this condition is changed. The nuclei become much more numerous, and of a more rounded shape, and in some places there is actual proliferation of round cells in their neighbourhood (Fig. 5). On transverse section the same thing is seen: a large increase of the deeply-stained nuclei. In some cases, apparently in those vessels where the disease is more intense, these nuclei become exceedingly numerous and lose their definite outline altogether, and leave an irregular, darkly-stained channel, in which with difficulty their outline can be detected. And here the outline of the vessel itself becomes irregular, and spider cells may often be seen in connection with them. The transverse section of the vessels shows that the proliferation of cells exists in the inner coat quite as much as in the adventitial coat or perivascular space.

In general paralysis the vessels present very similar appearances; and the changes which take place in them vary from these to a more marked degeneration.

In the early stages there is apparently simple increase of the nuclei of the vessel wall, and a rounding of their outline. In the more advanced cases the nuclei are so numerous that in some parts they appear more as a conglomerate mass than anything else (Fig. 6). The outline of the vessels is irregular, and darkly stained nuclei can be seen at their edges. But the same vessel may present both of these conditions. In the place where these nuclei are specially numerous there may often be seen small brown masses of what is probably hæmatoidin. The next stage shows the vessel still more irregular in outline; the nuclei are ill defined, and the vessel wall itself is darkly and irregularly stained. The last stages show the vessels uniformly but darkly stained, and no nuclei can be detected in their walls; and in frequent connection with them spider cells may be seen. These vessels also when stained with osmic acid show fatty degeneration in their walls. It is exceedingly difficult to get transverse sections of these vessels, but from examination of them it is clear that increase of nuclei takes place not only in the adventitial coat, but also in the inner ones. And it also becomes obvious that there is marked thickening of the whole vessel wall, including the adventitial coat. A single blood-vessel in the various stages of disease may often be seen.

I have also examined the vessels of the spinal cord in

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similar cases, but the results are not satisfactory owing to the impossibility of preparing specimens by the fresh method. But those prepared by ordinary methods show exactly the same appearances as are seen in sections of the brain prepared in a similar way. I have purposely omitted referring to the dilatation of the perivascular spaces so often mentioned by observers, as I have been unable to discover it in sections prepared by the fresh methods (see Figs. above).

Let us now compare the condition of the blood-vessels in general paralysis and contracted granular kidney. In the early stages of both—by early stage I refer to the extent of disease found in the vessels—there is, then, increase of nuclei with a corresponding (to some extent) increase of cells; this progresses still further until a regular fibrosis takes place. But this never appears to advance so far in chronic renal disease as in general paralysis. Obviously, then, in the latter disease something further takes place, and this something further appears to be a complete degeneration of the vessel wall. And, moreover, as seen by transverse section, many appear to be occluded.

Bevan Lewis, in his "Text Book of Mental Diseases," speaks of "the enormous development of nuclei along the lymph sheath," and he further states that "the perivascular lymph channels are the site of a nuclear proliferation and segmentation of protoplasm often so enormous as to entirely conceal the enclosed vessel from view."* By perivascular lymph channel must be understood a potential space between the tunica adventitia and the tunica media, which is not lined by endo- or epithelial cells; and by adventitia must be understood a delicate fibrous coat, and not a dense one as met with elsewhere. If this space, then, is to be filled by proliferated protoplasm and nuclei, or, in other words, cells, do they start from the cells which form the vessel walls or from transuded leucocytes? I am myself inclined to believe that this proliferation of cells takes place in other coats besides the adventitial, and that in the early stages, at all events, there is an actual increase of cells in the muscular and endothelial coats. This opinion is borne out by the examination of transverse sections of these vessels, where it is obvious that there is as much increase of the cells in the inner coats as in the adventitial. And, further, the cells in the early stages are often found to retain their

* "Text Book of Mental Diseases," pages 493 and 494.

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fusiform shape. Finally, the condition in chronic renal disease is much the same as in general paralysis. I may here state that I have not discussed the condition of the vessels in general paralysis with renal disease and general paralysis without, separately, because there appears to be no obvious difference between the two. In the later stages of general paralysis the adventitial coat and perivascular space become filled with cells; some from proliferation of the cells forming the wall, and some probably from transuded leucocytes. After a while these cells lose their outline and form, and leave nothing but a thickened and uniformly stained vessel wall, with some fatty degeneration and an irregular outline. In other words, the process here described is practically the same as takes place in any chronic inflammatory condition, and leaves behind it a true fibrosis.

I shall now attempt to describe the pathological process which takes place in the vessels, and briefly trace the results on the general brain substance. It has been shown by Heidenheim, Starling, and others that the cells which form the capillary walls actually take up the nutrient plasma of the blood and secrete it again for the nourishment of the surrounding tissue. Further, it has also been shown that the amount of this secretion is dependent on the extent of blood pressure, and that it can also be influenced by the presence of poisons in the blood stream. We know as a law in pathology that increase of tissue takes place according to the amount of work to be done by it. We start, then, with an increase of blood pressure, caused either by chronic renal disease or the presence of some poison in the blood. Either of these conditions is sufficient to cause an increase of secretion by the capillary walls. This increase of work must cause increase of the cell elements of the wall, and the increase of pressure in the vessels generally will lead to increase in the thickness of the vessel walls from the strain thrown on them, and thus can be accounted for the increase of cells in the different layers of the vessel wall. The increased secretion of nutrient plasma requires increase of the lymphatics to carry it off. This hyperplasia of the lymph connective tissue has been too well described by Bevan Lewis in his "Text Book of Mental Diseases" for me to attempt to add to it. The vessels then become thickened and inflammation is started—for it obviously is a chronic inflammatory trouble; proliferation of the cells takes place generally, together with transudation of leuco-

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cytes. In advanced cases there must even be small hæmorrhages, which account for the hæmatoidin present in the adventitial coat. This inflammation is of a slow character, and the ultimate change is fibrosis of the vessel walls, and probably even complete blocking of the lumen in some cases. The inflammatory products round the vessels also become organized, and finally form contracting fibrous tissue of the ordinary kind, and this further presses on the vessels and interferes with their functions. Thus is brought about a true cirrhosis, such as is found in the kidney or liver. This is the view which was held by Wiglesworth. Curiously enough he added this remark: "Though in several cases of the series taken for comparison with general paralysis the insanity had extended over many years, in none of them was there the smallest evidence of connective tissue increase, nor in our experience have we met with this in any cases other than general paralysis, except in cases of chronic Bright's disease."*

There is one more clinical point which must be considered, and that is the condition of the urine in general paralytics. Dr. J. Turner, who investigated the urine in these cases, stated that "albumen was absent in all but a few, and in these existed in the merest traces, and only during certain times of the day."† Unfortunately he omits to tell us the specific gravity. In the early stages of this disease, there is as a rule nothing worthy of remark. In the late stages it is different; but then the urine is much more difficult of examination. When any is wanted for testing it must be drawn off. And at the same time it is impossible to estimate the amount passed per diem—a point of almost as much importance as the presence or absence of albumen itself. In three bed-ridden cases which I was able to examine, the specific gravity was 1003, 1007, and 1013, and in one case a trace of albumen was present. I do not suggest that any conclusions can be based on three cases. I simply wish to make it understood that clinical signs of chronic renal disease may be present, and yet unobserved owing to the difficulties of examination.

The frequent presence of chronic renal disease in general paralysis, and the curious similarity of the blood-vessels of the pia and cerebral hemispheres in the two diseases, lead us to the question: What relation do these two diseases

* "Journal of Mental Science," Vol. xxviii., page 480.

† "Journal of Mental Science," Vol. xxxv., page 34.

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bear to one another? There are three possible views which are worth discussing. The first is that the chronic renal disease is responsible for the increase of arterial tension throughout the body, and that as a result of this there is general thickening of the arteries; that the increase of tension causes increased transudation through the capillaries of the cerebrum, and that the further lesions which follow are dependent on this transudation and thickening of the vessel walls; in fact, that the kidney disease is the prime factor of all the further trouble. That this is probably incorrect is shown by the fact that in some cases of general paralysis there is no apparent sign of kidney disease, and this shows that at all events general paralysis must in many cases commence before the kidney trouble.

The next view is that an arterio-capillary fibrosis is the commencement of both diseases, in fact, that they are both manifestations of a common condition. It was long ago suggested by Gull and Sutton that arterio-capillary fibrosis is a general disease of the vascular system in which the kidneys share. Although this is not generally accepted, is it not possible that it may after all be correct?

The third view, and one which goes hand in hand with the preceding, is that both diseases have a common cause. This common cause may act directly on only one set of organs, *i.e.*, the arteries and capillaries. Speaking of chronic renal disease, Coats says, "We have to look for an irritant," and further, that there are indications "that the irritant is carried to the kidneys by the blood."* Is it not possible that the same poison which induces chronic renal disease may also induce general paralysis? Perhaps the converse of this may be more accurate. What this poison is I cannot say, nor can we be sure that more poisons than one may not produce these conditions. That in some persons chronic renal disease should be the sole result of the irritant, whilst in others general paralysis is superadded, suggests that the ordinary cause of chronic renal disease is not the ordinary cause of general paralysis; but that the poison which induces general paralysis is capable of causing chronic renal disease also.

I do not pretend to say which of these views is correct, nor indeed to say that any one of them is. I only suggest them as possible, and I may add probable, explanations. The last view is the one I favour most.

One last point which may very properly be considered, is

* "Manual of Pathology," J. Coats, page 683.

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whether the convulsions so commonly met with in general paralysis are uræmic in origin? Out of 41 cases in which well-marked granular disease of the kidney was present only 41·5 per cent. had convulsions, whilst in the 9 cases in which renal disease was apparently absent 6 cases had convulsions, or 66·6 per cent. In some cases of course I am inclined to admit that the convulsions may be uræmic, but in the majority of cases I doubt it.

The main points I would then lay stress on are:—(1.) The frequency of contracted granular kidney in general paralysis. (2.) The similarity of the changes in the blood-vessels in both diseases, and the fact that they often cannot be distinguished one from the other. (3.) The two diseases are curiously inter-dependent, and in all probability have a common origin.

Dr. NICOLSON (Chairman) desired to make one or two remarks, which he hoped might be considered as offered rather in a suggestive than a critical spirit. Important as it was to sift the various conditions so closely interwoven in a complex question such as this, he wished to ask how far the differential features which had been indicated bore relation to the sex of the patients. Especially important was it that the nature of the poison which might influence the vessels in conditions of chronic renal disease and general paralysis should be elucidated. Dr. Bristowe had said that the kidneys in some cases of general paralysis were found free from advanced organic change, and his own experience (the Chairman's) was that there were a great many cases showing chronic renal disease not associated with general paralysis. As to how far it might be entertained that the same degenerative change produced either disease independently or the two conditions reacted one upon the other, it was impossible to hazard an opinion. He was glad to be able to speak in terms of the highest commendation of the work which Dr. Bristowe had produced, and he was sure the meeting would offer him their warmest thanks.

Dr. MERCIER said he joined very heartily in the note of praise sounded by the Chairman. The paper was thoroughly practical and founded upon definite observations, and it argued well for the success of the divisional meetings if this paper was a sample of those to be offered in the future. The observations contained in it were noteworthy. On the one hand there was an enormous number of cases of chronic renal disease occurring without any apparent association with general paralysis, and on the other hand they had a certain number of cases of general paralysis in which there was no evidence of renal disease, and in the third place, as Dr. Bristowe showed, a large proportion of cases of general paralysis in which renal disease was present. These facts seemed to indicate that, firstly, there was no necessary connection between renal disease and general paralysis, but, secondly, there was a connection of some kind between them, insomuch as the association of renal disease and general paralysis was exceedingly common, although the converse was certainly rare. It was at present premature to propose any theory with regard to a connection between the two conditions, because they were as yet ignorant of the initial pathological change. It might be that it was due to a poison circulating in the vessels, or to some initial vice in the constitution of the individual, and that it was merely a form in which the decay inevitable in advancing life showed itself. At any rate, the facts placed before them would serve as an excellent basis for numerous observations in the future, and the paper should be commended to the attention of the various scientific workers throughout the kingdom.

Dr. WEATHERLY wished to ask what was the percentage of persons who were alcoholics found in these cases of chronic renal disease and general paralysis. So

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far as he remembered, Dr. Bristowe had not mentioned whether he considered that alcoholism and general paralysis moved hand-in-hand to some extent, in view, too, of the fact that chronic renal disease was one of the principal outcomes of alcoholism.

Dr. STEWART had had experience of several cases of chronic alcoholism which had passed into general paralysis, and which had shown evidence of chronic renal disease. Although the number of his observations was not sufficiently large to draw any conclusion from, it was large enough to be striking.

Dr. BRISTOWE thanked the meeting for their cordial reception of his paper. He would answer as briefly as possible the queries put in connection with it. Firstly, as to the relation of sex. Out of 71 odd cases there were only four female general paralytics, and he could not say that there was anything especially notable about these. Secondly, with regard to a poison as a causal agent, such idea was suggestive only. The view given by Dr. Mercier that the degenerative change might only be a part of a general decadence of the body tissues was probably the correct one. In answer to Dr. Weatherly, he regretted that the statements on the part of patients or their friends in Somerset were so unworthy of acceptance as to make it unsafe for him to answer his question. He would much like to see statistics from other asylums dealing with the number of cases with chronic renal disease who died of general paralysis.

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*The Breaking Strain of the Ribs of the Insane.** An analysis of a series of fifty-eight cases tested with an instrument specially devised by Dr. C. H. Mercier.

By ALFRED W. CAMPBELL, M.D., Pathologist, County Asylum, Rainhill, Lancashire.

In the spring of 1893 we received from Dr. Mercier an instrument specially devised by that gentleman for the purpose of automatically registering the breaking strain of the human rib. It was accompanied by a letter, in which we were requested to experiment with the instrument on as many cases as possible and furnish him with the result. By that letter we were at the same time informed that he had sent similar instruments round to other asylums with a like supplication, and that he looked for the co-operation of a number of colleagues in enabling him to collect a number of cases sufficient to constitute a foundation for an accurate statistical record—a record which would, among other things, settle once and for all in which varieties of mental disorder it is that we are to look for ribs possessing a low breaking strain.

On account of the medico-legal importance of the question of the frangibility of the ribs of the insane, this scheme, needless to say, immediately received our hearty approval. A few preliminary trials proved, to our minds, the efficacy of the instrument, and I forthwith undertook the investigation, the results of which I propose communicating.

* Paper read at the Quarterly Meeting of the Medico-Psychological Association in London, on November 15th, 1894.

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