into the urethra are the only causes which may give rise to extravasation of urine in young patients, with the exception of rupture of the urethra by falls upon the perineum, and the subsequent obstinate form of stricture which ensues upon that accident. The treatment of such injuries and their consequences in no wise differs from that followed in the case of adults, but considering the firmness of the cicatricial tissue which forms at the site of these lesions, the rapidity of its contraction and the speed with which destructive changes in the kidneys supervene, and the fistulæ which form, it may sometimes be necessary to resort to some extreme measure in order to avert these after-consequences.

ABNORMALITIES OF THE PENIS.

On the many baneful effects which result from an elongated or contracted prepuce I have no space to dilate, and can only allude to their effects upon the urinary apparatus. Reference has already been made to cases of hydronephrosis, which are ascribed solely to this condition, and as a reflex effect may be mentioned nocturnal enuresis and daily incontinence, and all the symptoms of calculus, including even hæmaturia. The hypertrophy of the bladder which ensues from this cause has been pointed out by Sir James Paget. The eczematous state which so often exists at the end of the prepuce frequently starts as slight urethritis in the region of the meatus, by which urination is rendered painful and at the same time frequent, and which, if permanent, causes the meatus to contract, and renders its division by the scalpel a necessity. For these and very many other reasons connected with the effects of this condition in youth and in later life, I consider that the simple operation of complete circumcision should be performed at an early age wherever complete retraction cannot easily be performed, and whenever the prepuce considerably overlaps the glans.

The urethra of girls is not often the site of any surgical affection, but Mr. Davies-Colley has described a case in which the orifice of the ureter protruded through the meatus in a girl, aged 18 months. Mr. Croft has related a case of inversion of the bladder in a girl of 14 years, and Mr. Bryant has described a case of extreme prolapse of the female urethra occurring in a girl aged 6 years. The prolapse seems to occur as the result of straining in the later years of childhood. It does not cause much trouble in micturition, but the protrusion is tender and the mucous membrane often bleeds. All these conditions must be carefully diagnosed from urethral caruncle, which, common enough in women, is found occasionally to exist in children.

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THE INFLUENCE OF LOCALITY ON THE PREVALENCE OF MALIGNANT DISEASE.*

By EDWARD NOEL NASON, M.D. CANTAB.,
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THE subject matter of this paper is the result of an investigation which was begun about three years ago, and which was suggested to me by the apparently disproportionate frequency in the occurrence of malignant disease in some districts compared with others. In one locality cases of malignant disease occurred with alarming frequency, while in another locality in close proximity to the first but few were met with. Who could refrain from asking the question Why?

Before attempting to find an answer to this question I determined to make quite sure of the fact itself, and to eliminate as far as possible the elements of chance or coincidence.

It seemed to me that if the death-rate for malignant disease could be obtained for various registration areas which differed in certain particulars, a confirmation or the reverse of my impression could be arrived at. I therefore wrote to the Registrar-General, but the answer I received, though

promising some statistics, intimated that they would not be ready for some little time; and, moreover, I saw that they would embrace areas too large to be of any use for my purpose.

I then set to work to compile my own statistics for the districts in which I was chiefly interested. I have in consequence spent some considerable time in ascertaining and making a record of all deaths from malignant disease which have occurred in the registration districts of Nuneaton, Atherstone, Market Bosworth, and Ibstock during the years 1886 to 1896; and through the kindness of Dr. Nason, of Stratford-on-Avon, I have been able to obtain very similar statistics for the large registration area of Stratford-on-Avon.

A chart was prepared on which were marked the name, age, address, sex, and, where possible, the organ affected of nearly 500 cases in all. In doing this I have been able to divide the large registration areas into subdistricts and parishes, and thus with much greater exactitude to show that my impression was correct, for the large registration areas may contain two or more districts which, differing greatly both in physical characteristics and mortality from malignant disease, would counteract each other.

Taking the Market Bosworth Registration District first, I find this subdivided into Market Bosworth with a population of 6,100, and Ibstock with a population of 9,500. Each of these is again divided into a number of parishes most of which are too small to give separate statistics of any value on the result of a ten-years' survey.

Taking the two subdistricts, I find that 58 cases of malignant disease occurred in the Ibstock division while only 17 occurred in the Market Bosworth division, giving a percentage in the ten years of 0.61 in the former and 0.28 in the latter. This is a remarkable difference for two districts lying, so to speak, side by side, but it is even more remarkable that in Market Bosworth itself, with a population of 836 only, 1 death from malignant disease (carcinoma recti) was registered in the ten years, which would give a percentage of a little under 0.12.

The chief physical difference between these two subdistricts is that, as a whole, the Market Bosworth division has a much better fall, and stands on higher ground, Market Bosworth itself being 460 ft. above sea level, and having a steep slope to the west, south, and south-east. Ibstock, though 420 ft. above sea level, is still some 40 ft. below the surrounding country, and, moreover, has a small stream in close proximity, which Market Bosworth has not. The percentage of deaths from malignant disease for the whole district during the ten years is 0.48.

In the Atherstone District malignant disease is frequent, except in the large parish of Hartshill, where it is comparatively rare. The population of the whole of the Atherstone Registration District minus this parish is 13,316 with a percentage of deaths from malignant disease of 0.72 for the 10 years. The population of the parish of Hartshill is 1,485, with a percentage for the same period of 0.33. But, in reality, the difference is much more than this, when one comes to investigate the individual cases of death from malignant disease occurring in this parish. It happens that 3 of these cases had been patients of my own, and of these 2 were already suffering from carcinoma when they came from the Nuneaton district to reside, and, ultimately, to die in Hartshill, while the third, although registered in the parish of Hartshill, had lived in an outlying part of the parish close to the river Anker, where the physical characteristics were totally different from the rest of the parish.

Now, there is one most marked difference between this parish and almost all the others in the district. The parish of Hartshill, 460 feet above sea level, and 220 feet above the valley in which lie most of the other parishes, is on granite rock, and has a sharp fall in nearly all directions, and has no stream near it, except in the case of the outlying portion above mentioned. Atherstone itself, and nearly all the other parishes which go to make up the registration area, lie in the valley not far from the river Anker, which meanders through this district, is sluggish, is contaminated with sewage and liable to floods. In many of the smaller villages which lie along the banks of this stream the death-rate from malignant disease is very considerably above the average for the whole district, but the

* Read before the Birmingham and Midland Counties Branch of the British Medical Association.

population of these villages is individually too small to give data which are anything more than suggestive.

These points of difference led me in the case of the Nuneaton registration area to divide the district into two parts, in one of which were those parishes lying on low ground near the river, while in the other were those parishes lying on higher ground and at a greater distance from the river. Of the latter there were 4, of the former 5 parishes. The total population of the parishes lying near the river is 12,818, with 84 deaths from malignant disease, giving a percentage in the 10 years of 0.6. The total population of the parishes more or less removed from the river is 4,557, with 14 deaths from the same cause, giving a percentage of 0.3, or exactly half.

In the Stratford-on-Avon registration area, which comprises the subdistricts of Stratford, Wellesbourne, and Wootton Wawen with a total population of 21,893, no fewer than 178 deaths from malignant disease were recorded in the ten years 1886-96, giving a percentage of 0.81. Now almost every parish in these districts is in more or less close proximity to either the Avon, the Stour, or one of their immediate tributaries.

Dr. Nason, of Stratford-on-Avon, to whom the district is thoroughly known, has separated the parishes, over forty in number, into two divisions, placing in one, as far as possible, those parishes quite near the rivers Avon, Stour, or one of their tributaries, and in the other those parishes on somewhat higher ground and somewhat more remote from these streams. I then compared the mortality from malignant disease in the two cases, with the result that in the former case it was 0.9 per cent. in the ten years, while in the latter it was 0.6 per cent. These percentages, founded as they are upon a considerable number of cases, are most suggestive as showing that even in a district where all the parishes are situated in the vale of the Avon or one of its tributaries and none on very high ground, still the balance is 3 to 2 in favour of those which are higher and more remote from the streams.

All these statistics seem to point to one thing very clearly, namely, that the cases of malignant disease tend to group themselves chiefly about the low-lying land in the neighbourhood of the sluggish streams, or where there is little fall, and where the subsoil must in consequence be but indifferently drained. Furthermore, apart from statistics, I am convinced from direct observation made, especially in the Nuneaton district, that the closer to the stream the more frequent the occurrence of malignant disease. It may be that this connection only holds good where the stream is sluggish, contaminated by sewage and liable to flood, as is the case in all the districts I have specially investigated.¹

As further bearing out this connection, let me instance a large parish in the north of England from which I have been able to obtain some statistics. In this parish, the population of which is 4,000 and which covers a wide area, nearly all of which is on high, well-drained land with no sluggish streams, only 5 cases of malignant disease occurred in ten years. Now one corner of this parish slopes rapidly down to a river, and it is in this part of the parish, on the first rise above the river, that 3 of the 5 cases occurred, while the remaining 2 arose in a part of the parish which, though on absolutely high land, lay in what was relatively a hollow in which the ground was always marshy and undrained. The percentage mortality for this district is 0.125, as is also roughly that of a certain district in Derbyshire which chiefly consists of upland country; that is, the percentage for these chiefly upland districts is only one-seventh that for the Stratford-on-Avon district, and only one-fifth that for the Atherstone and Nuneaton districts.

Such a pronounced difference for different localities as these statistics show cannot be without meaning. So far I have confined my paper to recording observed facts, but what is the explanation of these facts? First, then, the facts point most strongly to some direct connection between residence in the neighbourhood of sluggish streams or ill-drained, sodden, contaminated soil and the prevalence of malignant disease. On what does this connection depend?

Leaving the solid ground of fact and venturing into the regions of conjecture, there are still a few steps further which we may take with safety, still some points which seem tolerably clear. We must admit some external agency as one of

the factors in the causation of malignant disease. Such external agency, whatever its nature, must be produced by, or have its habitat in, or at least be directly connected with, stagnant or nearly stagnant water or ill-drained soil. Persons residing in the near neighbourhood of such physical conditions would necessarily be more frequently brought under the influence of this external agency than those living at a greater distance. In this direction only, it seems to me, can we seek for an explanation of the marked increase in mortality from malignant disease in those districts where such conditions obtain. This external agency must act in one of two ways, either as the direct exciting cause or as an indirect predisposing cause. In the former case one must presuppose the existence of a micro-parasite as most probably the chief factor in the causation of malignant disease. This assumption explains certain peculiarities of malignant disease itself as well as of its distribution. In the latter case one must suppose that certain climatic conditions so influence the human body as to prepare the way for the development of malignant disease. This, however, would throw little light upon the disease itself, so that while not denying a possible predisposing influence of environment, I am inclined towards the former and more definite assumption.

If we assume that one of the factors in the causation of malignant disease is a micro-parasite, we must agree that such micro-parasite is most probably a protozoon, and may be comparable in some respects with the protozoon or protozoa associated with the various forms of malaria. If such an organism exists, it is not improbable that it may undergo changes both within and apart from its host, and through the medium of discharges gain access to streams or ill-drained soil. Here it may find suitable media for its development and multiplication. Under such circumstances, it would not be unreasonable to conclude that, as in the case of the organisms connected with malaria, exhalations from water or sodden soil thus impregnated might be the means of conveying the infection; this would also explain the undoubted existence of "cancer houses." The perfectly healthy human body may no doubt be quite proof against any amount of such organisms; but, given favourable conditions such as chronic tissue irritation, traumatism, degeneration of tissues from disease or senile changes, or the presence of "fœtal remnants" as suggested by Virchow, added to which may possibly be in some cases individual or inherited proclivity, and a lodgment of the micro-parasite might follow.

That the development of micro-parasites in animal tissues may produce proliferation of cell elements is unquestionable, as, for instance, in the case of psorospermiosis affecting the liver in rabbits, and also in the case of Paget's disease in the human subject. Whether such proliferation be due to the organism directly or to the chemical products of its growth and development is of secondary importance.

I am quite aware that the assumption of the connection between a protozoon and malignant disease lacks much direct evidence, but many competent and careful observers have described appearances found in microscopical preparations of both carcinomata and sarcomata consistent with this view. Another fact, which a study of the cases I have collected brings out, indirectly supports this assumption. When the organ or region in which the disease has developed is noted, it appears that in those districts on higher and better drained land where malignant disease is less common, a larger proportion of the cases which do occur have some more or less obvious predisposing cause, and, I am inclined to think, run a more chronic course. Here such cases as surface epitheliomata following definite irritation, carcinomata of breast, uterus or rectum are found in greater proportion. In close proximity to the streams, on the contrary, malignant disease of some of the less commonly affected organs or portions of the intestinal tract is found with unexpected frequency, and, I fancy, runs a more rapid course. This would suggest that in the neighbourhood of the streams, where the infective agent would presumably be in greater abundance, malignant disease attacks organs which would escape under more favourable circumstances.

Since writing this paper a paper has been published by Dr. Léon Noël in the *Revue des Maladies Cancéreuses* bearing upon this subject. The conclusions he arrives at confirm my own in a most striking way. He says: "Cancer regions exist

close to regions enjoying an immunity. These latter are generally in dry localities and some distance from streams. In these cancer regions one of two conditions prevail—either they are closely populated, or if the houses be spread about at some distance from each other a rivulet or stream connects them."

Having alluded to the disputed question of "heredity," I cannot close my paper without recording one series of cases, the occurrence of which can hardly be explained without that factor. In one family of two generations numbering 16 individuals reaching adult years 10 have died; of these 10, 3 have died of carcinoma of uterus, 2 of carcinoma of the stomach, and 1 of carcinoma of the liver, while of the 6 yet living 1 has a large tumour of the neck, and 1 a tumour of the arm, which has recurred after removal.

The facts which this investigation has brought out, and which may readily be confirmed by anyone who will take the trouble to tabulate all the cases of malignant disease occurring in his own neighbourhood, seem to me to be of considerable importance. The explanation I have suggested may not be the correct one, but of the facts there can be no doubt.

NOTE.

¹ From inquiries recently made it seems probable that malignant disease in cattle is influenced by locality in a precisely similar way and is much more frequently met with in those pastures which are low lying or bordering on sluggish streams than it is in the upland pastures. It is also more common among shorthorns than among other breeds.

ON THE STRUCTURE OF THE NEUROGLIA.

By JAMES R. WHITWELL, M.B.,

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Of late years a considerable amount of attention has been directed towards the neuroglia and sustentacular apparatus of the nervous system, more particularly since the introduction of Golgi's epoch-making method, and still later the surprising results achieved by Weigert in his more recent work on this subject. It is unnecessary to enter in any way into an historical survey of the various transition stages which have resulted in our present state of knowledge; it will be sufficient to indicate the two opposing camps into which neurologists and histologists have divided themselves on the subject.

1. The neuroglia is composed entirely of greatly ramified cells (glia cells), the branches of which pass everywhere in the interstices of the proper nervous elements.¹ Various kinds of these cells have been described,² and some writers consider that the glia cells form the distal portion of the lymphatic system (Meynert,³ Lewis⁴). Other functions have been attributed to them.

2. The neuroglia consists of a series of unbranching fibrils in the meshes of which certain cells lie, but not in organic continuity with the fibres, the so-called branching glia cells being an optical effect, the product of unsuitable methods (Weigert).⁵

It is undoubtedly true that the great bulk of authors believe the former theory to be true, and the examination year after year of preparations made by the Bevan Lewis or Golgi methods makes it difficult at once to believe that one could have been deluded by appearance to the extent that Weigert would have us believe, in spite of the fact that Ranvier's specimens prepared by maceration in dilute alcohol offer suggestions in the same direction.

On the one hand, then, neuroglia cells with processes can be clearly shown by more than one entirely distinct method, and, on the other, a method has been devised which resolves the previously obtained picture into component parts; it is, therefore, essential that some other method or methods must arise to add their weight to one or other side before any definite conclusion can be arrived at.

I would venture the suggestion that perhaps our conception of the neuroglia and sustentacular apparatus generally is somewhat narrowed owing to the difficulty of obtaining a comprehensive survey of it as a coherent system having an individuality of its own, and this is doubtless largely due to the methods commonly employed in demonstrating it, and I would here propose a method which is exceedingly simple

and yet gives a clear, though at first sight somewhat bewildering, view of its arrangement as a whole, a view which, like Weigert's nerve-fibre stain and his new neuroglia stain, displays one whole system to the necessary exclusion, or rather optical detraction, of the others. If any properly hardened (chrome, alcohol, picric formol) section of the central nervous system be placed on a slide and allowed to dry in the air, the more delicate nerve cells and their processes become optically obliterated in favour of the less hydrated and more highly refractile connective elements; these, however, form such a highly complicated and dense mass that comprehension of their arrangement is impossible, and it is necessary, in order to evolve the picture, previously to apply some reagent that will produce slight expansion of the section equally and in all directions. Many chemical bodies will do this with more or less success, such as glacial acetic acid, lactic acid, and rodinal, but probably the best for all purposes is hot concentrated caustic potash. The section then is dropped into a relatively large quantity of hot caustic potash, and allowed to remain for a few seconds only, when it is caught up on a slide and transferred to warm water to wash for a few seconds, and again taken up on a slide and desiccated in the air, the most correct picture being probably obtained from sections where on the slide the sectional area most nearly corresponds to that of the piece of brain from which it was removed, previous to its original treatment with the hardening agent. When sufficiently dry a cover glass may or may not be put on, the edges only, however, should be merely sealed with Canada balsam.

Fig. 1.— $\times 800$. Section of upper portion of cortex (asc. parietal), showing arrangement of fibrils of neuroglia. (These fibrils should all appear of the same diameter or nearly so).

On microscopic examination of this preparation with ordinary magnification but careful illumination, a more or less dense felted network of fibres is revealed, which may be seen to form a series of nests for the nerve cells, blood vessels, etc., and these can be readily seen *in situ* during the desiccation process. If this section be stained with any cell-staining reagent and mounted in Canada balsam, then the cell elements become visible, but the connective elements, being embedded in a substance so nearly their own refractive index, disappear.

The view presented by sections prepared this way is very striking, and shows clearly the vast sponge-like arrangement produced by a felted mass of neuroglia fibres, in the interstices of which the nervous and other elements lie. The arrangement of these fibres is at first difficult to follow on