the material was ejected from the inoculation wound, so that the dose which it received must have been smaller than that which was injected in the first instance. On March 24th Rabbit No. 1 died. There was great sanguineous cedema at the site of inoculation involving several glands. There was some congestion of the larger bowel. The liver was enlarged, congested, and showed a number of small white points which were irregularly scattered here and there over it. These points were irregular in size, never exceeding a millimetre in diameter, many being smaller. The spleen was enlarged and discoloured, portions being reddish and parts, especially towards one end, greenish in colour. Several enlarged and hyperæmic glands were discovered. The lungs showed inflammation in patches and a small amount of fluid was found in the pericardium. Pure cultures of the bacilli were obtained from the spleen and liver. On the 25th Rabbit No. 2 died. The post-mortem examination revealed similar conditions as in Rabbit No. 1. The spleen showed a similar discolouration, while the white points in the liver were much more numerous. Cultures of the plague bacilli were also obtained from the spleen and blood in this case.

On March 26th Guinea pig No. 4 (control experiment) died. A great tumour was found at the site of the inoculation of a hæmorrhagic character involving several glands. The glands of the opposite side were also enlarged. A sanguineous effusion surrounded the site of inoculation and extended over the abdomen. The lungs were affected with broncho-pneumonia and there were numerous areas of actual necrosis. Some fluid was found in the pericardium, but small in amount. The liver was enlarged, congested, and had some small white points studded over it. These ranged in size from a pin-point to that of a pin-head. The spleen was enlarged and absolutely studded over its surface and throughout its substance with white points. On March 20th two rabbits (Nos. 3 and 4) and one guinea-pig (No. 7) were each inoculated with 10 drops of a 24 hours' old bouillon culture of the rat bacterium which had been passed through a guinea-pig. On March 25th the guinea-pig died. The lesions in this case were very well marked and of the characters seen in the former cases of guinea-pigs inoculated with this microbe. The spleen was enormously enlarged. The lungs were slightly inflamed in patches. On March 26th Rabbit No. 3 died from causes which could not be ascertained. The post-mortem examination was kindly made by Dr. W. Ramsay Smith, the President of the Central Board of Health of South Australia, and Mr. J. Desmond, the Government veterinary surgeon of the same State. I was very pleased to have the assistance of these gentlemen, since they have had in Australia a rather extended experience in regard to the pathology and bacteriology of plague. The site of inoculation was occupied by a dry abscess the pus of which was tough and tenacious. All the organs were healthy except the liver, which was affected by animal parasites. Microscopic examination failed to detect any bacteria at all and tubes of agar which were inoculated from the liver, spleen, and blood remained sterile.

On March 28th I killed the remaining rabbit. Here, as in the former case, the site of inoculation was occupied by an abscess the pus of which was equally tough and tenacious. The lungs were affected by numerous hydatids; otherwise every organ in the body was quite healthy.

On March 26th two pigeons were each inoculated with five drops of a 12 hours' old bouillon culture of the rat microbe. Unfortunately while the inoculation was being made in the second pigeon the needle pierced the skin at the farther point and thus almost the whole of the fluid passed out among the feathers and but a small dose could have been left under the skin. The point selected for inoculation was the front of the chest between the delicate skin and the pectoral muscles. On March 31st Pigeon No. 1 died. At the post-mortem examination a tumour was found between the thin integument and the muscular tissue below, and had also infiltrated the muscular substance itself. The heart was absolutely empty in the ventricles and only a trace of blood was found in the right auricle. The liver was very deeply congested. No other abnormality was detected. Examination of the blood and of the juice of the liver showed innumerable bacteria which, in the case of the liver, showed extremely well-marked bi-polar staining. Pigeon No. 2 died on the afternoon of April 1st. The post-mortem examination revealed almost identical lesions. Cultures made on agar from the blood and liver juice in both these cases gave plentiful and absolutely pure cultures of the rat microbe.

Since, therefore, we have in the rat a disease which is

communicable to guinea-pigs but not to rabbits, and to which rabbits are also refractory even after it has been passed through the guinea-pig; and since, moreover, inoculation of the rabbit with this rat bacterium in its virulent form gives no protection against a subsequent inoculation with bubonic plague, it seems clearly proved that this rat plague cannot be bubonic plague. The peculiar susceptibility of pigeons to the rat disease also indicates the difference between that malady and bubonic plague. In future steps will have to be taken in case of rats being affected with a disease simulating plague to inoculate other animals than guinea-pigs. My experiments show that the rabbit is probably the best animal to use in conjunction with guinea-pigs.

ALCOHOL AND ARSENIC IN THE ETIOLOGY OF ALCOHOLIC NEURITIS.

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THE recent epidemic of arsenical neuritis amongst the beer-drinkers of the northern and midland counties has led to the discussion of several interesting points in relation to peripheral neuritis in general and that form which is the result of alcoholism in particular. The word "alcoholism" is used advisedly, for we find that medical authorities are by no means agreed as to what particular constituent of alcoholic beverages is responsible for the lesions in the peripheral nerves of their consumers.

Among the most notable opinions that have recently been put forward and emphasised by eminent medical men are (1) that ethyl alcohol *per se* cannot produce neuritis; and (2) that "alcoholic neuritis" only occurs in beer-drinkers and not in pure spirit-drinkers. It has, moreover, been widely suggested (3) that alcoholic neuritis is really a misnomer and that the causal factor in those cases to which we have been accustomed to apply the name may yet be found in arsenic acting in inconsiderable doses. The first of these three theories—the one which denies to ethyl alcohol a selective pathological action on the peripheral neurons—is difficult to prove or to disprove. The second and third theories may reasonably be expected to stand or fall under the test of clinical experience and such other tests as experimental investigation may suggest.

With a view to elucidating the facts which clinical observation in a large number of cases can disclose the author of this paper has conducted a careful investigation of the notes on 120 of the most recent cases of "alcoholic" neuritis which are to be found in the case-books at the National Hospital for the Paralysed and Epileptic, Queen-square, London. The above number includes only those cases in which there seems to be no reasonable doubt that immoderate drinking was, at any rate, a possible etiological factor and does not include those in which some other toxic agent had been shown to be present, either alone or in conjunction with alcoholism. The cases occurred during the last 12 years and in that time about 20 other cases of multiple neuritis were treated in the hospital in which alcoholism was a possible but not a reliable cause. If we take all the cases of multiple neuritis for the period they can be classified thus to show their relative numerical strength.

Cases.		Cases.	
Alcohol	120	Post-influenzal	3
Alcohol (doubtful)	20	Lead	21
Alcohol and marked tuber- culosis	7	Malaria	3
Alcohol and septicæmia	2	Arsenic	2
Septicæmia alone	4	Post-typhoid	1
Post-diphtheritic	34	Diabetic	5
		Unknown cause	5

In the study of these notes especial attention has been paid to the following points: (1) age; (2) sex; (3) habits in reference to alcohol; (4) changes of a nutritional, vaso-motor, or pigmentary nature in the skin, hairs, or nails; and (5) the result of treatment with arsenical drugs.

1 and 2. *Age and sex of the patients.*—These two points may be briefly dismissed. Among 120 patients there were

96 females and 24 males. The average age of the males was 42·8 years. The average age of the females was 38·5 years.

3. *Habits of the patients in reference to alcohol.*—In regard to this matter the notes are, on the whole, satisfactorily complete, and in quite a large proportion evidence as to both the quality and the quantity of drink taken has been obtained either from the sufferers themselves or from friends and relatives. It cannot be said that the story told by the former always tallied with the “friendly” version, but, taking the large number of cases in question, considerable value attaches to the statements thus obtained. I have classified the results of this inquiry into habits under as few headings as is possible, with a due regard to accuracy, in the following manner :—

	Cases.
Spirits only (quantities from half a pint to two bottles a day) ...	29
Spirits predominant (other forms admitted in moderation) ...	11
Spirits only, and in moderation ...	1
Spirits and wine in excess ...	3
Beer only and in excess ...	1
Beer predominant ...	1
Beer only and in moderation ...	3
Beer and wine in excess ...	1
Beer and spirits in excess ...	30
Beer, spirits, and wine in large quantities ...	3
Wine (port and sherry) in excess and only ...	1
Stout in moderation admitted ...	1
Stout and spirits ...	4
No mention of habits ...	11
Alcoholic excess without specification of form ...	20
Total ...	120

In the first class, that which contains the consumers of large quantities of spirits only, there are a considerable number in which, from the evidence of friends and patients alike, there can be no doubt that brandy, whisky, or gin was the sole stimulant consumed. Others base their claims to be included in this class on the evidence either of their friends or of their own admissions. It has been urged by some physicians that if the question and inquiry are only pushed far enough beer will always be found to be associated even with large quantities of spirits in the daily diet of these patients. It is scarcely credible, however, that a man or a woman who will unblushingly admit to consuming two bottles of brandy a day should display any bashful coyness in reference to an extra gallon or so of ale. On the other hand, out of 89 cases in which habits are noted there is but one in which there can be no reasonable doubt that beer alone, and beer in large quantities, was the only form of alcoholic liquor taken. As one would expect in the class from which hospital patients are drawn, it is among the mixed beer- and spirit-drinkers that the most numerous victims of this disease, are to be found and quite a large proportion of those who come under this head are connected with the liquor trade either as barmaids, publicans, or the wives of publicans. The figures given above undoubtedly point to the conclusion that in London, where there is a large beer-drinking community, it is among the consumers of pure spirits, either alone or in conjunction with beer, that the clinical picture of alcoholic neuritis is most frequently found.

4. *Changes of a nutritional, vaso-motor, or pigmentary nature in the skin, hair, or nails.*—In 57 of the 120 cases no special reference was made to the condition of the skin or of its appendages, and these are therefore valueless for the present purpose. In 23 cases it is specially noted that no skin changes were to be found. In 40 cases vaso-motor, trophic, or pigmentary abnormalities are described and their nature presents an interesting and useful study when brought into comparison with those changes which are known to be a consequence of arsenical poisoning. Under the head of trophic disturbance it is to be remarked that the skin on the hands and feet is generally described as (a) thin and glossy or shiny, or (b) soft, soapy, or boiled in appearance. Along with the thin shiny skin which is particularly observed on the digits is found striation, brittleness, or a reeded condition of the nails. Profuse perspiration, limited to the extremities, generally accompanies, and probably accounts for, the soft, soapy condition of the skin, which has been likened to that found in washerwomen’s hands. The colour of the skin on the hands and feet is usually described as white, but in some cases there have been purple or red patches, generally over joints in which adhesions are present or, in one case, over the palmar surface of the phalanges. In reference to pigmentation one case, that of a mixed beer- and spirit drinker, is found in which the skin is described as pigmented in the groins and over the abdomen. In another there were some pigmented scars on the shins,

but with these exceptions pigmentation is conspicuous by its absence. Vaso-motor changes, apart from perspiration, are not frequently noted, but in a few cases a congested appearance of the lower extremities, with or without oedema of the ankles, appears to be a feature.

In considering the above observations the fact is at once evident that the whole of the conditions mentioned with two exceptions (one of trunk pigmentation and one of keratosis of the plantar surfaces) are those which can be, and frequently are, met with not only in all forms of peripheral neuritis but also in other diseases in which the lower neurons are affected, such as progressive muscular atrophy, amyotrophic lateral sclerosis, and the like. These secondary skin changes are, indeed, the outward and visible signs of a disturbed nutrition due to an abeyance or alteration of the trophic function of the peripheral neurons and are quite distinct from the primary cutaneous changes in arsenical poisoning where the toxin at work exercises a specific influence on the cutis and cutaneous appendages. It is true that in the latter class of cases one may, and does, find the signs of secondary cutaneous atrophy present in addition, since arsenic shares with other toxic substances the power of producing pathological changes in the nerves themselves.

Two other notable features of my series of cases deserve a word or two in this relation. There is no mention of a single case of herpes or of erythromelalgia in the 120 cases. The absence of these two nervous phenomena is of particular importance because neither would be likely to escape observation in the hospital under consideration, where both have gained a large amount of attention. Yet it is said that amongst arsenical beer-drinkers both these physical signs are by no means uncommon. The non-occurrence of herpes, at any rate, cannot be explained on the ground that the dose of arsenic is insufficient, for I have on several occasions noted a crop of herpes following on small doses of Fowler’s solution administered over a very short space of time, and the causal or predisposing relation of that metal to herpes has received general acceptance and confirmation since Mr. Jonathan Hutchinson first brought it forward. In this connexion it is interesting to note that out of a very limited number of cases of diabetic neuritis which have come under my observation I have on two occasions met with herpes zoster. Arsenical and diabetic neuritis resemble each other, moreover, in the severe character of the sensory phenomena; in both diseases spontaneous and continuous pain, apart from muscular tenderness in the affected limbs, is a much more marked feature than is commonly the case in alcoholic neuritis.

The term “erythromelalgia” properly refers to a symptom-complex in which pain, local heat, and flushing, all aggravated or initiated by a dependent position of the affected part, are pathognomonic, and is distinct from the phenomenon of ordinary vaso-motor palsy, to which, unfortunately, the name has been sometimes loosely applied. As far as I can ascertain no true instance of this condition has been observed in a case of alcoholic neuritis, or indeed of any other form of multiple neuritis, at Queen’s-square.

5. *The result of treatment with arsenical drugs.*—More than one physician at the hospital has from time to time treated his cases of alcoholic neuritis with doses of Fowler’s solution, and the course of the disease in these patients whilst under the influence of this drug cannot be without interest in view of the part which arsenic may or may not play in the production of this morbid condition. Twenty-four cases were treated with arsenical solution in doses of two, three, or four minims given three times a day. In 17 of these the amount taken was nine minims and in four others 12 minims per diem. The period over which the drug was exhibited varied from one week to eight months and in the majority of cases it was from three to five months. The results obtained in the whole series of 120 cases may be thus compared with those obtained in the 24 where arsenious anhydride was administered :—

	Cured.	Greatly improved.	Improved.	In statu quo.	Deceased.
Arsenious anhydride 0·06 } to 0·12 gr. daily ...	3	12	9	0	0
No arsenical drug given ...	31	33	36	7	13

I would not for a moment contend that the favourable results obtained in the first part of the table were due to the administration of this drug; on the contrary, it must be allowed that Fowler's solution would, in all probability, only be used when the patients had passed the most acute stage in the disease. At the same time it is a striking fact that none of those cases were unfavourably influenced by the exhibition of arsenic and that at least two-thirds of them left the hospital either cured or well on the road to recovery.

It will probably be admitted by most physicians that the essential condition for recovery from this form of peripheral neuritis is only attained when all access to alcoholic stimulants is prevented. If arsenic be the toxic constituent of those stimulants one would not expect the cases, when the alcohol is withheld and the toxin administered in another medium, to run an invariably favourable course. This, however, has certainly been the case in my series and as far as clinical facts permit any conclusion to be drawn they must weigh heavily in the balance against the arsenical theory in the etiology of this disease.

Whether arsenic or alcohol is the cause of this disease there is no doubt that only a very small percentage of persons who, on account of their habits, are exposed to the risk of peripheral neuritis ever show any symptoms of the condition. Probably the incidence of the morbid process can be best accounted for by a special individual susceptibility to the poison, and, if it be assumed that arsenic is the poison at work, all cases of "alcoholic" neuritis should occur in persons susceptible to that mineral. On this assumption one would expect even the small doses administered for therapeutic purposes to be sufficient to prevent or, at any rate, to retard, the recovery of sufferers from this particular form of neuritis. That this expectation is not borne out by clinical experience leads to the conclusion that arsenic is not the chief etiological factor in alcoholic neuritis.

Another point of clinical interest is the absence of any necessary association between arsenical pigmentation and arsenical neuritis, and in the National Hospital for the Paralysed and Epileptic is afforded the opportunity of seeing a considerable number of patients who have been taking arsenic medicinally over long periods of time. Many of these present more or less pigmentation, but only two cases of peripheral neuritis, undoubtedly due to arsenic, have been observed in 12 years. Only a few days ago I stripped a patient who had been taking arsenical solution, to the amount of nine minims a day, fairly regularly for seven years in conjunction with bromide of potassium. The whole of the neck, the trunk, and the proximal parts of the limbs were covered with a typical arsenical pigmentation of a mottled sepia colour. No signs of cutaneous trophic changes or of peripheral neuritis were present. Still more recently I examined a man who had been taking six minims of the same drug daily for nine months. Eight months after he had ceased to take any arsenic he presented a similar condition of pigmentation in a less decided shade. Such cases represent the results of drug accumulation in persons whose nervous systems are not especially susceptible to the toxic properties of this metal. It would be interesting to know whether such cases of pigmentation are to be met with amongst heavy beer-drinkers in London who have not fallen victims to peripheral neuritis.

In recounting the results of my investigations I have purposely avoided reference to any of the clinical phenomena of alcoholic neuritis which do not help to elucidate the particular questions at issue.

One or two points may, however, have some indirect interest in this connexion. The absence of wasting and the presence of a peculiar hard condition of the calf muscles, accompanied by tenderness on pressure, has been a noted feature in one or two cases. This has been so only in mild forms of the disease and when the motor difficulty has been one rather of unsteady gait than of great paresis. Paralysis of the diaphragm has been of frequent occurrence in the fatal cases, but is not unknown in those which have recovered. Difficulty in swallowing has been recorded in a few instances. The loss of memory for time and place has been very general and, in the more severe cases, is a condition from which there is very little hope of recovery even when the activity of the limbs is restored. The presence of ocular nystagmoid movements on extreme lateral deviation and amenorrhoea are not infrequent features and are well known to most observers.

A summary of the evidence which I have obtained leads

me to think that, in London at any rate, (1) alcoholic neuritis is more often found in the sequel of spirit-drinking than in other forms of alcoholism; and (2) that clinical evidence is antagonistic to the idea that arsenic is the cause of alcoholic neuritis.

It has frequently been argued that spirits cannot produce neuritis because the latter disease is uncommon in Scotland, but, as far as I am aware, no modern statistics on this point have been made. I am strongly of the opinion that a numerical comparison of cases of alcoholic neuritis with the total population in Edinburgh, Glasgow, and London would throw an important light on this line of argument.

In conclusion, I have to thank the members of the medical staff at the National Hospital for the Paralysed and Epileptic for their kind permission to make use of their case-books for the purpose of this investigation.

Harley-street, W.

AN EXPLANATION OF THE VULNERABILITY OF THE APICES IN TUBERCULOSIS OF THE LUNGS.

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AND

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It has been generally admitted since the time of Laennec and Louis that the apices constitute the most vulnerable portions of the lungs when these organs become the seat of tuberculosis. Statistics collected from divers sources bearing on this subject vary somewhat, but they show that from 60 to 80 per cent. of the cases of pulmonary tuberculosis commence in the apices of the lungs, the initial lesion being rather more common on the right than on the left side, in the proportion of slightly less than three to two. Now, while there is a practical unanimity of opinion as regards the primary site of the disease in pulmonary tuberculosis, there is no sort of agreement among observers with respect to the cause of the peculiar vulnerability of the apices. Indeed, it may almost be said that our knowledge of the exact conditions which determine the special proclivity of the apices to tuberculosis is inversely proportional to the number of theories that have been advanced to elucidate them. Nevertheless, it is by no means improbable that some of the attempts which have been made to solve the problem contain at least the germs of the true explanation of the cause of the phenomenon under consideration, and for this reason, if for no other, it becomes necessary to enumerate and to briefly review the more important theories that have been advanced.

The view that has probably met with the widest acceptance attributes the apical site of the lesion to the comparative rigidity and fixity of the upper portion of the chest, whereby the movements of the contained lung are considerably curtailed. It has, moreover, been pointed out that sedentary occupations and certain forms of manual labour, notably digging, ploughing, &c., by tending to force the shoulders forward, would still further hamper the movements of the upper portion of the chest and hence of the lung. The vulnerability of the apices is attributed under these conditions to diminished functional activity and consequently lessened power of resistance to the tubercle bacillus, which may therefore be able to effect a lodgment in this portion of the lung. While it cannot be seriously disputed that the range of movement of the upper portion of the chest is less than that of the lower parts of this structure, it is by no means proved that *relatively* the expansion and mobility of the contained lung are not as great in the former as in the latter situation. Indeed, it is probable, as Woods Hutchinson has pointed out, that the activity of the upper portions of the lungs has been underestimated. In any event it cannot be admitted that the theory under examination satisfactorily accounts for the peculiar constancy of the site of the apical lesion which is found from an inch to one and a half inches below the summit of the lung.

A modification of the theory which has just been considered suggests a mechanical explanation of the vulnerability of the apices. Thus in consequence of the imperfect