

ARSENICAL POISONING  
IN  
BEER DRINKERS

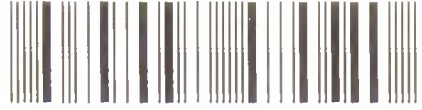
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*KELYNACK—KIRKBY*

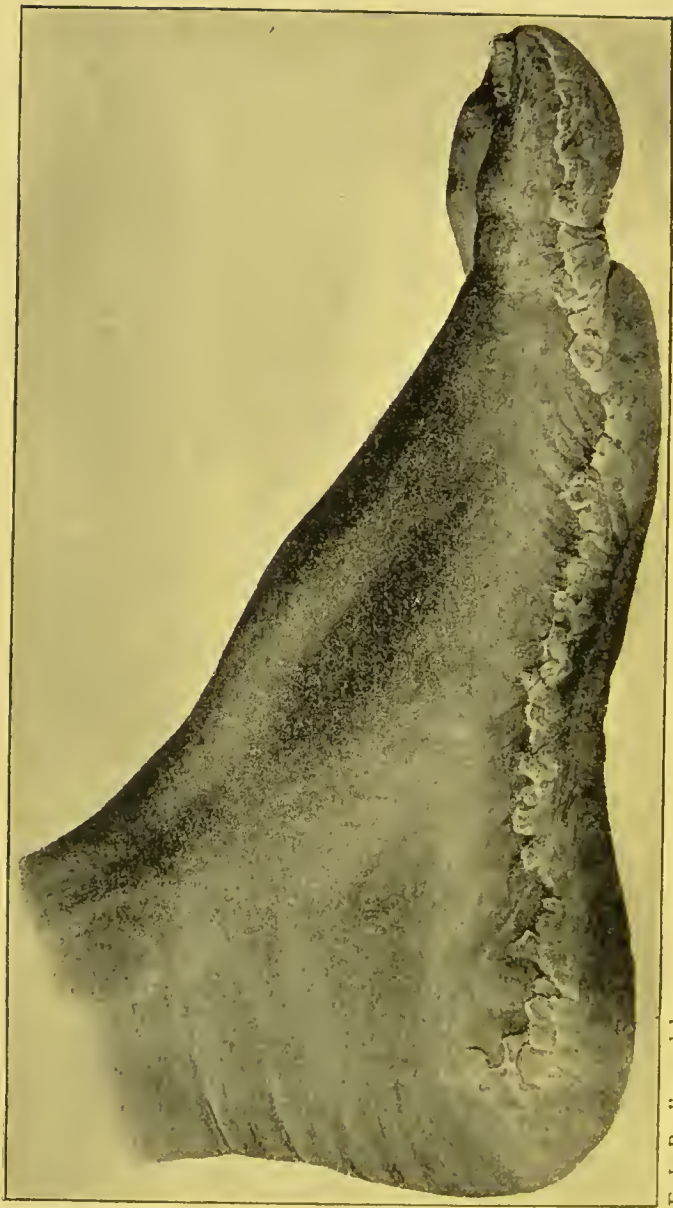
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E. L. Bradbury, del

KERATOSIS AND ERYTHEMA, WITH PIGMENTATION.

# ARSENICAL POISONING IN BEER DRINKERS

BY

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WITH SIXTEEN ILLUSTRATIONS



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## P R E F A C E

WE have been pressed to publish our notes on the recent epidemic of arsenical poisoning in Manchester and district. In order to assist in removing the difficulties which surround the question in its scientific aspects, we have put into book form what we consider are the more important results of our investigations. The urgency of the matter has precluded our making the research as complete as we could have desired.

Our best thanks are due to Dr. Julius Dreschfeld, Senior Physician to the Manchester Royal Infirmary; to Dr. Robert Forsyth, who, as medical officer to one of the largest firms of brewers implicated in the brewing of the arsenical beer, has rendered us invaluable service; and to the other gentlemen whose names appear in the body of the book.

We are much indebted to Miss Bradbury and Mr. W. S. Kelynack for their work in the production of the illustrations; to Mr. L. Roy for assistance in the chemical portion of the investigation, and to Messrs. Jewsbury and Brown, in whose laboratories the chemical portion of the work has been carried out.

Without the ready help of several firms of brewers it would have been impossible to have procured the many varied and

interesting samples which have enabled us to make a fairly comprehensive survey of the contaminated materials.

The Bibliography by no means exhausts the published records dealing with the toxicology of arsenic; it has been selected with a view to illustrate, as far as possible, the distinctive features of the present epidemic of chronic arsenical poisoning and the methods in use for the detection of minute traces of arsenic.

T. N. K.

W. K.

*December 20, 1900.*

# ARSENICAL POISONING IN BEER DRINKERS

## PART I

### INTRODUCTORY

PERIPHERAL neuritis in alcoholic subjects has long been recognised as a well-defined clinical entity, and, especially through the writings and teaching of Dr. Dreschfeld,\* the late Dr. Ross,† Dr. Bury‡ and others, has been a condition particularly well known to the medical profession in Manchester and district.

Multiple peripheral neuritis is unfortunately a very common affection in Lancashire amongst alcoholics, and for at least twenty years has been a prolific cause of paralysis. The subjects affected are almost invariably beer drinkers. Some observers go so far as to claim that peripheral neuritis never develops simply in spirit drinkers. Many cases, however, have certainly occurred in imbibers of 'mixed drinks.'

Recently the number of cases of so-called 'alcoholic paralysis' has increased to such an extent that during the latter part of 1900 epidemic proportions were reached.

This at first was not unnaturally thought to arise from

\* Dreschfeld, Julius : 'On Alcoholic Paralysis,' *Brain*, 1884-85, vii. 200 ; 'Further Observations on Alcoholic Paralysis,' *Brain*, 1885-86, 433.

† Ross, James : 'Alcoholic Paralysis,' *Medical Chronicle*, 1889-90, xi. 353 ; also 'A Treatise on Peripheral Neuritis,' by James Ross and Judson Bury, 1893, 121. Bibliography.

‡ Bury, Judson : 'Multiple Symmetrical Peripheral Neuritis,' 'Allbutt's System of Medicine,' 1899, vi. 675. Recent Bibliography.

increased drinking, but it soon became apparent that many of the patients presented unfamiliar features. Large numbers of cases came under observation at the various Medical Charities, and many were met with in private practice in working-class districts.

Suspicion soon fell on the beer, the principal drink of the majority of the affected persons. The people themselves and some of the brewers early admitted that something was 'wrong' with the beer. In some districts the sufferers labelled their malady with the name of the brewery from whence came their disease-producing drink. In Salford the presence of conspicuous pigmentation of the skin led to the popular designation of the affection as 'khaki disease.' A man recently returned from Canada spoke of his condition as 'foot and mouth disease.'

Thus some considerable time before the exact nature of the irritant became apparent many members of the profession and a large number of the persons affected realised that 'the beer was to blame.'

In the investigation of the present outbreak we have been enabled to avail ourselves of exceptional opportunities for the study of almost every variety of case occurring amongst the very poor people seeking medical assistance at the Pendleton Branch of the Salford Royal Hospital; and through the kindness of members of the medical staff of the Manchester Royal Infirmary, cases have been investigated in that institution. Further, through the courtesy of medical officers of health, superintendents of hospitals, and numerous private practitioners, it has been possible to examine not only a very large number of cases in Manchester and Salford, but many also in Liverpool, Blackburn, Heywood, Bacup, and elsewhere.

Suspicion being aroused that the poisoning arose from arsenic in the beer, we sought the co-operation of Dr. Robert Forsyth, medical officer to one of the largest firms of brewers in the district. Dr. Harold Bailey also rendered us the greatest assistance in procuring samples of beer such as was being consumed by the affected patients.



To Dr. Reynolds,\* however, is due the credit of first directing attention to arsenic as the probable cause of the epidemic.

As the result of our investigations† we had the satisfaction of localising the source of the introduction of the arsenic into the beer within a few hours of the announcement of the nature of the poison to the public, and we did our utmost to see that immediate steps were taken to insure as far as possible the arrest of the poisoning.

Although much further work will be necessary before the whole of the pathological, chemical, and hygienic features of the 'outbreak' are made clear, we venture to think that no essential link in our research has been omitted, as our investigation has been designed and conducted throughout on scientific lines.

1. Arsenic in quantities sufficient to account for the symptoms complained of was separated from the beer which was actually being consumed by the affected cases;

2. Arsenic was found in the secretions of the patients presenting symptoms of arsenical poisoning;

3. Arsenic was isolated from the beer received direct from the breweries supplying the local retailers;

4. Arsenic was found in varieties of glucose and invert sugar used in the brewing of the very beer in which the arsenic had been detected, and such as was being taken by the affected persons; and

5. Finally, arsenic was detected in the tissues of affected cases.

### Extent and Duration of the Poisoning.

Since the precise nature of the poisoning amongst beer drinkers in Manchester and Salford has been ascertained, evidence has accumulated to show that the extent of the

\* 'An Epidemic of Peripheral Neuritis amongst the Beer Drinkers in Manchester and District,' *British Medical Journal*, 1900, November 24, 1492.

† *Medical Press and Circular*, 1900, November 28, 555.

malady has been very widespread, cases being reported from many parts of the country.\*

Dr. Niven, the Medical Officer of Health for Manchester, in his official report† expresses the view that at least 2,000 cases have come under medical observation in his district. He also adds, 'There will, no doubt, be a good many more with minor degrees of illness which have not been seen by a medical man.'

Dr. Tattersall, Medical Officer of Health for Salford, also shows‡ that in that borough returns indicated an increase in the deaths from 'peripheral neuritis,' 'multiple neuritis,' and 'alcoholic neuritis,' commencing in the third week in July, and amounting in nineteen weeks to 41. 'In addition, during the same period, there were 25 deaths certified to be due to "alcoholism," or a total of 66 in the past four months, as compared with 22 in the first seven months of the year, 39 in 1899, 31 in 1898, and 27 in 1897.'

Many persons in towns in the immediate neighbourhood of Manchester have also been severely affected. Thus at Heywood Dr. Hitchon, the Medical Officer of Health, considers that '200 or 300 people have suffered.'

Dr. Nathan Raw, Medical Superintendent of the Mill Road Infirmary, Liverpool, gives valuable returns,§ showing that as regards the large union hospital under his care, containing 800 beds and with between 4,000 and 5,000 admissions annually, 'in the year 1898, 26 cases of alcoholic neuritis were admitted, and that the greatest number in any month was 4. In the year 1900, up to December 8, no less than 143 cases were admitted, and practically a case a day was admitted during the last four months.'

\* It has been stated that cases have occurred at Accrington, Alderley-Edge, Ashton-under-Lyne, Ashton-in-Makerfield, Bacup, Birkenhead, Birmingham, Blackburn, Bolton, Bromley, Burnley, Chester, Crewe, Darlaston, Darwen, Denton, Haslingden, Heywood, Huddersfield, Ilkley, Leamington, Leeds, Liverpool, London, Macclesfield, Market-Drayton, Oldham, Ormskirk, Penrith, Skipton, St. Helens, Stourbridge, Warrington, Wednesbury, Worksop, and a number of country places.

† *Lancet*, 1900, December 15, 1752.

‡ *British Medical Journal*, 1900, December 1, 1587.

§ *Medical Press and Circular*, 1900, December 12, 612.

Like returns which could be given from other centres all clearly indicate that arsenical poisoning has been not only extensive, but in many centres extremely serious.

The rural districts have also contributed their share of cases. One of the worst paralytic cases we have met with is now bed-fast in a village.

Careful inquiry in different centres goes to show that many cases date their first symptoms as far back as Easter, 1900. We have also good reason to believe that 'arsenicated beer' has been in circulation in some districts for over a year, and it seems very probable that it may ultimately be shown to have been in use, although possibly containing much less arsenic, for even a very much longer period. Most of the cases, however, in Manchester and Salford first came under medical observation during the last few months of 1900. One of the earliest cases of Addisonian-like pigmentation, which we have had the opportunity of investigating, dated the illness from about Whitsuntide, 1900.

The experience of Dr. Raw at Liverpool seems to show that in that city also 'the contamination first occurred probably about last June.'

Regarding Heywood, the Medical Officer of Health states\* that 'a case or two was seen before Whitsuntide, but the disease occurred in an epidemic form immediately after the Whitsuntide holidays, and fresh cases have continued to be seen until the last fortnight.'

### Social Position, Sex and Age of the Sufferers.

The majority of the cases have occurred amongst persons of the working class. Many have been extremely poor, hence the striking fact that large numbers of sufferers have been met with in workhouse hospitals and attending out-patient departments.

The lower classes in Salford have suffered greatly, and not a few deaths have occurred. On the other hand, some districts of Manchester, as far as we can ascertain, have been

\* *Medical Press and Circular*, 1900, December 5, 583.

hardly affected. But while the poor and destitute classes have been most involved, and cases seeking gratuitous medical assistance have undoubtedly generally been 'alcoholic,' it is necessary to very definitely point out that in private practice many cases have been met with in strictly moderate drinkers. We have also investigated several cases presenting unmistakable evidences of chronic arsenical poisoning where there was every reason to believe that no more than from one to two pints of beer or stout a day had been taken.

The patients have been of both sexes. The proportion has varied somewhat in different localities. In our out-patient department at Pendleton large numbers of both men and women have been examined.

In places like Heywood men seem to have suffered in greater number than women. The medical officer says: 'Out of 60 or 70 cases, 11 only have been women.'

In one family in a country place, where the wife stayed at home and the husband was away at work in a neighbouring town all day, the woman was rendered helpless by almost complete paralysis of both upper and lower extremities, while the man only presented slight symptoms. Both persons were 'strictly moderate' in the use of the bottled beer, which was bought in quantities from one brewery only. The beer was found to contain  $\frac{1.6}{100}$  gr. of arsenious acid per gallon. A bottle obtained direct from the brewery gave 1.4 gr. per gallon, and a sample of glucose from the same source 0.05 per cent. (5 parts in 10,000).

Persons of all ages have been affected. The greater number of the patients have been middle-aged, but we have examined cases at both extremes of life. Children have not altogether escaped, and even infants at the breast have presented undoubted evidences of arsenical poisoning. These cases will be referred to later.

#### Kind of Alcoholic Beverage taken.

The cases presenting indications of arsenical poisoning have almost invariably been beer drinkers. Some few,

however, have confined themselves to stout. Many 'took anything they could get.' In not a few cases enormous quantities have been drunk, but, on the other hand, some persons have been seen where there was every reason to believe the amount taken was very limited. One young woman presented very characteristic symptoms after partaking of only a pint of stout daily, a quantity she had been accustomed to for years. Examination of the stout, which was always obtained from one and the same public-house, showed it to contain  $\frac{4}{100}$  gr. per gallon.

We have been unable to meet with any evidence of arsenical poisoning in any persons limiting themselves to the use of brandy or whisky. It is a remarkable fact that even in confirmed drinkers in this district who have restricted themselves, according to their own account, to spirit, peripheral neuritis is so rare that we are not prepared to substantiate a single case met with during recent years.

## PART II

### CLINICAL

#### Complaint of the Patient.

GENERALLY speaking, there has been a great similarity in the statements of the patients regarding the troubles for which they sought medical aid. Usually they came complaining of pain and weakness in the extremities, particularly the feet. The morbid sensations were described as 'pins and needles,' 'numbness,' 'pricking,' 'burning,' 'scalding,' 'lurching,' 'springing,' and 'like walking on hot bricks.' Some were chiefly anxious about their difficulty in walking. More advanced cases were described by their friends as 'paralysed,' and in severe cases they were often found absolutely bed-fast. A few laid great stress on 'numbness,' 'aching,' and 'pins and needles' in the finger-tips, and that they were frequently 'dropping things.' Some sought advice because the skin of their hands was getting thick, and thus interfering with their work. Many said that their hands and feet were both 'getting thick,' while the skin 'kept peeling' or was 'crumbling off.' In some cases the pains were general, and it was not uncommon for patients to declare that they had 'rheumatism all over.' A considerable number sought advice at the Skin Hospital on account of 'rashes' and 'eruptions,' with oftentimes irritation and troublesome itching. Generally the poorer patients have not been particularly observant of the pigmentation. In some persons, however, usually women, the increasing darkening of the skin was the chief feature to attract atten-

tion. Not a few were much troubled with 'smarting and itching' of the eyes, sufficient in some instances to cause them to attend the Eye Hospital. A common complaint was 'cold in the head,' 'running of the eyes and nose,' or even 'influenza.' Some said that the tears 'scalded the cheeks.' Many had become 'husky,' and a few were so hoarse as to make speaking difficult. Cough and irritation of the throat caused trouble to some. A few patients came complaining of nausea, vomiting, and diarrhoea, but usually the history or even presence of these symptoms was only elicited on inquiry.

### General Characters.

Many of these cases can be recognised at a glance.

In a well-marked case the aspect is most characteristic. The patient presents a dull, 'heavy' appearance. The face is congested and dusky, often mottled and blotchy, and with sometimes distinct cyanosis. The eyes are suffused, watering, and often with tears visibly overflowing. This may be so marked that the sufferers are constantly mopping the running eyes. When the eyelids have been rubbed with dirty fingers there may be evidences of slight suppuration. A puffiness about the eyes is often noticeable, but the œdema may be more extensive.

The gait and posture is often unmistakable. Walking is painful and difficult, and the patients progress slowly in a gingerly and halting manner. There is often distinct reeling, and an ataxic gait is sometimes well marked.

When standing, the patient shuffles from one foot to another, and seeks support by leaning against anything convenient. He is usually anxious to sit down as soon as possible, and when given the opportunity, 'flops' into the chair. In bad cases there may be considerable difficulty in rising again. The hands are often held in an unaccustomed position, and it is very common to find the patient quite unconsciously rubbing the fingers with the palmar surface of the distal portion of the thumb. This rolling movement is not altogether unlike that seen in paralysis agitans. It

evidently arises from the various paræsthesiæ experienced more particularly in the tips of the fingers.

In an affected district comparatively mild cases can readily be recognised as they stand at the doors of their houses with dusky faces and tearful eyes, or as they shuffle about their homes and loiter at street-corners. Many of the cases present a distinctly 'alcoholic' aspect, but this is by no means always so.

When detailing their troubles it is often apparent that there is much mental sluggishness.

Frequently there is general wasting, and many patients complain greatly of the 'loss of flesh.'

In many bad cases the temperature is raised, and is oftentimes of an irregular type.

### Manifestations in Connection with the Cutaneous System.

Lesions of the skin are met with, if carefully looked for, to a greater or less extent in almost every case. They differ much, however, in form and distribution.

#### (1) Pigmentation.

Pigmentation, when present, constitutes one of the most conspicuous and characteristic features. It varies greatly both in intensity and extent, sometimes being so slight as to be readily overlooked; while in others it may be so deep and so general as to give the patient the appearance of a mulatto. Generally it is most marked in exposed parts, over pressure areas, and in normally pigmented regions, thus agreeing closely with the distribution in Addison's disease. The tint varies from a faint brown, as from exposure to the sun, to a dull black. It often resembles a 'vagabond's pigmentation,' and has in many instances been mistaken for dirt. One nurse remarked that her patient on admission to hospital was washed three times without visible improvement. Many of the female cases have been much disconcerted at their growing duskiness.





E. L. Bradbury, del.

FIG. I.—PIGMENTATION OF SKIN OVER BREAST, SLIGHT DESQUAMATION ABOUT NIPPLE AND AREOLA.



The face is often but slightly involved, but in not a few is distinctly pigmented, and when associated, as is often the case, with a certain amount of congestion, gives the patient a gipsy-like appearance. Sometimes distinct patches of pigment may be seen about the eyelids. The neck, especially over the back and sides, is often very dark, and the axillæ, loins, nipples and areolæ, and abdominal walls are frequently of a deep-brown colour (Figs. 1, 10, 11). The pigmentation is usually most intense about the nipples, around the umbilicus, over the genitals, in the perineum, and at the anus. In many men, even when pigmentation is but little marked elsewhere, the nipples and areolæ may be almost black. This has even attracted the attention of some of our dullest patients. In some instances the dark skin over and around the nipple has assumed an almost 'ichthyotic' appearance. About the ischial tuberosities patches of pigmentation may occur, also over other pressure areas, as, for instance, the shoulders, buttocks, and prominent vertebral spines, and in such areas pigmentation may be found when the skin is but little affected elsewhere. Scars and old cicatrices are usually non-pigmented, but the lineæ albicantes may show a distinct brownish discoloration, as in a case seen through the kindness of Dr. Orchard at the Withington Hospital (Fig. 2). Many cases very closely resemble Addison's disease, both in their general appearance and in the distribution of the pigmentation, and in not a few cases the patients have, indeed, been so regarded. In some hospitals deaths have occurred and been certified as resulting from Addison's disease, and on post-mortem examination have been found to present no characteristic lesions. The best-marked cases of pigmentation usually occur in women, and especially those of naturally dark complexion. Most of the Addison-like cases seem to have suffered less severely from prolonged neuritic symptoms, and certainly generally recover more quickly than many of the non-pigmented cases; but in some, at least, where the pigmentation has been intense, well-marked 'erythromelalgia' has occurred. One of the best-marked cases of this Addisonian type occurred in a married woman, aged

thirty-five, seen on November 12 in consultation with Dr. J. W. Crawshaw. His careful description so well indicates the condition of the patient that we here quote it somewhat fully:

M. H. B., a woman aged thirty-nine years, had a holiday in the Isle of Man from June 1 to June 9, 1900. For some time before she went away she had noticed a troublesome watery discharge from the eyes and nose. In the third week of June, after she returned home, she became aware of a brown discoloration on the left side of the neck and the adjacent part of the top of the left shoulder. The point of the right elbow also was discoloured. Pigmentation occurred next on the anterior and external aspects of the knees, just above the patellæ. In a few weeks the discoloration had appeared practically over the whole body. She does not remember any redness, but says that at first the right elbow, which was one of the regions first noticed to be pigmented, was painful and tender. She has also noticed that the skin has peeled off the forearms and hands, and the soles of the feet.

About the middle of August she first felt tenderness and pain in the soles of the feet. At first this was noticed on rising in the morning, and on getting warm in bed at night, at which time there was much burning and tingling. The pain was also described as like 'pins and needles.' These symptoms gradually increased in severity, and walking became very painful. The toes became stiff, and the legs very soon tired on walking. She also noticed a general and gradually-increasing feeling of weakness on exertion.

Coincident with the onset of pain in the feet she began to have 'pins and needles' in both hands, and she noticed the peeling of the skin. At this time, also, gastric symptoms began to be developed. The most prominent of these was vomiting, at first only in the morning, but in a week or two it occurred during the day as well, but she did not suffer any pain. She says that a drink of beer was vomited in a few minutes, and seemed also to produce an attack of diarrhœa. For some weeks the bowels were very loose.

Chest and throat symptoms also appeared. There was very marked hoarseness of voice, and a persistent troublesome cough, unaccompanied by any expectoration. All this time since the onset of the illness there had been marked running from the eyes and nose, and the general weakness slowly increased. She became unable to get out of bed in the last week of October.

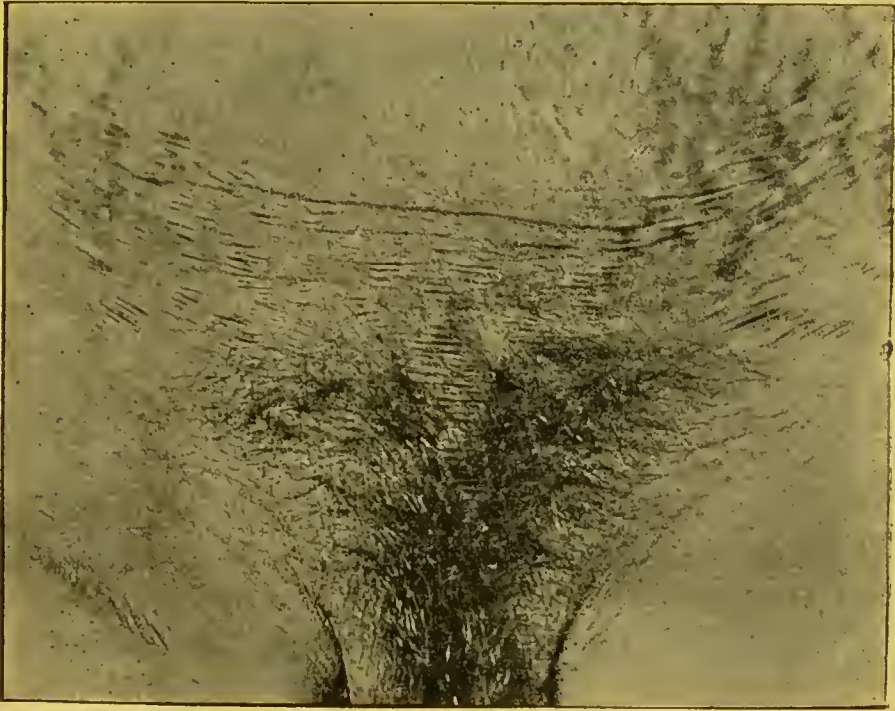


FIG. 2.—PIGMENTATION OVER ABDOMEN, ESPECIALLY MARKED  
ALONG LINEÆ ALBICANTES.



She has been in the habit of drinking at least four gills of beer a day: one in the morning, one at dinner, and one at supper; one was generally taken early in the evening. One or two days a week more would be taken, but on very few occasions was more than eight gills taken in a day. This amount has been taken regularly for a year or two before the onset of the illness, and during the course of the illness also. The amount taken has been most carefully inquired into, and, as the patient fully understands the importance of the inquiry, her answers may be relied upon.

The amount of ordinary food taken during the illness has been but little, the appetite for solid food having been very poor. No other single article of diet likely to be the cause of the illness has been taken. The beer was always of a 'sixpenny' kind, and obtained regularly from the same firm. She never drank any stout or spirits. She had no medical treatment previous to my attendance on her, and has taken no medicine containing arsenic.

#### PRESENT STATE.

The face appears flushed and dusky. The eyes are congested and watery, and a slight watery discharge is seen exuding from the nostrils.

*Pigmentation.*—The most noticeable feature is a brown pigmentation of the skin, which is present over the whole body, with the exception of the soles of the feet, palmar surfaces of the hands, and a small extent of the legs for 3 inches or so above the ankles. It is intensely marked round the neck, gradually fading off towards the chest and back and the shoulders; also over both knees, on the upper and outer aspects; in the axillæ, around the nipples and umbilicus, and the skin about the genitals. There is a distinct band round the waist, where her clothing would press, and also round the upper part of the legs, where the garters were tied. One or two prominent vertebral spines in the lower dorsal region are also extremely pigmented. The backs of the hands and forearms are also deeply coloured, but not quite so much as the other regions mentioned. In all these situations, which it will be noticed are exposed either to the influence of the weather or to pressure or friction, the colour is a deep brown. Over the rest of the body, with the exception of the palms, soles, and ankles, the coloration is very noticeable, but is much paler in tint. The tint of the deeper-coloured regions gradually fades into that of the lighter-coloured parts everywhere, except, as will be described later, in the hands and feet. On close inspection the

pigment is seen to be unevenly deposited in most of the regions. This is perhaps most noticeable on the backs of the hands and forearms, and also on the front of the chest. The ground-work of the skin is deeply pigmented, but small areas, varying in size from  $\frac{1}{16}$  to  $\frac{1}{8}$  inch, are considerably lighter in tint than the adjacent portion of skin, and some of them seem to be quite free from pigment. The appearance presented conveys the idea that the pigment, having first been deposited evenly, had been washed out by small drops of water. In the neck the hair-follicles are much lighter in colour than the rest of the skin. No pigmentation can be seen in the mucous membrane of the mouth.

*Desquamation and Thickening of Skin.*—Over the greater portion of the skin, but particularly the back, a branny desquamation is noticeable. The skin of the palms of the hands and soles of the feet is rough and thickened, and is seen to be peeling, especially in the furrows of the palms and fingers. The skin over the joints of the fingers on the dorsal surface is markedly thickened, particularly over the joint between the first and second phalanges of the left index and middle fingers, where pressure would occur on supporting the body in such a position as is assumed while scrubbing the floor. On the dorsum of the feet the pigmentation is well marked, though not so evenly distributed as over the rest of the body. The pigment stops abruptly at a line running round the foot at a level of about  $1\frac{1}{2}$  inches from the ground at the heel, and approaching nearer to the ground towards the toes. Just above this line the pigment seems to be heaped up, and is more intense in tint than the colour of the dorsum, towards which it rapidly pales. Below this line the skin of the soles and sides of the foot is dusky bluish-red (cyanosed). This is most marked at the sides of the foot, where the skin is thinnish, and the abrupt change from pigmented skin to cyanosed skin is extremely noticeable. On pressure, which is very painful, the area becomes pale, and slowly assumes its former colour on removal of pressure. There is a marked increase in the perspiration of the soles and sides of the feet below the line of pigmentation. In the upper extremities the pigmentation also stops abruptly just above the thenar and hypothenar eminences, and at the borders of the hands, but the heaping up of pigments is not present here in the way that is noticed in the feet. The nails of the hands seem hardened and brittle, but otherwise normal. The toenails are somewhat thickened, and those of the smaller toes show a tendency to separate from their matrices. The surface of the nails is smooth. No erythematous or papular eruption is noticed on any part of the body. There has been no complaint of any itching.



*Nervous System.*—No complaint of spasm or cramp of the muscles of the legs or elsewhere is made. There was much tremor of the hands when first she went to bed, but that has passed off to a great extent. There is no paralysis of any muscle, but the muscular power seems diminished in the legs. The soles of the feet are markedly hyperæsthetic. There does not seem to be any anæsthesia of the legs or hands. The muscles of the calves are extremely tender on pressure. The superficial reflexes are present. The knee-jerks are present, but very feeble. There is no alteration in the mental condition, which is perfectly clear.

*Circulatory System.*—The heart is not enlarged, but the sounds are weak, particularly the first sounds at the apex. The pulse is soft and regular.

*Digestive System.*—The tongue is coated with white fur. Much complaint is made of thirst. The appetite is very poor. There is no abdominal pain or discomfort. For several weeks vomiting has been very frequent, most of the food taken being rejected. The bowels have been very loose during the same time. Since she has been confined to bed, and beer has not been taken, both the vomiting and diarrhœa have ceased, and light milk food digested without any difficulty.

*Respiratory System.*—A troublesome cough is present, without expectoration. The voice was very hoarse, but is now quite clear, having improved along with the vomiting and diarrhœa. There is little evidence of bronchitis.

The beer taken by this patient, on examination, was found to contain  $\frac{2}{100}$  grain of arsenic per gallon.

Four samples of urine have been tested, and in each of them arsenic was found. The first was a small specimen, but the remaining three (28 ounces, 48 ounces, and 58 ounces) represented the whole of the twenty-four hours' urine. An interval of three days elapsed between the passage of the last specimens.

The description of the above case very clearly indicates the curious arrangement of the pigmentation which has been noticeable in a large number of instances. The small rounded areas of lighter coloured or non-pigmented skin scattered all over the dark background gives a mottled, or rather spotted, appearance, which, when present, is most characteristic of

chronic arsenical poisoning. These little circular patches are not met with merely around hair follicles, as has been stated, but may occur plentifully in almost any part of the body, and even in regions where hair follicles are but few, or altogether absent (Fig. 1).

It is interesting to note that so far we have met with no case showing distinct pigmentation of the mucous membranes.

The palms of the hands and soles of the feet are also usually free from discoloration.

## (2) Erythematous Lesions.

Erythema has occurred in a large number of the cases. This varies greatly in extent and intensity. Generally it has been most marked in the hands and feet. When affecting the latter it has usually been associated with much pain, and a condition of 'erythromelalgia' has resulted, which will be referred to later. The erythema of the feet has usually been of a purplish-pink colour. Frequently the feet are hot, but in some cases they present a distinctly cyanosed aspect, and are cold. Many patients have complained bitterly of their feet and toes being like ice, and feeling frozen. The erythematous patches in the feet are often bathed in a foul-smelling sweat. Hyperidrosis may also be very conspicuous about the hands.

The generally marked bilateral symmetry of the erythematous areas would seem clearly to indicate dependence on nervous involvement. In the case of an infant affected through the milk of its mother, who was suffering from acute arsenical neuritis, the soles of the feet were abnormally red, and in the case of a child a little over two years of age there was well-marked erythema about the hands and the toes and soles of the feet, as well as in the region of the elbows and knees. In slighter cases the erythema of the hands is most commonly limited to the distal part of the fingers.

Extensive areas of erythema may surround the knee and

elbow-joints, being sometimes best marked on the extensor surfaces. In the case of an old man the erythema involved the region of the left elbow, and was evidently of an inflammatory character, for there was an œdematous-like infiltration of the subcutaneous tissues.

As already indicated, the face may be distinctly erythematous; but in working people exposed to wind and weather, and purpled by alcoholic indulgence, it is often difficult, or even impossible, to apportion the influence of the arsenic in its production.

In severe cases more or less general erythema of the body may occur. Some of these cases have been mistaken for scarlet fever, and the similarity is heightened by the subsequent occurrence of extensive desquamation.

### (3) Papular Eruptions.

Cutaneous lesions of a papular type have also been common. Usually these have been most marked on the extremities, but sometimes more or less general over the whole body. They have at first often been separate or discrete, but in many they have coalesced to form distinct patches. Frequently the papules remain small, but sometimes they have been as large as an ordinary pin's head.

Patients have occasionally presented eruptions not unlike some of the papular syphilides.

In some instances the 'rash' has somewhat resembled that of measles.

The papular eruptions have often been associated with much itching and discomfort. By scratching they may readily be converted into minute 'sores,' which, when produced in areas where the cuticle is appreciably thickened, heal badly.

### (4) Vesicular Formations.

Vesicles have been noticed in not a few cases. In some patients the discharge from the same has caused distinct

stiffening of the linen (*eczema arsenicale*). The dried serous exudation can sometimes be seen forming 'crusts.'

**Herpes** has been met with in a considerable number of cases. Several practitioners state that they have recently met with numerous examples. In some of these cases of 'epidemic herpes' no other very distinct indication of arsenical poisoning has been noted. Dr. Robert Forsyth tells us that in his practice he has recently met with a number of cases of herpes, six in the course of the intercostal nerves, and one each involving superficial cervical, lateral nasal, ilio-inguinal, and last dorsal nerves. 'Although all these patients were beer drinkers, yet the other sensory troubles were developed to only a very slight extent.'

**Urticaria**.—Small areas of circumscribed œdema have exceptionally been seen, and some patients have presented a condition of skin practically identical with 'nettle rash.'

#### (5) Bullous Lesions.

Large blebs have been met with in a few instances, but are by no means common. Blisters may also occur in the keratosed areas, especially when the patients have continued to do much walking.

#### (6) Pustules and Boils.

Suppurative lesions have also not infrequently been seen. Possibly some of these may have resulted from self-inoculation occurring during the scratching dependent on the itching, which has greatly troubled many persons.

Boils have been met with, more particularly in the axillæ and about the genitals and buttocks. In some of these cases there was a mild degree of pyrexia.

#### (7) Desquamation.

Exfoliation of skin has occurred in a very large number of cases. In many this has been of a branny or furfuraceous

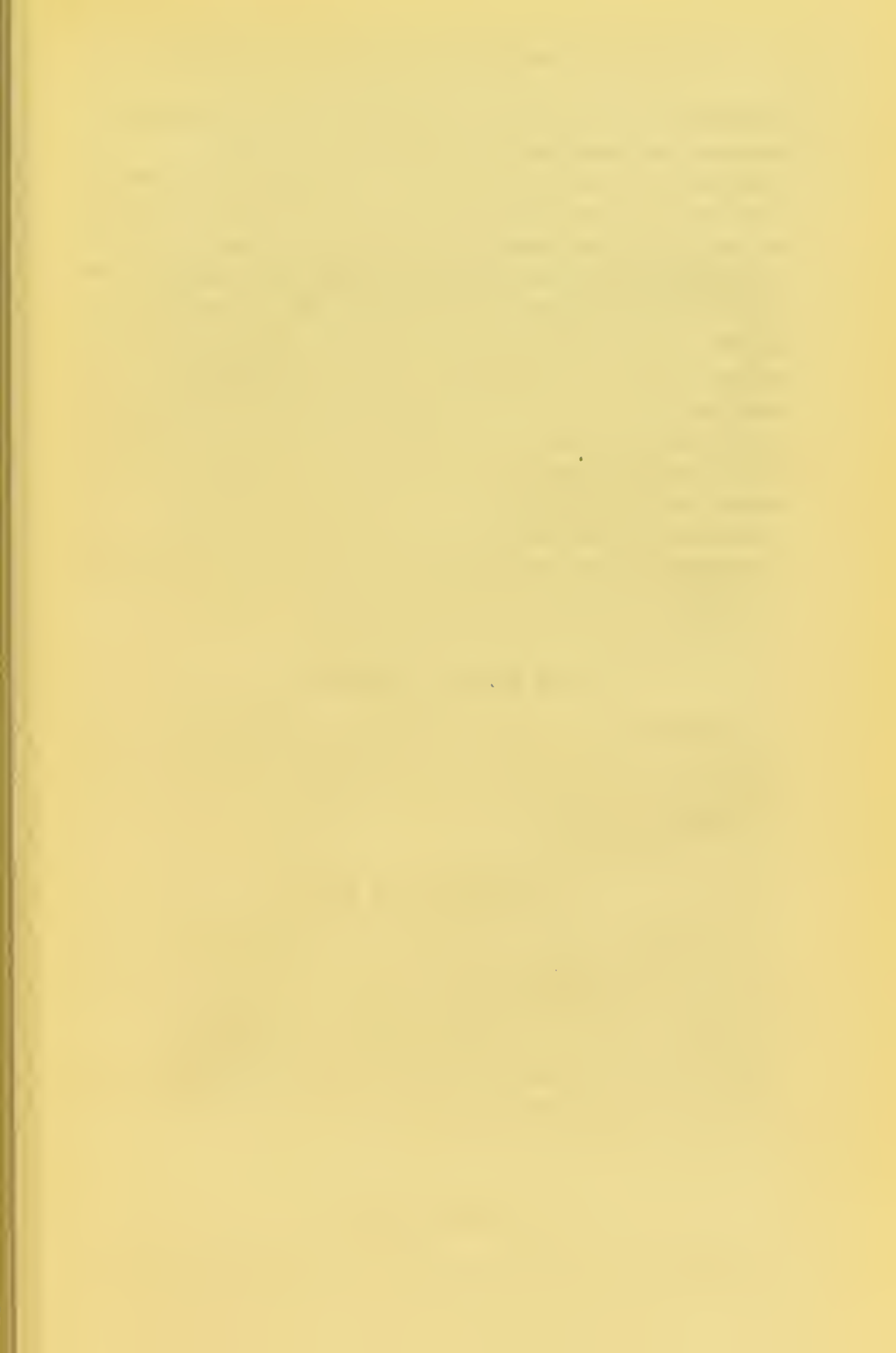




FIG. 3.—'DROPPING' OF FEET, SLIGHT ATROPHY OF MUSCLES, THICKENED AND SEPARATING CUTICLE, AND PIGMENTATION.

character, while in others the cuticle has separated in large flakes. One woman complained of the 'crumbling away' of dirty skin from the sides of her chest. The same patient also stated that her hands were so hard and cracked that she found it impossible to keep them clean. Some cases shed the skin almost like examples of pityriasis. From one case under the care of Dr. Dreschfeld 2.6 grammes of shed cuticle were readily collected for chemical examination, and found to contain a considerable quantity of arsenic. One nurse stated that the only way of getting rid of the scales was to take the bed-sheet out and well shake it. In some regions, especially over the lower parts of the abdomen, the pigmented cuticle has come away in large flakes, leaving a fairly normally pigmented skin beneath. In some instances, where no general evidence of desquamation is apparent, slight separation of the cuticle in thin scales may be noticed at the junction of the areola with the ordinary skin of the breast (Fig. 1).

### (8) Thickening of Skin.

Keratosiis, or thickening of the cuticle, has been a conspicuous feature in a very large number of cases. This has been especially marked about the hands and feet, although not altogether limited to them (Frontispiece). Some have sought medical advice because the hands were getting so thick that they could not well close them, and their work was thereby much interfered with. The cuticular thickening is generally most marked over the heels and about the balls of the toes (Fig. 3). The hands are also frequently affected, especially over the thenar and hypothenar eminences and around the knuckles. In some cases the thickening may involve practically the whole of the hands and feet. Some working men have noticed that the thickened skin readily cracked, and the 'sores' thus produced were usually slow in healing. In some few cases more or less general thickening of the skin has occurred. Not a few persons have by soaking their feet in water, or by the application of local preparations, endeavoured to soften the skin, and many speak of the way

in which they have from time to time detached large portions of the thickened cuticle. Sometimes it has been remarked that the skin has 'come off' several times.

As already indicated, in some of these cases, when walking is persisted in, distinct blisters form in the keratosed areas.

### (9) Hyperidrosis.

Excessive sweating has been well marked in a large number of cases. Usually this increase in the activity of the sweat glands has been limited to the hands and feet, and generally has been most conspicuous in the latter. Even when the erythema was not excessive or diminishing in amount, the feet were frequently found bathed in a somewhat foul-smelling secretion, and often when the extremities were cold clammy perspiration covered them.

Many of the patients complained greatly of the number of times they had been compelled to change their socks, which quickly became 'soaked through.'

### (10) Rarer Lesions of the Skin.

**Psoriasis-like** conditions have occasionally been met with. We have seen cases in which white, dry, powdery scales have been formed about the extremities, and usually on the extensor surfaces; but they have sometimes been present on the face and scalp.

**Necrosis** of the skin has occurred in bad cases. The Sister of a large ward in a public hospital stated that many of the cases were giving the nursing staff much trouble by the readiness with which bedsores formed.

### (11) Alteration in the Nails.

Changes in the nails have been frequent; they become hard, thick, and brittle. In a considerable number they have been cast off. Many patients have themselves remarked that the nails have grown with unaccustomed rapidity, and the







FIG. 4.—TRANSVERSE RIDGING OF NAILS.

cutting of them was more difficult than usual. In one case transverse ridging on every finger-nail indicated the distinction between old and new nails (Fig. 4).

### (12) Changes in the Hair.

The hair in many cases, particularly in females, has become detached in considerable quantities. Some few thought the hair had grown more rapidly than usual before or during the illness. The hairy scalp often presents an erythematous aspect, and a more or less general scaly dermatitis of this region has even been met with.

### Erythromelalgia.

At this point, midway between a consideration of the cutaneous and nervous manifestations, reference may be made to the curious condition which is perhaps best described as 'erythromelalgia.'

This affection is characterised by two main features: erythema and pain. It has been very well marked in a very large number of the cases, and has caused much distress.

The erythema has varied much in intensity. In some it has been slight and easily overlooked, while in others it has been rather that of an acute dermatitis with, in some instances, a certain amount of œdema. The colour has varied from a bright red to a purple. Most usually it has been of a purplish-red.

The distribution is very characteristic. It is almost always more or less symmetrical. It involves the soles and borders of the feet most markedly. In some the hands present a somewhat similar condition. The erythematous border, often slightly undulating and frequently clearly defined along the edges of the feet, has generally been readily recognised in this class of case. The dorsum of the foot is usually not involved (Frontispiece).

As already indicated, the erythematous areas have often been found covered with sweat, and frequently have felt cold

both to the patient and to the examiner. In the acute stages they have generally been described as 'hot and burning.'

The pain in many instances has been severe: movement of any kind has always aggravated it, the erect position has usually increased it, and walking in severe cases has been rendered impossible.

In many instances patients have not been able even to bear the weight of the bed-clothes on the affected feet. In the case of a child a little over two years of age, where we found distinct erythema of the feet, the first thing to attract attention to the condition was the fact that the little sufferer was always wanting to take her shoes and socks off.

Almost every degree of erythromelalgia has been met with. In almost all cases pressure has increased the pain, and in acute cases even merely touching the foot caused the patient to exclaim. Sometimes exposure to cold has brought temporary benefit.

### Nervous System.

The poisonous effects of the arsenic have been in nearly all cases most apparent in connection with the nervous system. Most of these have manifestly been of 'peripheral' origin, but some patients have shown symptoms which cannot but be regarded as 'central.'

#### SENSORY DISTURBANCES.

These constitute in the majority of cases the earliest and most marked of the nervous derangements. It would seem as though arsenic—at least, in its preliminary influence—attacked the sensory fibres more readily than the motor. All varieties of sensory disorder may occur.

**Hyperæsthesia of the Skin** is a very marked feature, particularly in many cases of the 'erythromelalgic' type. Frequently, as already indicated, the slightest touch over the erythematous areas causes the most acute distress. Even the weight of the sheet could not be borne by some, and it



FIG. 5.—PARALYSIS OF LOWER EXTREMITIES, WITH MUCH WASTING OF MUSCLES.



became necessary to keep the bed-clothes off the lower extremities by some form of 'cradle.'

**Hyperæsthesia of the Muscles** is also usually well marked, but perhaps most distinct in 'mixed' cases—that is to say, where both alcohol and arsenic had to be considered as combined in their ætiological influence.

**Hyperalgesia**, or an increase of the common sensation of pain, is frequently present. A pin-prick may cause intense distress, and the pain may persist for some time. Pressure of the muscles, especially those of the calf, and most commonly in females, may cause the patient to scream with the pain thus caused.

**Anæsthesia** is occasionally met with in some of the more chronic cases.

**Analgesia** has been observed in a few instances, but is exceptional.

**Neuralgia**, or attacks of paroxysmal pain, may be experienced in the course of the affected nerves. In some cases a slight jar to the bed has caused pain to 'shoot' upwards along the inflamed nerves. Such have been mistaken for the 'lancinating' pains of locomotor ataxia. Others have complained of pain like 'sciatica.' In many instances pressure over the nerve-trunks will cause pain and tingling in the area of their distribution, and even twitching of the muscles.

**Paræsthesiæ**, or abnormal sensations of different kinds, and very variously described, are frequently complained of, and, as already indicated, they are generally said to be like 'pins and needles'; but sometimes sensations as of heat and cold are experienced, and occasionally a patient will describe a feeling as of being 'scraped.' In the majority of cases the paræsthesiæ have been almost limited to the feet and hands, but occasionally the numbness has been experienced over the whole of the lower extremities. Even the head and trunk may be involved.

**Alteration in the Rate of Conduction** seems noticeable in many cases. In some of the more chronic forms of neuritis it would appear to be distinctly delayed.

**Derangement in the sense of temperature** may occur. Thermo-anæsthesia is sometimes well marked. The husband of one patient put an oven plate as hot as he could hold to his wife's feet, and she declared it to be cold.

**The muscle sense is impaired** in some cases. This may explain, at least in part, the occurrence of the ataxic manifestations.

#### MOTOR IMPAIRMENT.

In almost every case more or less involvement of the muscles occurs, and there is generally lessened power, loss of tone, wasting, and in some instances distinct inco-ordination.

**Paresis and Paralysis.**—The degree of impairment of the muscular power varies from a slight paresis in mild cases to complete paralysis in severe forms (Figs. 3, 5, 6, 7, 8, 9, 12, and 13).

Muscular weakness is usually general, but the extremities are principally involved.

The lower limbs are in most cases chiefly affected, but the degree of paresis varies greatly. Some patients continue to walk about throughout the whole course of the malady, although readily getting tired, and often manifesting a hesitating, shuffling, or unsteady gait. Many who insist on walking about admit that they cannot go far, and are soon eager to sit down or seek support by leaning against a wall or anything else convenient.

In bad cases complete paralysis occurs. The worst cases are usually seen in 'alcoholics,' but we have met with almost total loss of power in both extremities in the 'strictly temperate.'

The muscles of the feet and legs are principally affected, but those of the thigh may also be much weakened.

The paresis of the hands is sometimes comparatively slight, the clumsiness in handling things being in these cases apparently due to the more marked involvement of the sensory fibres.

But in severe cases there may be almost complete loss of





FIG. 6.—‘DROPPED’ HANDS FROM PARALYSIS OF EXTENSORS,  
WITH MUCH MUSCULAR ATROPHY.



power in the hand. We have seen one woman, apparently almost a pure case of arsenical neuritis, where the hands were helpless. Not infrequently the hands are found 'dropped' (Figs. 6 and 15).

Usually in both upper and lower extremities the extensors are more enfeebled than the flexors, and the small muscles of the hand are frequently much involved.

The muscles of the back are in severe cases also considerably affected. Even patients who persist in walking about have difficulty in sitting down slowly and rising again. Bad cases cannot sit up in bed without assistance. The abdominal and thoracic muscles may be enfeebled. We have met with several instances in which distinct paresis of the diaphragm was apparent.

The ocular muscles, as far as we have observed, have not been involved, but Dr. Robert Forsyth states that he has observed oculo-motor paralysis in one of his cases.

**Tremor** is met with in some cases, principally in the 'alcoholics'; but in the more distinct examples of 'primary arsenical neuritis' it has not usually been a conspicuous feature.

**Convulsions** have been reported to have occurred, but we have met with no example in our large series of cases.

**Cramp.**—Painful tonic spasm of certain muscles has been in many cases a distressing symptom. It has usually been worse in 'alcoholics.'

The calf muscles have been principally involved, but many localise the cramp to the region of the toes, and particularly about the extensor tendons of the big toe.

Frequently the attacks are so severe as to cause the patient to scream.

There can be but little doubt that the 'alcoholic' influence has greatly accentuated the toxic action of the arsenic in very many instances.

**Contractures** have been observed in some cases; but apparently these were—at least, in most instances—confirmed alcoholic subjects.

## REFLEX DISTURBANCES.

**Superficial.**—The superficial reflexes are often present, and the plantar may be exaggerated even in cases of long standing; when lost, the plantar reflex is often the first to return.

In bad cases all superficial cutaneous reflexes may be absent.

**Deep.**—The knee-jerk in bad cases is generally absent, but in many acute and severe cases we have found it exaggerated. In one case it was present on one side and absent on the other.

In cases where it has disappeared and recovery is speedy the knee-jerk can often be elicited early.

Ankle clonus is, of course, never observed.

**Visceral Reflexes.**—A few cases have presented some difficulty in connection with the act of micturition; but this has probably been due rather to local conditions than nervous derangement.

## TROPHIC AFFECTIONS.

Undoubtedly most of the cutaneous lesions are to be considered as of tropho-neurotic origin.

The erythema, erythromelalgic condition and urticaria-like eruptions can only be satisfactorily explained by angio-neurotic irritation. Herpes zoster and most of the other skin lesions are undoubtedly to be considered as manifestations of trophic derangement.

Glossy skin' has also been well marked in many patients.

A tendency for bedsores to develop has been noted in severe cases.

Wasting of the muscles has rapidly developed in many instances. The extremities suffer most, and particularly the calf muscles and those of the hands and feet, and in such muscles as the interossei and adductor pollicis the atrophy may be extreme (Figs. 6, 7, 14, and 15).

Reference has already been made to the trophic disorders of the nails and hair (Fig. 4).

A passing note may here be made as to the increased secretory action of the lachrymal and sweat glands.

Qualitative and quantitative changes in the electrical

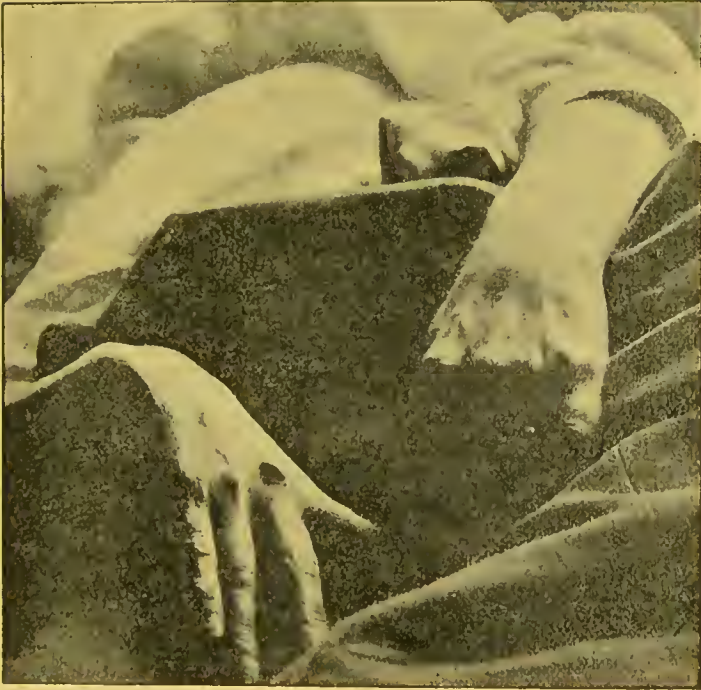


FIG. 7.—'DROPPED' HANDS FROM PARALYSIS OF EXTENSOR MUSCLES, WITH MUCH WASTING.



reactions have been well-marked, and the so-called 'reaction of degeneration' has been obtained in bad cases.

It is also interesting to observe that in several instances before neuritic symptoms developed an increased appetite and feeling of general well-being had been present, apparently depending upon the tonic action of the arsenic when taken in what may have been medicinal quantities. This had been very well marked in the case of a lady seen in consultation with Dr. Bennett.

#### PSYCHICAL MANIFESTATIONS.

Mental symptoms have been present in a large number of cases. In the chronic soakers these have often been more or less of the well-recognised 'alcoholic' type; but others have presented characters which warrant the view that they were dependent upon the presence of the arsenic. Some patients complain of 'night startings,' 'nightmare attacks,' and experience auditory and visual hallucinations. In one case complaint was made that the patient saw 'faces' when dozing off to sleep, which always disappeared on the eyes being opened. Visual hallucinations are most frequently met with at night, and seem always to take the form of 'persons,' thus differing much from those complained of by alcoholics. Insomnia has been a troublesome condition in many instances.

Some cases finally sink into a semi-comatose condition; but even when verging on coma, some improvement may occur if all alcohol is prohibited, as was demonstrated in the case of a woman seen in consultation with Dr. Harold Bailey on November 29.

This case presented several features of interest, and has been well reported by Dr. Bailey:

On October 9, 1900, I was called in to attend a married woman, aged forty-one years, residing in Pendleton, she having slipped and sprained her left ankle. Rest and the application of lead and opium lotion to the injured joint were prescribed. The swelling around the joint subsided, and the pain, which was severe, abated somewhat; but at the end of a week the patient began to

complain of pains and tingling in the left foot, and she was unable to stand upright, and was obliged to remain altogether in bed. Cramps in the calves of both legs were next complained of, and the feet and legs became exceedingly painful to pressure on any part of them. She also complained of the weight of the bed-clothes, and of being unable to sleep at night owing to the intensity of the pains. After another week the patient noticed that her hands were becoming affected, saying that they felt numb to the touch, though painful sensations like 'pins and needles' were present. She could not use her hands, moving the fingers with difficulty. Her appetite began to fail, the tongue became slightly coated, and vomiting of yellowish bile occasionally occurred.

Before being confined to bed the patient had been accustomed to have beer for supper, and she admitted having taken a glass or two since. I called at the patient's house on the morning of November 21, and sent out for a jug of the beer which she was in the habit of drinking. This was obtained from the shop whence she had been getting her beer, and on its being analysed by Mr. Kirkby was found to contain 0.14 grain of  $As_4O_6$  per gallon. A sample of urine from the patient failed to show the presence of arsenic, though in the case of another patient of mine who had drunk the same beer, and was suffering from symptoms of arsenical poisoning, the urine showed a faint trace of arsenic.

The condition of the patient became gradually worse, the weakness of the limbs increasing, and there being, in addition, considerable general wasting. On making a detailed examination on November 29, the following state of affairs was noticed: The patient lay on her right side in a drowsy, heavy condition, with the eyes half-open and the knees drawn up. She opened her eyes slowly when asked to do so. She could recognise me, mentioning my name. She complained of her head, saying that it felt as though drums were playing in the street. Dark-brownish pigmentation of the skin was present on the neck, the axillæ, the abdomen, the thighs, and the legs. There was flaky desquamation of the skin over the lower part of the abdomen. Over the calves of the legs the skin was roughened and desquamating. The legs and hands could be moved slightly without the patient being roused, but on making more extended movements she complained of pain (Fig. 7). The left foot was dropped, and the skin was thickened; on the right foot keratosis was well marked, especially over the heel. The patellar reflex was absent on both sides. The tongue was red and moist, the pupils reacted readily



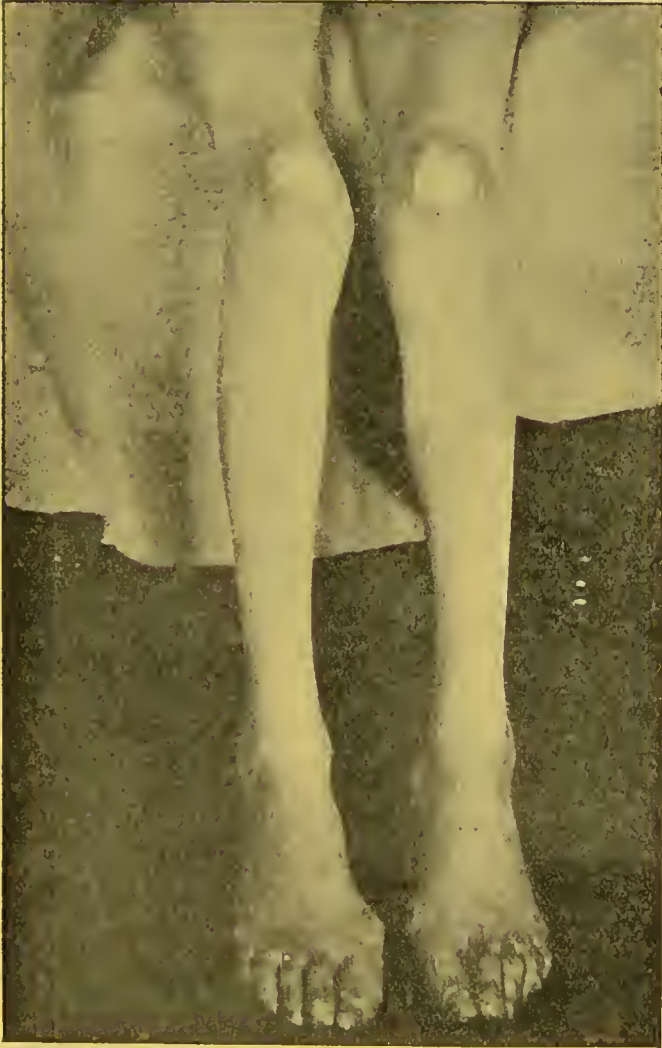


FIG. 8.—PARALYSED LOWER EXTREMITIES, WITH MUSCULAR WASTING AND SLIGHT PIGMENTATION.



to light, the eyes were somewhat watery, but there was no nasal discharge. The heart-sounds were regular, but feeble; the first sound was hardly to be detected. The pulse was 100 per minute, and exceedingly feeble. The respirations were twenty-four per minute; there was slight movement of the diaphragm. The chest moved, as a whole, without much lateral expansion. The temperature was normal. During the five days ending on December 4 the patient's condition remained much the same, though more nourishment was taken, and the comatose state was not so well marked.

On December 20th the patient was still alive, although in a very serious condition.

### Affections of the Respiratory Passages.

The mucous membrane of the respiratory passages is congested in many cases. If the nose is not found 'running,' usually moisture from serous discharge will be seen immediately within the nostrils. The 'catarrh' often involves the larynx, and very many patients have complained of 'huskiness' and alteration in their voice. In some few it has been so marked that the patients could only phonate with difficulty.

There may be irritable cough. Distinct bronchial catarrh has been present in some cases.

The lungs apparently do not suffer directly, at least to any extent, but I believe it will be found that some deaths have occurred from respiratory failure due to paralysis of the diaphragm.

The intercostal muscles have certainly been weakened in some instances.

In severe cases the breathing becomes quick and shallow, and sometimes presents distinct 'periodic' characters.

Occasionally vague pains about the chest have been complained of.

### Disorder of the Circulatory System.

Many of the excessive beer drinkers present the usual evidences of cardiac enlargement, and some show signs of muscle failure; but in the majority of cases arising in strictly

moderate indulgers there seems usually to have been no direct action of the irritant on the circulatory apparatus.

In some cases, however, cardiac asthenia has occurred, and given rise to serious symptoms of heart failure. The pulse in bad cases is always of low tension, frequently quickened, and readily influenced by changes in position. Fainting attacks may occur.

### Changes in the Blood.

Well - marked anæmia has occurred in many cases. Generally there has been a diminution in the amount of hæmoglobin, and also in the number of red corpuscles. A slight increase in the leucocytes has been observed.

### Digestive Derangements.

No very marked indications of digestive disturbance have been met with in the majority of cases.

Nausea and loss of appetite have oftentimes been present ; but some cases have remarked with surprise that previous to their illness their appetite had been unusually good, and, with some, friends had remarked on their healthy appearance. Probably this was due to what may be called the ' medicinal effects ' of the arsenic before it had exerted its toxic action.

In many the appetite has remained good throughout the illness, and even when this has fallen off during the severer stages, it has generally quickly returned under appropriate treatment.

Vomiting and diarrhœa, with some slight abdominal pain, have occurred at the commencement of the illness in a certain number of the cases. In, perhaps, the majority there has been no conspicuous gastro-intestinal derangement. This, to many, seems to have been a perplexing fact ; nevertheless, in a large number of cases the involvement of the peripheral nerves and the affection of the skin have been practically the only evidences of arsenical poisoning.

One working brewer who was in the habit of tasting the glucoses used in the brewery noticed that he was experiencing

abdominal discomfort, and that his finger-tips were getting 'numb.'

The tongue may be 'furred,' and in some few instances presents an appearance best described as 'silvery.' The mucous membrane of the mouth is not pigmented. We have not met with true ulceration of the gums or fauces. There may be slight catarrh of the pharynx. Salivation has not been marked in the cases we have investigated. Diarrhœa is exceptional, and colic is but seldom complained of; some have experienced epigastric pain and slight general abdominal discomfort.

Stubborn constipation calls for active treatment in many cases.

### Urino-Genital Disturbance.

The urinary organs generally present but little evidence of derangement. Occasionally some slight discomfort is experienced in micturition, the act being accompanied by 'smarting' or pain at its close, one man describing the condition as being 'like something sticking.'

In severe cases the urine is high coloured and may contain a little albumen.

In several cases arsenic has been detected in the urine, but our experience is that when the arsenicated beer has been stopped the arsenic has quickly disappeared from the urine.

Our experience is in accord with that of Dr. Nathan Raw at Liverpool, who expresses the opinion that arsenic is eliminated by the kidneys only for a very short time after the cessation of the drug. He reports:

'I examined carefully the urines of thirty-one chronic cases of arsenical poisoning, but failed to find any traces of arsenic; but in two cases of recent acute illness I found arsenic on the first and second days after admission, but never afterwards.'

In a number of cases there has been considerable irritation about the genitals, and the formation of boils has been noted in some instances.

### Cases occurring in Young Subjects.

In the present remarkable outbreak of arsenical poisoning even infants and children have not altogether escaped.

On Monday, December 3, a mother, aged thirty-two, was seen at the out-patient department at Pendleton, with well-marked arsenical neuritis. She was confined nine weeks previously. 'Stout' was subsequently taken. Four weeks previous to seeking medical advice mother and child were well; then the woman experienced 'numbness' of the fingers, 'lurching' and 'jumping' at the bottom of the feet, 'running' and 'smarting' of the eyes, and she became hoarse. At the same time the child began to vomit after every nursing, and wasted. The mother had tearful eyes, marked erythema and keratosis of the feet, pigmentation of the skin, much sensory involvement of the distal parts of the upper and lower extremities, and walking was very painful. There had never been any nausea, vomiting, or diarrhoea, and the secretion of milk was plentiful. The infant was puny and much wasted; the eyes were 'running,' the child 'snuffled,' and the feet were slightly erythematous. The mother was directed to immediately cease taking stout, and stop nursing.

On Thursday, December 6, both patients were again seen. The woman was distinctly better, and stated that since she 'stopped the breast,' and gave cow's milk and barley-water, the baby had ceased vomiting. The coryza and nasal catarrh had disappeared, and the child was manifestly much improved.

A sample of the milk was examined, but no distinct evidence of arsenic could be obtained. The clinical features, however, clearly warrant the view that the infant had been receiving toxic doses of arsenic in its mother's milk. That arsenic may be so excreted is a well-known fact.

On December 17 both patients were again carefully examined, and found to be rapidly improving. The woman still showed distinct 'tearful' condition of the eyes, which she said readily 'watered' when she went out of doors. The pigmented skin was desquamating (Fig. 10). Slight paræsthesiæ were still complained of. The child was now taking breast milk again, which appeared to cause it no discomfort. It was, however, puny, and presented evidences of malnutrition.

On November 29 a somewhat similar case was investigated

through the kindness of Dr. J. H. Taylor, whose description is so graphic that it is best given in his own words :

Mrs. M.'s case is of interest, as during the course of her attack she was delivered normally of a child at full term, and continued to suckle it for several weeks. She had been accustomed to drink about a pint of beer per day. At the beginning of September a faint rash appeared on her arms, and her eyes began to water. She was confined a fortnight after the rash appeared, was attended by a midwife, and says 'she had an easy time.' She remained in bed a fortnight, during which she took no beer, and the rash disappeared entirely. Child healthy. A fortnight after confinement 'her milk began to go,' and she again began to take beer, as she says, 'to make milk.' A few days afterwards the rash again appeared on her forearm, and her eyes became intensely painful and red.

I first was called in on November 19 to see the baby. I found it suffering from gastro-intestinal catarrh, with vomiting, moderate diarrhoea, furred tongue, but with no rash, and only slight redness about the eyelids. Its cry was hoarse, and it had a frequent, slight cough. Temperature  $101^{\circ}$ .

Inquiry showed that it had never taken anything except the breast, and as I saw at once that the mother was herself ill, I advised her to wean it for a time. She did so, and in a few days the child was quite well. Examination of the mother showed at once that her condition was due to arsenical poisoning. The rash had the typical characters and distribution, except that it was only slight on the face. There was also injection and tenderness of the eyes. The rash was worst on the forearms and thighs, and the sensory disturbances, such as numbness and tingling of hands and feet, were marked. In addition, there was complete anæsthesia of the toes, not even a deep pin-prick being felt. She said she had to look where she placed each foot in walking, as she could not feel the floor. No distinct motor weakness, knee-jerks normal, no mental derangements. Slight cough, apparently from laryngitis, voice only a whisper, and walking painful. Tongue covered with brown fur. Great nausea and loss of appetite, but vomiting only once. No abdominal pain, moderate constipation, micturition normal.

I procured two samples of the beer she had used, and found one free from arsenic, but the other contained quite a large amount. I have also analysed her urine, and found traces of arsenic in it a week after she ceased taking beer. I procured also a small quantity of milk from her breasts, but analysis failed

to show any traces of arsenic in it. The fact that it was not obtained till a full week after she ceased taking the beer may perhaps account for this, for the illness of the child would certainly be easily accounted for by excretion of arsenic in her milk.

On December 2 a still more remarkable case was seen with Dr. John Brown at Bacup. Dr. Brown has carefully reported this unique case, and we therefore quote from his description :

The patient was a bonny-looking little girl, aged two years. She had been unwell for some days, suffering from pains in the feet, legs, and arms, which were thought to be rheumatic pains. Evidently her feet felt hot and uncomfortable, for she wanted her shoes always off. The child was too young to describe her subjective symptoms, so that it was necessary to rely on the objective ones. Her face was flushed, her eyes were watery, and there was a slight running from her nose. The cutaneous symptoms were as follows: There was no pigmentation of the face, neck, thorax, axillæ, abdomen, or groin. Erythematous areas existed over the arms and forearms in the region of the elbows, being most marked on the extensor surfaces. The palms of the hands were red, especially over the thenar and hypothenar eminences, and about the tips of the fingers. In the lower extremities there was marked erythema over both knees, and on the right side above the patella there were several distinct, irregular, brownish patches, evidently due to pigmentation in the superficial layers of the skin, and not arising from effusion of blood. There were similar pigmented spots above the left knee, but neither so well marked nor so extensive. There was erythema of the soles of the feet and the toes, with a distinct border to the erythema along both sides of the feet and around the heels. As the child sat on the lap of a relative the feet looked 'dropped,' as if the extensors were paretic, but there was no distinct paralysis. There were no impairment of the tactile sensation, no muscular hyperæsthesia, no plantar reflex, and no dorsal extension of the toe; the knee-jerks were absent.

The child's father keeps a public-house, and although so young, she was accustomed to get little 'sups' of beer from the kindly-disposed customers at the bar. I have carefully tested samples of the beer, and have found arsenic present.



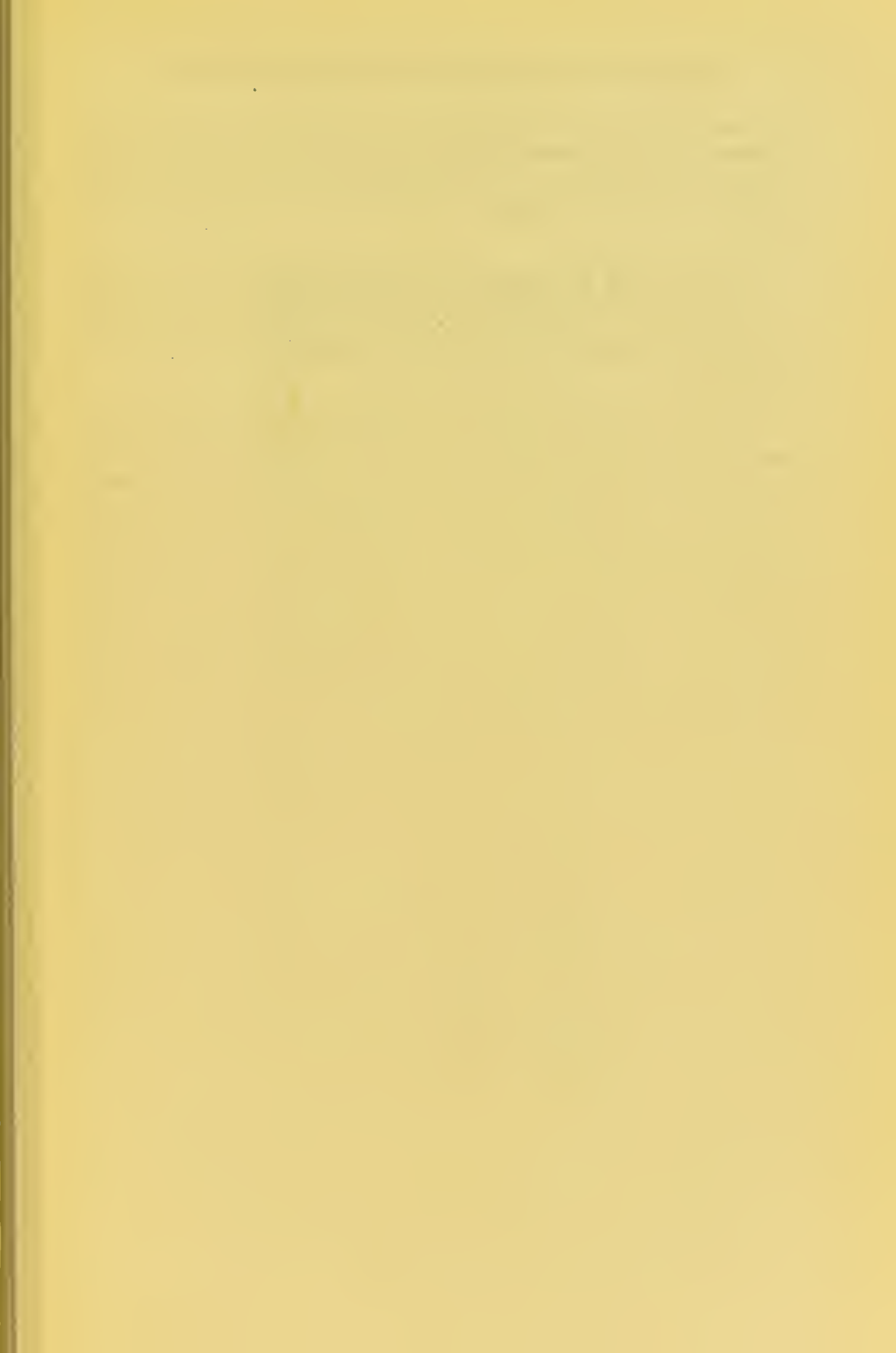




FIG. 9.—'DROPPED' HANDS AND FEET.

### Clinical Varieties.

A study of recent cases of peripheral neuritis clearly indicates that three distinct groups may be readily differentiated :

1. Arsenical neuritis occurring in strictly temperate persons ;

2. Arsenical neuritis occurring in chronic alcoholics.

3. Neuritis occurring in chronic alcoholics, and presenting no evidences of arsenical poisoning.

Many examples of all forms have come under observation during the last few months. It is only with the study of the two first groups that we are at present concerned. The distinction between (1) non-alcoholic and (2) alcoholic cases is not always to be made easily, or without careful inquiry. After thorough investigation, we are, however, convinced that in connection with the present 'epidemic' a large number of 'strictly moderate' drinkers have been affected, and some very seriously.

Nearly all cases have presented more or less well-defined evidences of 'neuritis,' but very great variations have been observed. According to the predominant features a more or less definite clinical classification seems possible :

1. *The Mixed or Common Neuritic Type.*—The form which has undoubtedly been most frequently met with has been one in which evidences of sensory, motor, and vaso-motor disturbance have all been present, although in very varying degree. Generally even in this form the sensory and vaso-motor derangement has preceded the motor enfeeblement.

2. *The Sensory Type.*—The sensory form of derangement has been one of the most conspicuous of the neuritic group.

Even when considerable sensory involvement has occurred, many cases were found capable of walking about, and a considerable number continued their work for some weeks.

In not a few motor symptoms have been inconspicuous throughout.

3. *The 'Erythromelalgic,' or Vaso-Motor Type.*—This has

been well defined in many cases, and, indeed, in a certain number the erythema and pain in the feet have been almost the only definite clinical features.

4. *The Paralytic Type*.—This form has not been confined to chronic alcoholics, and many who have taken quite small quantities of the affected beer have rapidly lost almost all power of walking.

In two specially severe cases which had taken beer from the same brewery, both hands and feet were almost entirely powerless, and when seen medically the profound paralysis constituted the main clinical feature.

5. *The Ataxic Type (neuro-tabes peripherica)* has been met with in not a few cases and has led to the condition having been confounded with locomotor ataxia. The muscular inco-ordination is usually most noticeable in the lower extremities.

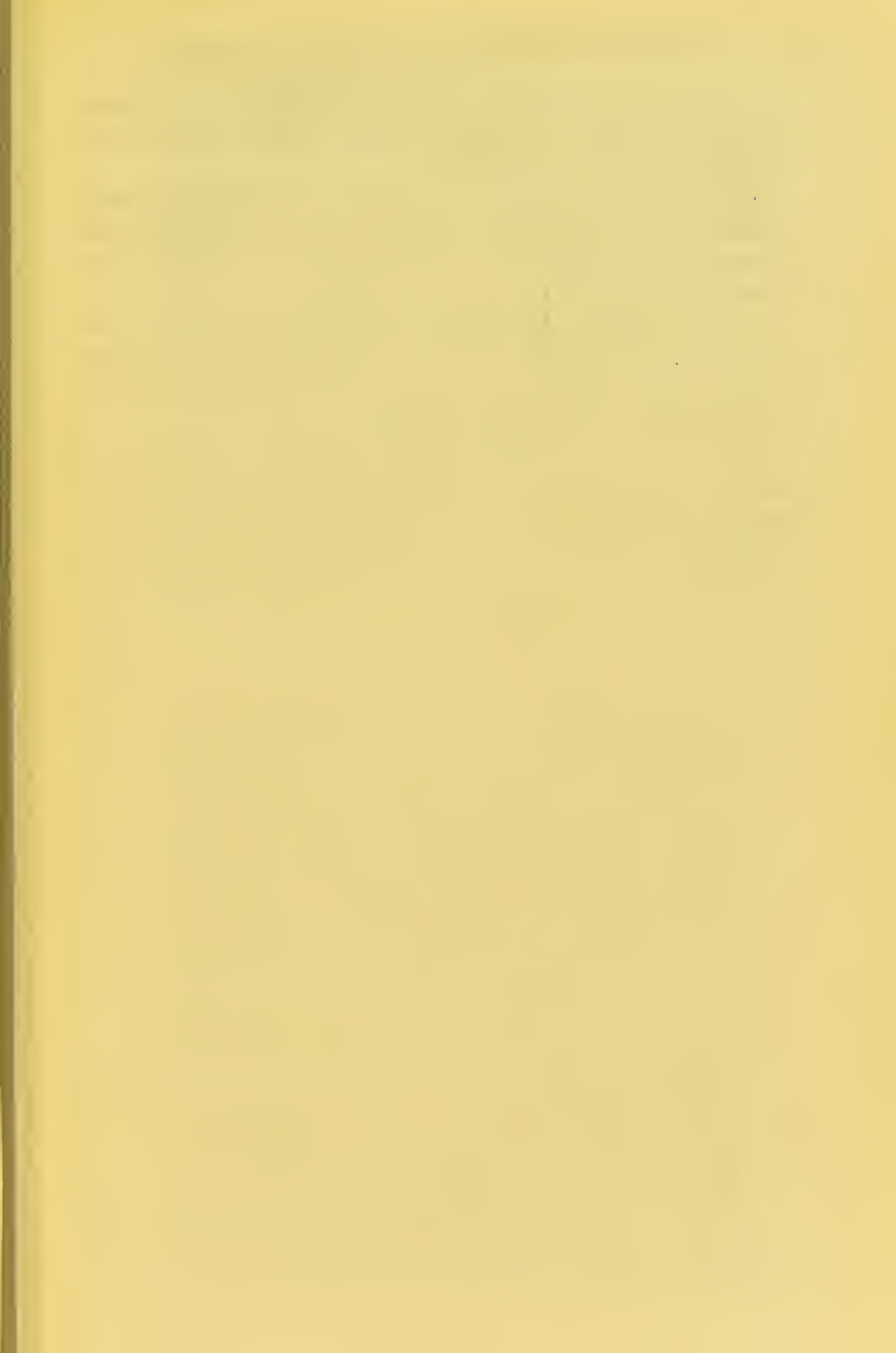
6. *The Atrophic Type*.—In some few cases atrophy has developed with great rapidity, and apparently quite out of proportion to the severity of the neuritis. In some the hands have presented an appearance almost identical with that seen in progressive muscular atrophy. In others the most marked wasting has been confined to the lower extremities (Fig. 12). In one case the pectoral muscles were greatly wasted, and presented fibrillary twitchings.

In some rapid atrophy of nearly the whole of the muscular system has been noted (Fig. 15).

7. *The 'Herpetic' Type*.—In a number of cases 'herpes' has developed as the earliest and oftentimes the only definite manifestation of arsenical poisoning.

There can be no doubt, however, that many of the recent cases of 'epidemic shingles' have been due to this agent.

We have met with a striking example in a brewer who, knowing that something was 'wrong with his beer,' sampled the different brews with a view to ascertaining which were the affected ones. He developed 'herpes,' and subsequently noticed a more or less general desquamation of the skin. Some of his workmen were affected with 'blisters' about the feet and body, and said that their feet felt as though they were treading on 'broken oyster shells.'



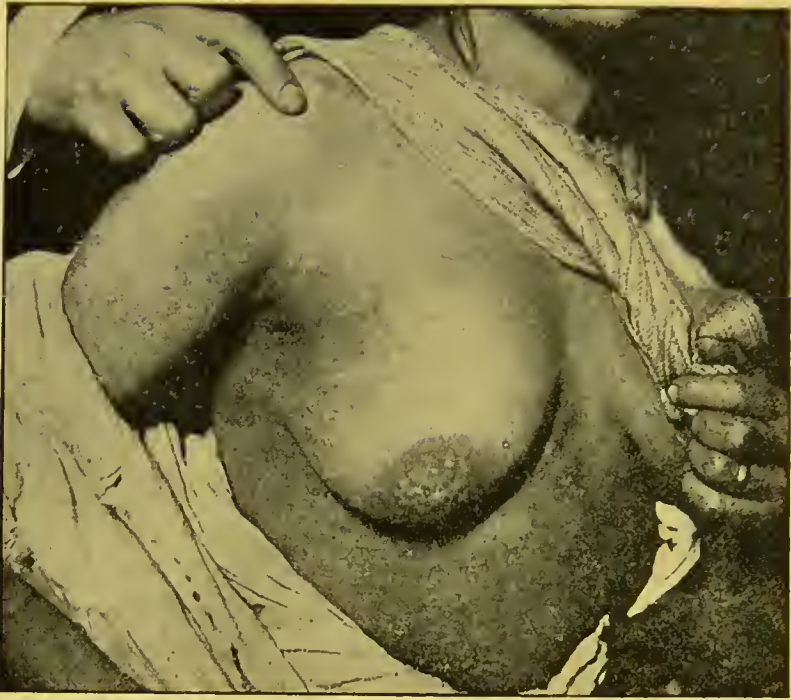


FIG. 10.—PIGMENTATION ABOUT ARM, AXILLA, SIDE OF CHEST AND OVER ABDOMEN.

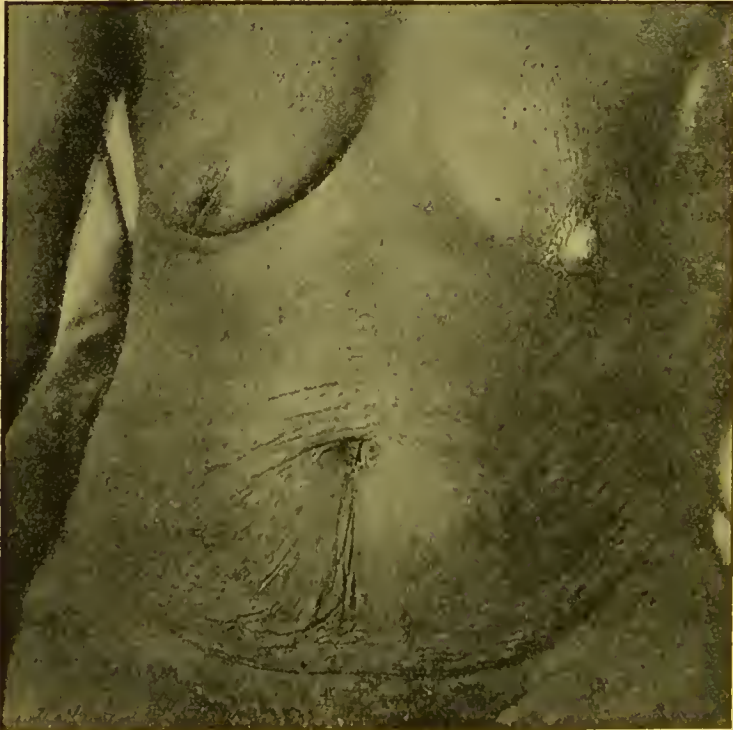


FIG. 11.—EXTENSIVE PIGMENTATION OF BODY.

8. *The Pigmentary, or Addisonian, Type.*—Cases belonging to this class, both as regards character and distribution of the pigmentation, have in many instances closely resembled ‘Addison’s disease.’

In not a few, however, the area of discoloration has been very irregular (Figs. 1, 2, 10 and 11).

In many the neuritic symptoms have been comparatively slight, but some, however, have suffered severely.

9. *The ‘Catarrhal’ Type.*—This form is exceptional. Still, some cases have occurred where ‘running of the eyes and nose,’ and a catarrh of the respiratory and alimentary passages have been the only, or, at all events, the first and most conspicuous, evidences of arsenic in the system. We have seen one case where the patient attended for some time at an eye hospital, and finally diagnosed her own condition from reading of the ‘epidemic’ in the daily press. The discomfort in the feet had been so slight as to be considered merely ‘rheumatics,’ and medical attention was apparently not directed to it.

The cases met with in suckling infants belonged to this type.

### Diagnosis.

Although since the latter part of September beer had been under suspicion as the cause of the marked increase in the number of cases of peripheral neuritis and the unusual symptoms associated therewith, yet it was not until the discovery of the arsenic in the drink that a certain diagnosis could be arrived at.

A retrospective consideration of many of the cases of unusual multiple neuritis and cutaneous affection which have come under observation during the present year are now seen undoubtedly to have been dependent on arsenical irritation. It is only fair, however, to allow that peculiar difficulties surrounded the early recognition of these cases, and prevented their true characters being generally recognised until the number had assumed ‘epidemic’ proportions.

It is unnecessary here to discuss in detail the differential

diagnosis of these cases; that will have been sufficiently indicated in the preceding pages. It seems, however, desirable to call attention to some of the more important distinctions between arsenical neuritis and the so-called 'alcoholic' form, and also to refer briefly to some of the affections which have been confounded with arsenical lesions in the present outbreak.

The cases occurring during recent months have chiefly differed from so-called 'alcoholic' neuritis in the following respects:

1. They have not been confined to excessive drinkers, but many strictly moderate persons have suffered, and oftentimes severely.

2. The acute onset, rapid development, and severe course of the neuritis has been very marked in a large number of cases.

3. The sensory involvement has generally been much more conspicuous than in ordinary alcoholic neuritis.

The hyperæsthesia of the skin and muscles has been extreme in many instances, and in nearly all cases far more marked than in any other forms of neuritis usually met with.

4. The paralytic symptoms when present have usually developed rapidly.

5. The 'erythromelalgic' symptoms, which have been such a striking feature in so many of the affected cases, are only very occasionally present in 'alcoholic' neuritis, and never to the same extent.

6. Ataxia has been a more distinct and constant feature than in ordinary peripheral neuritis. Quite a number of the cases have presented most apparent inco-ordination of the lower extremities, involving to some extent also the upper.\*

7. 'Cramps' and 'tremors' have generally been less note-

\* It is interesting in this connection to refer to a valuable paper published nearly fourteen years ago, by Dr. Charles Dana, of New York, on 'Pseudo-Tabes from Arsenical Poisoning, with a Consideration of the Pathology of Arsenical Paralysis.' *Brain*, 1887, vol. ix., 456. A valuable bibliography, including over one hundred references, is also given.





FIG. 12.—ATROPHIC PARALYSIS, WITH MUCH WASTING,  
AND 'DROPPED' FEET.



worthy features than in the common form of peripheral neuritis. When 'cramp' has been experienced, it has often been situated in the feet, particularly about the toes, and especially in the big toe, rather than in the calf muscles.

Tremors have occurred in some cases, but have been inconspicuous in the majority, and certainly much less seldom met with than in ordinary alcoholic neuritis.

8. Pigmentary and numerous other cutaneous lesions have been present in a large number of the cases, and clearly indicated the true origin of the affection. Arsenic is probably the only drug which will produce such typical 'herpes' as has been common during recent months.

9. Nutritional changes in the cuticle, nails, and hair have occurred in many cases.

10. Catarrhal symptoms have also been very conspicuous in a considerable number of the cases. The suffused conjunctivæ and œdematous face have given many of the patients a very characteristic aspect, and such is but seldom seen in the ordinary cases of peripheral neuritis in alcoholic subjects.

11. Finally in mild cases and those of moderate severity the withdrawal of the contaminated beer has led to speedy improvement.

Within a few weeks of our discovery of the source of the arsenic, the greater number of the male 'ambulatory' cases attending our out-patient department at Pendleton had returned to work. The women generally have suffered more severely, and their improvement is usually slower.

Of the severe cases bed-fast in hospitals many improve very slowly, and with some it seems likely that recovery will be quite as tedious as in the cases we have hitherto been accustomed to deal with.

Many of the recent cases of arsenical poisoning have given rise to great difficulty and much perplexity in diagnosis. They have been confused with the following affections :

*Addison's Disease.*—A number of cases have for long been considered and treated as Addison's disease, and some at least

have been so entered on the death certificate. The error is comparatively easy, for in not a few of the cases we have seen the character and distribution of the pigmentation has very closely followed that of Addison's disease. The absence of persistent asthenia and vomiting, and the presence of 'erythromelalgia' and other manifestations of peripheral neuritis, have in almost all instances clearly indicated that the cases were anomalous. The occurrence of desquamation and other cutaneous lesions associated with 'running of the eyes' and other slight catarrhal symptoms had been also noted some time before the discovery of arsenic was announced.

*Erythromelalgia* has for nearly twenty years been recognised as a well-defined affection,\* so that it is not extraordinary that the symptomatic erythromelalgia should have been in some instances mistaken for the 'idiopathic' form. It is interesting to note that our experience of the present epidemic goes far to substantiate Dr. Weir Mitchell's contention that erythromelalgia is dependent on peripheral neuritis.

*Locomotor Ataxia* has been occasionally confused with arsenical neuritis. As already indicated, a considerable number have presented evidences of inco-ordination, and in many of these the 'knee-jerk' has been absent. Even the shooting pains along the nerves, not uncommon in the very severe cases, have been thought to be the characteristic 'lightning pains' of locomotor ataxia.

*Landry's Paralysis* has been suggested by the course followed by some of the cases, especially those in which a rapidly developing paralysis involving both upper and lower extremities has not presented marked sensory symptoms.

*Progressive Muscular Atrophy* has been simulated by several cases. In one man the appearance of the hands was practically identical with that seen in this condition, but careful inquiry left no grounds for doubting that he was suffering from arsenical poisoning.

\* See article by Dr. Thomas Barlow, 'System of Medicine,' edited by Dr. Clifford Allbutt, 1899, vol. vi., 607.

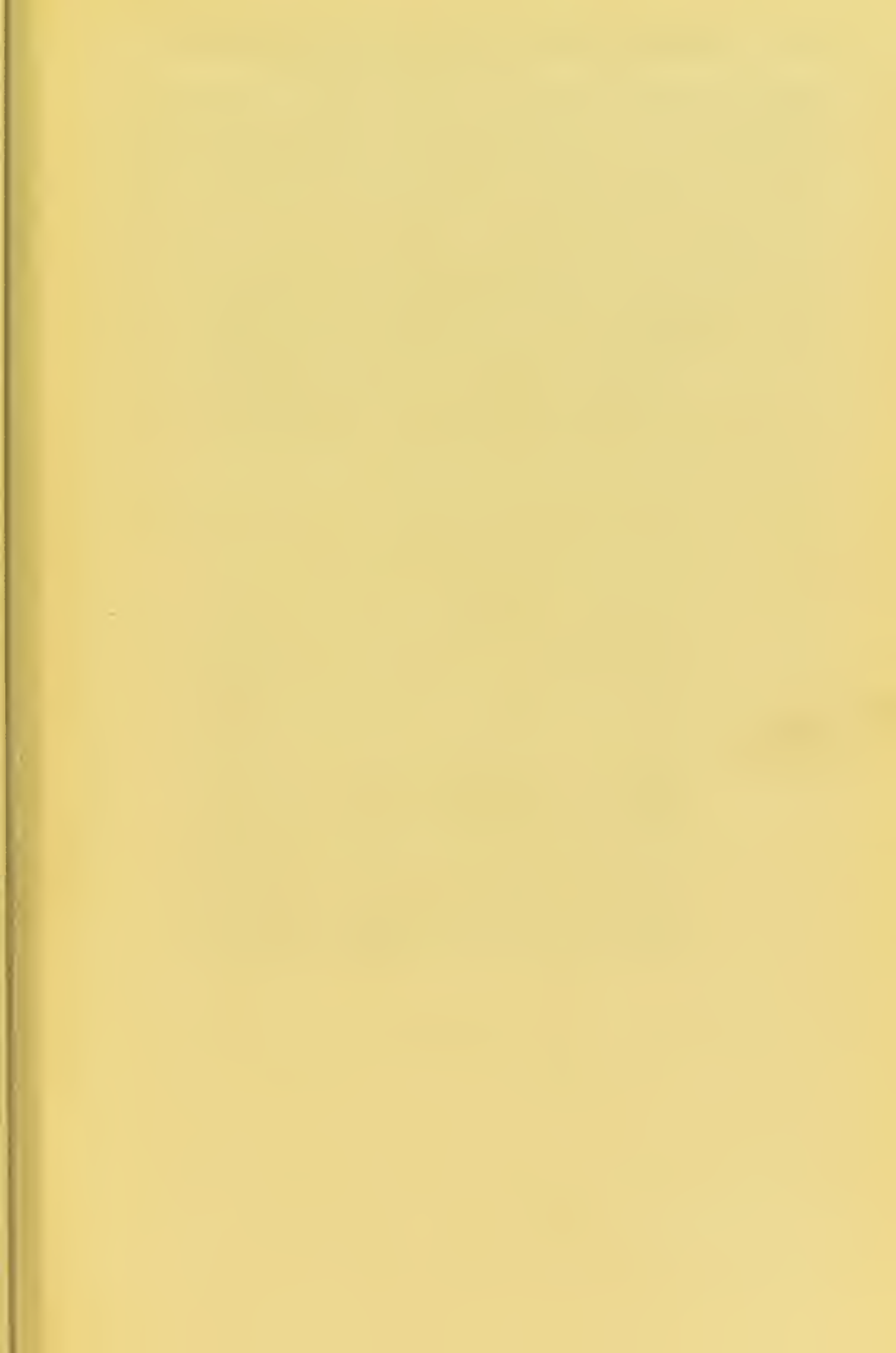




FIG. 13.—COMPLETE PARALYSIS OF LOWER LIMBS WITH MUCH ATROPHY, NAILS THICKENED, AND SLIGHT PIGMENTATION OF SKIN.

*Various Skin Diseases*, as would be expected, have been confused with the arsenical 'eruptions,' and numbers of cases have sought relief at skin hospitals.

*Scarlet Fever* has been suggested in some instances by the presence of marked erythema and subsequent desquamation.

*Rheumatism* has been complained of by large numbers of the affected cases, and some patients have even sought relief by visiting health resorts famous for the relief of this affection.

*Beri-beri* has also been confounded with cases of arsenical neuritis.\* Dr. Conolly Norman,† the Medical Superintendent of the Richmond Asylum, Dublin, has very kindly sent us a copy of his valuable clinical study of beri-beri occurring in Dublin, which clearly shows how closely many cases of this supposed parasitic neuritis may resemble arsenical neuritis.

### Prognosis.

Almost every degree of chronic arsenical poisoning has been met with in the cases under consideration. Some forms have been exceedingly severe, while in others the involvement has been so slight as to give rise merely to some vague subjective disturbances. Thus almost every variety of prognosis has been rendered possible.

At the present time it will be sufficient to briefly summarise our general impressions:

1. Arsenical neuritis occurring in 'alcoholics' has, generally speaking, led to more severe results than when occurring in strictly moderate drinkers.

2. Recovery has in very many cases been rapid on prohibiting the use of the contaminated beer. When all forms of alcoholic drinks have been stopped, recovery has seemed more speedy than in those cases where the use of spirits has been continued.

\* See articles by Drs. Newall and Prytherich, *British Medical Journal*, 1900, December 1, 1591; and Dr. Ronald Ross, *Lancet*, 1900, December 8, 1677.

† 'The Clinical Features of Beri-Beri,' by Conolly Norman, F.R.C.P. (Irel.), 1899.

3. Erythromelalgia and various paræsthesiæ have often persisted for many weeks, and sometimes, according to the patients' statements, for quite three months after all beer had been stopped.

4. In some cases cutaneous lesions continued to develop for many weeks after the drinking of all arsenicated beer had been prevented. In a case under the care of Dr. Dreschfeld, almost every form of the elementary and secondary lesions described by dermatologists has been met with during the course of the illness.

5. The cases in which the paralytic and atrophic manifestations were most marked have generally been slow to show amendment, and large numbers of these are under treatment in various parts of the country, and probably many will never perfectly recover.

6. Where 'herpes' has been most marked, general symptoms have usually been slight and restoration rapid.

7. The deeply pigmented cases seem generally to have suffered less as regards neuritic symptoms, but nevertheless a large number of the 'Addisonian type' have also presented marked erythromelalgia.

8. In favourable cases the knee-jerk has rapidly returned, and often when pigmentation and other cutaneous involvement have been present the skin has quickly desquamated.

It is necessary, however, to remember that in many of the cases when first coming under medical observation, and presenting acute neuritic symptoms, the knee-jerks have been exaggerated.

9. Electrical testing has shown in convalescing cases an absence of the reaction of degeneration.

10. Even when there were evidences of general arsenical intoxication, and the patient somnolent and semi-comatose, improvement has occurred when the affected beer has been stopped.

Death has resulted in a considerable number of instances. In perhaps most of these the subject has been a confirmed alcoholic. We have had the opportunity of very carefully investigating with Dr. Crawshaw, of Weaste, such a case





FIG. 14.—GENERAL MUSCULAR ATROPHY.



in the person of a middle-aged married woman, and as the history presents many points of interest we give it in Dr. Crawshaw's own words :

For nearly twelve months the patient has suffered from morning sickness, loss of appetite, furred tongue, etc., due to gastric catarrh from alcoholism. About three months ago she first noticed a feeling of weakness in the legs, which gradually got worse. She became easily tired on walking short distances, and suffered much from pain in the feet and calves. A sense of numbness and tingling was felt in the hands. About the same time a rash appeared on the hands, arms, and neck. It was red and burning, and itched very much. The patient described it as being 'like scarlet fever.' After this subsided the skin peeled off in various parts of the body. She says that 'thick skin peeled off the hands and feet.' The hair came off freely at first, but not much recently. The eyes have been very 'smarty' for several weeks, and have been 'running a good deal.' Very little discharge from the nose. A troublesome cough has been present for some weeks, but without expectoration. Hoarseness has been very pronounced and persistent for nearly two months. Vomiting has been frequent. No diarrhoea. The bowels have been constipated throughout.

The patient presents a decidedly alcoholic appearance. The face is dusky, flushed, and somewhat puffy. The eyes are watery, and the conjunctivæ somewhat inflamed. The skin over the forehead and at the sides of the face in front of the ears is slightly pigmented, the colour being a light brown. The superficial vessels over the cheeks are dilated. There is marked pigmentation of the skin in various regions of the body. This is most noticeable round the neck, in the axillæ, around the nipples and umbilicus, and in the lower part of the abdomen and in the groins. In these regions the pigmentation is uniform, and gradually shades off into the normal skin. Over the upper arms and in the hands the pigment is differently deposited. In these situations there are small spots of pigment varying from one-eighth to nearly a quarter of an inch across, with quite clear skin between them. The spots are more numerous on the upper arms and forearms, less numerous on the hands. In the hands the spots are not confined to the dorsal surfaces, but there are several large pigmented spots on the palms. Some of these spots, particularly on the backs of the hands, are intensely dark in colour. A slight desquamation is noticed in several regions; most marked in the pigmented areas on the trunk. The skin of the hands is thickened

and is noticed to be peeling slightly. The fingers are 'glossy.' In the feet, especially the soles, the skin is much thickened, and is peeling off in thick flakes. No change is noticed in the nails. The hair is decidedly thin.

No spasm or cramp is complained of. Tremor of the hands is present, but is not pronounced. There is marked weakness of the muscles of the legs and feet. The great-toe is dropped, and there is very little power of extension either of the toes or feet. The flexor muscles are not so markedly weakened. There is considerable weakness of the muscles of the forearms and hands, and also of the back. The muscles of respiration are unaffected. Tingling and numbness of the hands are complained of. There is, however, no anæsthesia. The feet are extremely tender to the touch in some places, particularly in one or two of the smaller toes. In the centre of the sole there seems to be paræsthesia. There is marked loss of the sense of heat; the husband of the patient says that she can easily place her feet on an oven-plate, so hot that he cannot bear his hand to touch it. The reflexes, superficial and deep, are abolished. There is a slight amount of dusky redness of the soles of the feet, however, amounting to the condition of erythromelalgia. The mental condition is characteristic of alcoholism. Her memory is very defective, particularly for recent events. She is rather irritable, and soon gets confused if asked many questions. There is considerable depression of spirits, and a slight tendency to delusions. The heart is not enlarged. The pulse is soft and regular. The tongue is covered with white fur. The appetite is very poor. No pain in the abdomen. Vomiting is frequent, particularly in the mornings. No diarrhœa. The cough is frequent, and the voice hoarse. No bronchitis. No disorder of special senses or of genito-urinary system.

The amount of stout or beer taken has varied considerably, and it is difficult to arrive at anything like a certain estimate. From two to four pints a day have been taken regularly, probably more at times.

A sample of porter bought from the same shop from which she habitually procured her supply was examined, and found to contain  $\frac{8}{100}$  of a grain of arsenic per gallon. A sample of beer, of which she had taken a little, brewed by the same firm, was found to contain  $\frac{7}{100}$  of a grain per gallon. The urine was examined on two occasions at an interval of six days, but no arsenic was detected.

The patient steadily grew worse, and death occurred on December 17th.

### Treatment.

Comparatively little need be said regarding the treatment of these cases of arsenical poisoning from beer-drinking. The nature and source of the irritant once detected, clear indications for general management are readily apparent.

In the majority of cases, when the contaminated beer was stopped, improvement at once commenced.

In some cases the use of other kinds of alcoholic drinks was persisted in, and usually, as far as could be estimated, with distinctly prejudicial results. One man, after some months' abstention from beer, drank rum and whisky to excess for nearly a week, with the result that the old pains in the feet recurred. There can be but little doubt that in many cases the irritant action of the arsenic has been much accentuated by the use of alcohol.

It is to be hoped that no mere sentimental opinions will minimise the evil arising from the only too common abuse of all alcoholic beverages.

This aspect of the case has been recently stated so ably by Dr. Judson Bury in his opportune paper\* on the treatment of arsenical neuritis that we venture to quote from his article :

‘When we know that patients who visit our hospitals have been in the habit of taking 10, 20, and even 30 pints of beer a day, and as a result are gradually but surely losing their physical and mental powers, and then reflect on the present arsenical panic, we begin to wonder why there has never been an alcoholic panic. The scare with regard to poisoning by arsenic has been fully justified, but surely consternation regarding poisoning by alcohol might be looked on as equally natural.

‘There appears to be a curious difference in the relationships of doctors and patients in respect of alcohol and to other poisons. If a doctor finds that his patient is taking lead, arsenic, or mercury in poisonous doses, he tells him so, and

\* *British Medical Journal*, 1900, December 8, 1629.

urges him to discontinue his dangerous practice. But if alcohol in large quantities is being taken, the doctor requires more courage to tackle his patient, for he runs the risk of offending, and possibly of losing, his client.'

Dr. Bury goes on to show that 'the gain in self-respect ought to compensate for the temporary loss of a client,' and quotes Dr. Thomas Barlow's searching question :

'What can be more humiliating to us as medical men than to have repeatedly to attend people who every day are shortening their lives and converting a remediable condition into a hopeless disease, whilst we stand with folded arms, or write prescriptions, and have not the courage to tell them what is right and stick to it?'

The general principles of the treatment of peripheral neuritis are so well known, and have been so fully defined in the standard articles on the subject, that detailed description would be out of place here.

Reference may, however, be made to certain measures which have proved of benefit during the recent outbreak in this district.

*Rest.*—Local and general rest must at once be enforced and severe cases kept in bed. From what we know of sufferers in different parts of the country, there can be but little doubt that many have greatly aggravated their sufferings and lengthened their illness by neglecting to insure complete rest for the inflamed nerves and irritated tissues.

*Nursing.*—Unfortunately, many of the sufferers have not been in a position to obtain the care and attention which their condition rendered necessary.

Some of the cases have been so helpless that they were unable to feed themselves or even turn in their beds.

In the acute stages a water-bed is very desirable for severe and debilitated cases. In many of the cottages of the poor it has been pitiable to witness the crude methods of kindly-disposed neighbours in their attempts to minister to the sufferings of their friends.

In those cases where cardiac weakness is marked the greatest care must be exercised.



FIG. 15.—GENERAL WASTING, EXTENSIVE ATROPHY OF EXTREMITIES, AND 'DROPPED' HANDS AND FEET.





*Diet.*—It is a remarkable fact that many patients throughout their illness have suffered from practically no derangement of digestion, and have continued to eat and enjoy their usual food. In some mild cases appetite has even been increased.

In other cases a certain amount of gastro-intestinal catarrh has given rise to temporary dietetic difficulties.

In severe cases the tongue has been furred, the bowels constipated, and appetite diminished or lost.

A mild, bland, non-irritating diet, with plenty of fluid, has been generally indicated.

*Drugs.*—It is not without interest to note that arsenic has for long been recognised as an agent having marked influence over the peripheral nerves, and its use in multiple neuritis has been recommended. One of the most recently published treatises on medical treatment states that for ‘alcoholic neuritis preparations of arsenic are sometimes valuable.’ It has also been proposed to treat erythromelalgia by means of the same agent. Arsenic is also advised for Addison’s disease. It is to be hoped that these suggestions have not been acted upon in any of the present cases. The recent experience will have been of service in enforcing the importance of always carefully observing the condition of patients who are taking arsenic in any form.

In the acute stages sedatives have been necessary, and the administration of opium preparations has been imperative. Hypodermic injections of morphine have also been given.

Bromides and chloral have not proved satisfactory in bad cases, and ordinary hypnotics have been of but little good.

Salicylates of quinine and soda have been given in early and comparatively mild cases. We have not been able to observe that iodide of potassium exerted much influence.

Antipyrin, phenacetin, and the like preparations have sometimes proved of temporary benefit in relieving the neuralgic pains.

Purgatives have often been necessary, as a large number of the cases have been much troubled by constipation.

Strychnine is a drug to be avoided in all cases presenting acute manifestations, but is of service when recovery is occurring.

Digitalis must be given in cases where cardiac asthenia occurs.

During convalescence the anæmia will call for bland preparations of iron. Quinine and other tonics may be administered with advantage. It will be well to avoid all preparations of so-called 'medicated wine.'

*Local Applications.*—Fomentations, lotions, ointments, and the like, have been of much service in alleviating some of the local conditions.

The erythromelalgia has generally been relieved by the application of such a preparation as lead and opium lotion. Sometimes hot fomentations applied from time to time have seemed useful.

When itching has been troublesome anti-pruritic measures have often brought temporary relief.

For the keratosis salicylic ointment has been of use.

*Baths* have been indicated in many of the cases, and there can be but little doubt that suitably applied hot water and vapour baths in selected cases would have proved of great service. Unfortunately, in most instances such agencies were not available.

*Massage.*—In the acute stages massage is to be absolutely prohibited. When, however, the neuritic symptoms will allow of gentle movements being made without pain, massage should prove useful if gently applied, and for a short time only, but gradually increased in vigour and duration as the condition of the patient allows.

*Special Exercises.*—During convalescence carefully regulated exercises prove of great service in the re-education of the muscles. In cases of ataxia and marked inco-ordination of the hands and feet Fraenkel's method may be employed with advantage, whereby the affected muscles are again trained in their respective duties.

*Electricity.*—In the resolving stage electricity carefully regulated and applied in the form of the galvanic and

faradic currents, or by means of the electric bath, may prove of great service.

*Convalescence.*—Large numbers of cases are now progressing towards this condition. Doubtless in time most of the patients will recover much of their power, but there is reason to believe that a large number will be permanently injured.

Many of the paralytic and atrophic forms will take many months of the most careful management before much improvement can be expected. As many of these cases, from their alcoholic habits, are particularly predisposed to tuberculosis, it seems undesirable that they should be retained in general hospitals. As soon as possible they should be removed to country districts, or, at all events, so placed as to be able to avail themselves of the restorative influences of sunlight and fresh air.

### Pathology.

A study of the recent outbreak has opened the way for much speculation, and directed attention to many lines of research which will require considerable time and special methods of investigation for full elucidation.

A number of cases submitted to pathological examination are still in their legal aspects *sub judice*, hence detailed reference is obviously impossible at the present time.

The recent epidemic of arsenical neuritis has shown the need for a careful reconsideration of the question of the true ætiology of so-called 'alcoholic' neuritis. Is it possible that cases occurring prior to the outbreak have arisen from the same or a similar cause, and not from alcohol itself? Certainly the frequency of peripheral neuritis in beer-drinkers, and its rarity in spirit-drinkers, would seem to prove conclusively that the amount of alcohol taken was, at all events, not the sole ætiological factor.

But while beer-drinkers, at least in Lancashire and district, have for long been peculiarly prone to develop degenerative processes, especially in nerve and cardiac structures, there is good reason to believe that partakers of

other kinds of alcoholic drinks are also liable, although to a less extent, to similar regressive changes.

Recent researches\* go to show the desirability of submitting all kinds of alcoholic beverage to careful investigation, with a view to the isolation of the various injurious constituents which undoubtedly exist at the present time in so many. Chemical investigation in the near future is likely to throw much new light on their chemical and pathological effects.

Until recent years comparatively little has been definitely known concerning the morbid histology of affections of the nervous system due to arsenic.

Jarschka in 1882 appears to have been the first to suggest that the paralysis occurring in chronic arsenical poisoning was due to a peripheral neuritis, and Putnam seems to have been the earliest to confirm this. Subsequent observations and experiments tend to show that the morbid results are not confined to the distal portions of the nervous system. In arsenical as in other forms of toxic neuritis the lesions are to be looked upon as essentially due to a degenerative process involving spinal, motor, and sensory neurones. As Mott shows, the changes are generally only visible in the remoter portions, and are of the nature of a primary Wallerian degeneration, viz., 'breaking up of the myelin, proliferation of the sheath of Schwann, swelling of the axis-cylinder in some places, attenuation in others, and finally its rupture and destruction.'

In connection with the marked paralysis and extreme atrophy of the extremities which has occurred in many of the recent sufferers, it is of interest to remember that several observers have described changes in the ganglia cells of the anterior horns of the spinal cord.

Regarding the effects of chronic arsenical poisoning on the other tissues of the body but little need be said. A widespread degeneration is characteristic. Most of the organs

\* Brunton, Lauder, and Tunnicliffe, F. W.: 'Concerning Certain Apparently Injurious Constituents of Potable Spirits.' *Lancet*, 1900, December 8.

and muscles of the body present more or less extensive fatty degeneration. Oliver states that 'the degeneration is sometimes as marked as that met with in phosphorous poisoning.' A recognition of this fact throws much light on many of the clinical manifestations.

Our researches tend to show that while arsenic is rapidly eliminated by means of the kidneys, certain tissues retain it long after all means of introduction of the poison have been stopped.

In a fatal case occurring in an elderly woman a trace of arsenic was found in the liver and a very faint trace in the skin taken from the front of the abdomen.

It is to be hoped that the medical histories of all the cases now under observation will be carefully recorded, as thereby much valuable information will be forthcoming respecting the pathology of peripheral neuritis and the pharmacology of arsenic.

## PART III

### CHEMICAL

#### Historical.

UNTIL within the last two months, as far as our researches have been carried, no evidence is to be found as to the presence of arsenic in beer. In the returns of the analyses, made in the Somerset House laboratory, of beers from 1844 to 1897,\* there is nothing to indicate that arsenic was ever contemplated as a possible impurity. The only suggestion that has been met with of such a possibility is made by Dr. Blyth† in these very significant words: 'It is possible for arsenic to be found in beers manufactured from glucose, for in certain kinds of the latter arsenic is occasionally discovered, the substance probably having been introduced by the use of an arsenical sulphuric acid in the process of manufacture.'

#### Examination of Beer for Arsenic.

The number of available methods for the detection of small quantities of arsenic in organic fluids is not large, and each of them is attended by somewhat formidable possible errors, either of judgment or experimentation. Where, however, only extremely minute quantities are likely to be

\* 'Minutes of Evidence taken before the Departmental Committee on Brewing Materials.' London, 1899.

† 'Foods: their Composition and Analysis,' by A. W. Blyth, M.R.C.S., F.I.C., etc. London, 1896.

present, as in the case of the beer which was suspected of causing the chronic arsenical poisoning, the difficulties of the detection of the poison are greatly increased. In this epidemic it became evident, as soon as suspicion had been aroused as to the presence of the arsenic in the beer, that it could only be there in very minute quantity, because the symptoms exhibited by the patients in only a few cases pointed with any certainty to the poison being arsenic.

**Marsh's Test.**—The attempt to obtain evidence of the presence of arsenic in beer by the direct application of Marsh's test is likely to fail unless the poison is there in considerable quantity. In the first place, many of the figures which have been recorded as indicating the delicacy of the test are very misleading, not because of the lack of exactitude in carrying out the test, but because of the manner in which the experimental results are expressed; because of the failure to indicate all the conditions under which the test was carried out; also because of the want of agreement among chemists as to what constitutes the test of delicacy—the smallest actual amount of arsenic placed in the apparatus and revealed, or the strength of the weakest solution submitted to its operation. It may happen that the poison is present in the beer in quantities too small to be revealed under the most favourable conditions. A further and greater trouble is the retarding action which the organic matter of the liquid has upon the evolution of arseniuretted hydrogen. This retardation is not a consistent factor; it appears to vary in accordance with the character of the beer. Beers brewed with the less proportion of sugar, and therefore with the larger proportion of malt, will contain a larger proportion of dextrin; this appears to be in large measure the retarding constituent. To obtain the arsenic from the beer by destruction of the organic matter is the only satisfactory method to adopt if an indication is to be obtained with Marsh's test. This may be effected by evaporating to dryness, and then either distilling with strong hydrochloric acid or with a mixture of hydrochloric acid and ferrous chloride (Beckurts). In submitting the

acid distillate to the apparatus, the precautions recommended by the Committee of the National Health Society\* should be adopted in order to avoid loss of arseniuretted hydrogen. The value of this method is restricted to the actual detection of the poison, and notwithstanding the ingenious quantitative arrangement of Sanger,† it does not readily lend itself to the valuation of, and discrimination between, very minute quantities of arsenic.

**Reinsch's Test.**—As in the case of Marsh's test, comparative results are almost if not quite unobtainable. Although it is generally conceded that this method possesses an advantage in withdrawing all the arsenium from the fluid, it is frequently overlooked that when large quantities of organic matter are present, boiling for several hours may be required for entire separation.

With Reinsch's test it is not easy to verify the nature of the deposit upon the copper when present in minute quantity. This drawback is serious, in view of the fact that when used for organic fluids the copper, upon being heated, may give a layer of copper chloride and organic matter. Not only is the copper liable to be stained by other substances, but when the arsenium exists as a very thin film it is easily oxidized in drying the copper foil, and may be to a large extent lost before sublimation is properly effected.

Sufficient has been said to show that the most serious drawback attaching to the two foregoing tests is the possibility of overlooking quantities of arsenic which would in ordinary circumstances be called small, but which in such an article as beer, consumed as it is sometimes in large quantities, are in reality very large and dangerous.

**Fleitmann's Method.**—This depends upon the liberation of hydrogen by heating together metallic zinc and a strong solution of caustic soda or potash. If a little arsenical solution be introduced, arseniuretted hydrogen is produced, and is allowed to act upon a piece of white filter-paper moistened with a drop of solution of silver nitrate. A black colour is

\* *British Medical Journal*, 1883, vol. i.

† *American Chemical Journal*, 1891, xiii. 431.



obtained, due to the production of metallic silver. Aluminium or magnesium may be substituted for the zinc. This is an extremely delicate qualitative test, but it may give deceptive indications because of the ease with which the silver salt is reduced by the action of light or by the organic matter of the paper.

**Biological Reaction.**—Bujwid,\* Morpurgo,† Gosio,‡ and others have suggested the use of the mould *Penicillium brevicaulis* as a means whereby small quantities of arsenic may be detected. A properly prepared nutrient medium is impregnated with the arsenical matter and sown with the mould. After a more or less lengthy stay in the incubator, the characteristic alliaceous odour of arseniuretted hydrogen can be detected. It is stated that 0.01 milligramme of arsenic can be detected after an incubation of twenty-four hours.

**Gutzeit's Test.**—To ascertain with anything like certainty the absence of arsenic from a complex organic liquid like beer by means of any of the foregoing tests is a matter of more than ordinary difficulty. Quantities of the poison, which could be ignored with safety in many substances, assume dangerous proportions in beer, which is partaken of in such large quantities and so regularly by many people. It is therefore imperative that the utmost care should be exercised to avoid falling into the error of deciding that a beer is arsenic-free if such is not the case. The manipulations necessary to the operating of Reinsch's and Marsh's tests introduce the danger of losing a trace of arsenic before the final stage is reached. These considerations suggest the use of Gutzeit's test, in the operation of which the manipulations are reduced to a minimum. A negative result in the presence of arsenic is an extremely remote possibility.

This method was recommended and used by Vulpius,§ Flückiger,|| and Ritsert¶ for the detection of arsenic in

\* *L'Union Pharmaceutique*, xlvi. 293. † *Oesterr. Chem. Zeitung*, i. 167.

‡ Allbutt, T. C.: 'A System of Medicine.' London, 1897, vol. ii., 989.

§ *Apotheker Zeitung*, 1889, April 10.

|| *Archiv der Pharmacie*, (3), xxvii. 1.

¶ *Pharmaceutische Zeitung*, 1889, 104.

glycerin. Without tracing the history of the process, it will suffice to say that this process, when conducted in the manner and with the precautions suggested by Siebold\* and by Paul and Cownley,† may be relied upon not only to give valuable negative indications, but, if used with skill and discretion, to give information as to the approximate proportion of arsenic present. As originally suggested, the test consisted in the action of arseniuretted hydrogen, produced by the action of hydrochloric acid upon zinc in the presence of arsenic, upon a piece of filter-paper moistened with a drop of solution of silver nitrate. As adopted in the British Pharmacopœia for testing glycerin, a solution of mercuric chloride is substituted for the silver nitrate solution. This latter solution (silver nitrate) is decidedly the more sensitive, but it possesses two very serious disadvantages—darkening is induced by light and by the organic matter of the paper, and it is very readily affected by sulphuretted hydrogen. The action of arseniuretted hydrogen upon a dried spot of mercuric chloride solution on filter-paper results in the production of a warm yellow, orange or orange-brown colour, according to the quantity of arsenic present or the length of time the action is allowed to continue. The mercury compound, or, rather, compounds, produced is stated by Partheil and Amort‡ to be first  $\text{AsH}(\text{HgCl})_2$ , and subsequently  $\text{As}(\text{HgCl})_3$ . As in the case of the silver salt, so in the mercury salt sulphuretted hydrogen is a disturbing factor, but to a very much less extent. Generally sufficient sulphur must be present to produce on lead subacetate paper a stain with a metallic lustre before the mercuric chloride paper is affected at all.

A series of experiments made to ascertain the relative sensitiveness of mercuric chloride paper and lead subacetate paper showed that 0.04 milligramme of potassium metabisulphite produced a strong stain with a distinct metallic lustre on the lead paper, but only in the best light could the

\* *Year-Book of Pharmacy*, 1889, 416.

† *Pharmaceutical Journal*, (3), xxiv. 685; *Ibid.*, (4), x. 688.

‡ *Berichte der deutschen chemischen Gesellschaft*, xxxi. 594.

very faintest shade be detected on the mercuric chloride paper. When the quantity of the potassium salt was reduced to 0.01 milligramme, the stain on the lead paper was scarcely diminished in any degree, but on the mercuric chloride paper no coloration was apparent. The potassium metabisulphite was used because of its stability as compared with other sulphurous acid compounds, and because it is so generally used in brewing operations.

The first stages of staining due to the sulphuretted hydrogen simulate the yellow stain caused by arsenic, but a very little experience serves to discriminate between the two. The arsenical stain, which must be examined by daylight, is always, even when extremely faint, of a rich warm yellow colour, and increases in intensity through a bright orange colour to, when intense, a rich orange-brown colour; the sulphur stain is always colder in tone, when very faint being of a dull lemon colour, passing through a leaden yellow to a dull leaden-brown colour. In order to obviate the action of sulphuretted hydrogen it has been proposed that oxidation of the sulphur compounds by the agency of iodine should be effected, but this needs to be carried out with the greatest care, and excess of iodine must be avoided by making use of starch mucilage, which should only be coloured the faintest blue. If excess of iodine is introduced, not only is the generation of the hydrogen retarded, but vapour of iodine causes the filter-paper to assume sometimes a blue colour, probably due to the presence of acid vapour producing the well-known cellulose reaction, and sometimes a brown colour.

Not only is it necessary to use zinc and hydrochloric acid free from arsenic, but also free from sulphur. If these are available, the best method to adopt to diminish the risk of error of wrong interpretation of the stains is to eliminate, as far as possible, from the beer all substances likely to give rise to sulphuretted hydrogen.

### The Application of Gutzeit's Test to the Testing of Beer for Arsenic.

**Preparation of Beer.**—The most important and essential step in preparing the beer for testing is the elimination of sulphurous acid gas in order to obviate, as far as possible, the effects of sulphuretted hydrogen upon the test-papers. Sulphur compounds are almost always present in beer as 'preservatives,' and are introduced in various forms and under various names, such as 'bisulphite of lime,' 'monocalcic sulphite,' 'K.M.S.' (potassium metabisulphite), 'kalisaline' (potassium sulphite), 'sulphosite,' 'phylax' (sodium bisulphite), the bisulphites of soda, potash and magnesia, the sulphites of lime, potash, soda and magnesia, and sulphurous acid. A plan which is effectual is to acidify the beer, evaporate to dryness on a water-bath, and then dissolve the residue in distilled water. In order to obtain comparative results it is also important to ensure that the arsenic present is in the arsenious condition before being tested. The state in which it is present in the beer can only be a matter of conjecture. Probably it is introduced as an arsenate derived from the arsenical sulphuric acid with which the glucose is made; but if sulphites are used in the finished beer some of it may be reduced to the arsenious state. It is, therefore, always advisable to boil the concentrated beer with a little sulphurous acid to insure reduction of the whole of the arsenic compound; in some cases it has been found that this has the effect of increasing the arsenical stain as compared with stains obtained from the same beer which had not been so treated with sulphurous acid. The whole of the sulphurous acid must be eliminated by thorough boiling.

**The Reagents.**—The hydrochloric acid and the zinc should be rigorously tested for arsenic by allowing them to react, and causing the evolved hydrogen to play upon a test-paper of mercuric chloride for three or four hours at least. The so-called pure hydrochloric acid of the shops frequently reveals more than traces of arsenic when submitted to

this test. To prevent disappointment only the 'redistilled' article should be 'accepted in the first instance. Zinc rod having a diameter of 5 millimetres\* is the most suitable for the purpose, as it is easily broken, and the length therefore readily adjusted. Some samples are much less brittle than others; these should be avoided as they contain metallic impurities, which by their presence accelerate the evolution of the gas to such an extent as to cause excessive and troublesome frothing. The brittle samples which maintain a metallic surface when placed in hydrochloric acid are the most suitable. The use of platinic chloride is to be avoided on account of the property it sometimes manifests of fixing the arsenium—a feature which is sometimes overlooked when using it in Marsh's test. For making the test-papers a solution of mercuric chloride, 1 part in 20 parts of distilled water, is used. The strong solution of subacetate of lead of the Pharmacopœia answers excellently for preparing the lead test-papers.

**The Test.**—Nine c.c. of prepared beer (reduced) is diluted with distilled water to 15 c.c., and finally made up to 20 c.c. with pure hydrochloric acid (specific gravity, 1.16). This mixture is equally divided between three test tubes of equal length and diameter. Other 6 c.c. of prepared beer, in this case not reduced with sulphurous acid, is diluted with water to 10 c.c., and made up with hydrochloric acid to 13.3 c.c., and divided between two test-tubes. Plugs of cotton-wool are prepared for loosely stopping the mouths of the tubes, and four discs of pure white filter-paper of close texture are each moistened with one drop, from the same small glass rod, of the solution of mercuric chloride. In addition, one paper disc is moistened with one drop of solution of lead subacetate. The mercuric papers are used dry, but the lead paper in the moist condition. When everything is prepared, in each test-tube is placed a piece of zinc rod 15 mm. long and 5 mm. in diameter, the cotton-wool plugs are inserted and two mercuric papers and the lead paper are placed as

\* This can be obtained from most of the first-class dealers in fine chemicals.

caps on the first three test-tubes, and two mercuric papers are placed on the second two test-tubes. The mercuric tubes are duplicated because even when the utmost has been done to insure uniform conditions in each test-tube the hydrogen is occasionally not evolved at an equal rate in each. When the rate of evolution is very sluggish in any tube, it may be accelerated by very gentle warmth. In the absence of arsenic and an excessive quantity of sulphur compounds the mercuric papers remain unstained, but in the majority of cases a brown stain is found on the lead paper. Arsenious acid in the proportion of 0.01 ( $\frac{1}{100}$ ) gr. per gallon will produce a faint yellow stain on the mercuric papers in one hour. One hour seems, therefore, a suitable time limit for the process, beyond which there is no need to go.

In order to obtain an approximate value of the amount of arsenic present, standard tests with weighed quantities of arsenious acid should be put up in the same way, taking care to maintain uniform conditions. These must be carried out with an arsenic-free beer, otherwise if water is used an error of as much as 50 per cent. may arise, the evolution of the gas in the beer being scarcely more than one-half the rate it is in water. With each set of experiments for the day it is desirable to put on a new set of standards, as the colours are to a certain extent affected by light. The standards useful are 0.05 mgm. of arsenious acid ( $\text{As}_2\text{O}_3$ ), 0.04 mgm., 0.03 mgm., 0.02 mgm., 0.01 mgm., and 0.005 mgm. In addition to the standards, control tests of reagents made up with water and beer should always be carried out. In this way one comes within measurable distance of obtaining uniform conditions of testing.

The chief and undoubted value of this test is the certainty with which it indicates the presence of arsenic; if one part of arsenic is present in 7,000,000 (seven million) parts of fluid, it will indicate its presence. There is absolutely no danger of a poisonous quantity being overlooked. The errors which are likely to arise are due to its extreme delicacy; they may be avoided if due care is taken. But other errors may be introduced if the utmost care is not taken to exclude

contaminated materials and apparatus. For instance, test-tubes should not be used a second time unless they have been thoroughly cleansed by boiling in moderately dilute pure sulphuric acid; zinc rod should on no account be used again if it was previously used in an arsenical tube.

### The Results obtained with Gutzeit's Test.

The opportunities for applying this test and arriving at a true estimate of its value have been great. One of the largest breweries in the Manchester district submitted for examination all the different beers which they had upon the premises, as well as others which were specially brewed, with a view to elucidating the matter in hand. In order to estimate aright the influence of sulphur compounds in the application of the test, a sample of beer was brewed with an average amount of glucose free from arsenic, and a good proportion of sulphurous preservative. By following the procedure set forth, no liability to misinterpret the results obtained was exhibited. Numerous experiments have been made to gauge its trustworthiness by making additions of arsenious acid to arsenic-free beers, and submitting them to an operator who was ignorant of their composition. Although a process of estimation such as this appears to lack that definiteness which is ascribed to a gravimetric analysis, it is questionable if really it is any less accurate when the numerous operations of a gravimetric analysis are considered. But no further claim is made for the following figures than that they are close approximations to the actual proportion of arsenic present in the beers.

In order to safeguard an important examination of this character, and to arrive at results which might be presented with some degree of confidence, it has been necessary to make between 600 and 700 experiments.

In the following tables the results of the estimations are expressed in grains of arsenious oxide (white arsenic,  $As_2O_3$ ) per gallon. From a purely scientific point of view it would, perhaps, have been preferable to use the

element, arsenium (As), as the basis of calculation; but we have adopted the former alternative in order to facilitate a correct apprehension of the dosage.

Table of Beers, Porters, Stouts, etc.

| ARTICLE.            | ARSENIOUS OXIDE.<br>GRAINS PER GALLON. | REMARKS.                      |
|---------------------|--|-------------------------------|
| BREWERY A.          |  |                               |
| 1. Draught beer     | Nil                                    | Bought since outbreak.        |
| 2. " "              | "                                      | "                             |
| 3. Bottled ale ...  | 0'04                                   | Bought Nov. 27.               |
| 4. " ...            | Faint trace                            | From brewery; brewed Aug. 8.  |
| 5. " ...            | 0'18                                   | " " Nov. 9.                   |
| 6. " ...            | 0'28                                   | " " Oct. 29.                  |
| BREWERY B.          |  |                               |
| 7. Draught bitter   | Nil                                    | From brewery; brewed Nov. 15. |
| 8. Bottled stout    | Very faintest trace                    | " " " 7.                      |
| 9. Pale ale ...     | Faintest trace                         | " " " 14.                     |
| 10. Draught stout   | 0'03                                   | " " " 14.                     |
| 11. Pale ale ...    | 0'16                                   | Bought Nov. 15.               |
| 12. Draught ale ... | 1'40                                   | From brewery, September.      |
| BREWERY C.          |  |                               |
| 13. Beer ...        | Nil                                    | From brewery. Malt only.      |
| 14. " ...           | "                                      | " "                           |
| 15. Wort ...        | "                                      | " "                           |
| 16. Beer ...        | "                                      | " "                           |
| 17. " ...           | "                                      | " "                           |
| 18. " ...           | Very faintest trace                    | " "                           |
| 19. " ...           | Very faintest trace                    | " "                           |
| 20. " ...           | 0'01                                   | " Malt and Glucose.           |
| 21. " ...           | 0'04                                   | " "                           |
| 22. " ...           | 0'04                                   | " "                           |
| 23. Pale ale ...    | 0'05                                   | " "                           |
| 24. Beer ...        | 0'05                                   | " "                           |
| 25. " ...           | 0'07                                   | " "                           |
| 26. " ...           | 0'07                                   | " "                           |
| 27. " ...           | 0'08                                   | " "                           |
| 28. " ...           | 0'09                                   | " "                           |
| 29. " ...           | 0'09                                   | " "                           |
| 30. " ...           | 0'10                                   | " "                           |
| 31. " ...           | 0'11                                   | " "                           |
| 32. Stout ...       | 0'14                                   | " "                           |
| 33. Beer ...        | 0'14                                   | " "                           |
| 34. " ...           | 0'14                                   | " "                           |
| 35. " ...           | 0'14                                   | " "                           |
| 36. " ...           | 0'18                                   | " "                           |
| 37. " ...           | 0'20                                   | " "                           |



Table of Beers, Porters, Stouts, etc.—*continued.*

| ARTICLE.            | ARSENIOUS OXIDE.<br>GRAINS PER GALLON. | REMARKS.             |
|---------------------|--|----------------------|
| BREWERY D.          |  |                      |
| 38. Stout... ..     | Faintest trace                         | From brewery.        |
| 39. Bitter beer ... | 0·07                                   | "                    |
| 40. Best XX ...     | 0·07                                   | "                    |
| 41. Common X ...    | 0·09                                   | "                    |
| BREWERY E.          |  |                      |
| 42. X ale... ..     | Nil                                    | From brewery.        |
| 43. Stout... ..     | "                                      | "                    |
| 44. Luncheon ale    | "                                      | "                    |
| BREWERY F.          |  |                      |
| 45. Best beer ...   | Nil                                    | From brewery.        |
| 46. Stout... ..     | "                                      | "                    |
| 47. Common beer     | 0·03                                   | "                    |
| BREWERY G.          |  |                      |
| 48. Beer ... ..     | Nil                                    | From brewery.        |
| BREWERY H.          |  |                      |
| 49. Beer ... ..     | Faintest trace                         | From brewery.        |
| VARIOUS.            |  |                      |
| 50. Beer ... ..     | Nil                                    | Bought.              |
| 51. " ... ..        | "                                      | "                    |
| 52. " ... ..        | "                                      | "                    |
| 53. " ... ..        | "                                      | "                    |
| 54. " ... ..        | "                                      | "                    |
| 55. " ... ..        | "                                      | "                    |
| 56. " ... ..        | "                                      | "                    |
| 57. " ... ..        | "                                      | "                    |
| 58. " ... ..        | "                                      | "                    |
| 59. " ... ..        | "                                      | "                    |
| 60. " ... ..        | "                                      | "                    |
| 61. " ... ..        | "                                      | "                    |
| 62. " ... ..        | "                                      | "                    |
| 63. " ... ..        | "                                      | "                    |
| 64. " ... ..        | "                                      | "                    |
| FROM PATIENTS.      |  |                      |
| 65. Beer ... ..     | Nil                                    | Brewery A., Nov. 28. |
| 66. " ... ..        | 0·02                                   | " "                  |
| 67. " ... ..        | 0·03                                   | " "                  |
| 68. Stout... ..     | 0·04                                   | " "                  |
| 69. Beer ... ..     | 0·07                                   | " C.                 |
| 70. " ... ..        | 0·07                                   | " "                  |
| 71. Porter ... ..   | 0·08                                   | " C.                 |
| 72. Beer ... ..     | 0·14                                   | " A.                 |
| 73. " ... ..        | 0·14                                   | " A.                 |

The various beers, etc., may be placed in four groups :

- (a) Exceeding  $0.1$  ( $\frac{1}{10}$ ) gr.  $\text{As}_4\text{O}_6$  per gallon.
- (b) Exceeding  $0.03$  ( $\frac{1}{30}$ ) gr.  $\text{As}_4\text{O}_6$  per gallon, but less than  $0.1$  ( $\frac{1}{10}$ ) gr.
- (c) Less than  $0.03$  ( $\frac{1}{30}$ ) gr.  $\text{As}_4\text{O}_6$  per gallon.
- (d) Gave no reaction in one hour, and returned as arsenic-free.

The specimen marked No. 12 is worthy of special notice. It was speedily recognised as having a very unusual effect upon the persons drinking it, and as early as November 7 the brewer had it submitted to analysis, but nothing deleterious was found in it. However, other samples were sent for examination, and these were variously reported upon as severally containing  $0.8$  gr. (approximately) per gallon,  $1.12$  gr. per gallon, and  $1.36$  gr. per gallon. Without any previous preparation  $20$  c.c. of this beer gave a distinct mirror in a Marsh-Berzelius tube upon being heated for one hour ; there was no difficulty in obtaining distinct recognisable crystals of arsenious oxide with Reinsch's test.

Nos. 18 and 19 were brewed from all malt and hops, but were nevertheless contaminated with arsenic. The brewing materials of this particular firm were, with the exception of the brewing sugars, found to be free from arsenic. Subsequent brews, however, have been found to be free from arsenical contamination. The suggestion that arsenic is present in the brewing apparatus, such as india-rubber tubing, is worth investigation ; but a much more likely source of contamination is to be found in the plant of the brewery, which has been used for brewing arsenical beers for at least several months, as well as in the yeast, which will probably be found to be contaminated with arsenic after having undergone a period of fermentation in an arsenical beer.

### The Introduction of Arsenic into Beer.

The quantity of arsenic discovered in the first beers which were examined indicated that whatever the material might be which was the means of introduction, the poison must be

present in that particular material in quantities more pronounced than traces. How it came about that possible sources of introduction external to the brewery were neglected in the investigation has already been explained. Suspicion naturally fell upon those substances in the preparation of which sulphuric acid is used. There is an impression among manufacturers that the better varieties of sulphuric acid are still made from brimstone. The stress of competition is sufficiently great to tempt some to use the pyrites sulphuric acid even if the brimstone acid could be obtained. There is no doubt that the pyrites acid can be, and is, effectually freed from arsenic if so required. Still, the danger is not a hidden one to those who are familiar with the state of trade in this commodity. Unfortunately, or perhaps fortunately, the suspicion proved to be well founded, and considerable quantities of arsenic were found in invert sugar.

**Invert Sugar.**—This is produced by the action of sulphuric acid, about 2 or 3 per cent., upon cane sugar under the influence of heat. The resulting compound consists of glucose and fructose. The free acid is neutralized by the addition of chalk, and the calcium sulphate is separated by filtration. In order to obtain a preparation of a paler colour, the liquid is more or less decolorised by passing it through animal charcoal. It is then brought to a suitable consistence by evaporation. Any arsenic present in the sulphuric acid is almost certainly retained in the sugar as an arsenate. The inversion of the sugar may be carried out to a greater or less extent, in accordance with the length of time the acid is allowed to act upon the sugar, and with the temperature employed. The proportion of fructose (lævulose) will increase with the increase of time or temperature. Lævo-saccharum, lævuline, lævulose-saccharum are invert sugars in which the process has been carried out until the opticity is lævogyre. Dexvert and dextro-saccharum are invert sugars not so fully inverted. Many other names are used to designate the invert sugars of particular firms.

**Glucose.**—This, in the brewing and confectionery in-

dustries, is a technical term having a meaning quite distinct from its purely chemical significance. It embraces all those substances which are more correctly denominated 'starch-sugar.' Starch—maize starch, sago starch, rice starch, or potato starch—is submitted to hydrolysis by means of dilute sulphuric or hydrochloric acid. The conversion of the starch ( $C_6H_{10}O_5$ ) into dextrose ( $C_6H_{12}O_6$ ) proceeds more or less rapidly according to the proportion of acid employed, and the temperature to which the mixture is subjected. From 6 to 8 lb. of sulphuric acid is the quantity usually employed for the conversion of 1 cwt. of starch. When solution of iodine ceases to give the starch reaction, and alcohol in the proportion of two volumes to one volume of cooled liquid no longer produces a precipitate, conversion is then considered to be almost complete. The acid is neutralised with chalk or whiting. Sykes\* says in this connection, 'Tested with litmus paper, the liquid shows only a faint reaction'—that is, we presume, a faint acid reaction. If this is correct, the probability of calcium arsenate, supposing this salt to be formed, remaining in the sugar is almost converted into a certainty. After removal of the calcium sulphate, the liquid is more or less decolorized by treatment with animal charcoal, and then evaporated in vacuum pans to a suitable concentration for crystallisation. On the Continent a considerable proportion of the glucose would seem to be made from potato starch, and that of American origin from maize starch. The process as followed in America differs in two important particulars from that followed in this country. In order to obtain the maize starch free from oil, which the fruit contains to the extent of from 6 per cent. to 7.5 per cent., the embryo or germ has to be separated by a process of sifting and winnowing. It appears that the American manufacturers largely use hydrochloric acid for hydrolysing the starch, and neutralise by means of soda; in this manner the operation of filtration is obviated, but a proportion of

\* Sykes, W. J.: 'The Principles and Practice of Brewing.' London, 1897.

sodium chloride remains in the finished product. Glucose contains from 60 to 80 per cent. of dextrose; maltose is often also present, the proportion sometimes reaching 14 per cent. or even more; the residue consists of unfermentable carbohydrates, dextrine, mineral matters, and water.\*

Table of Brewing Glucoses and Invert Sugars.

| ARTICLE.                | AS <sub>4</sub> O <sub>6</sub> PER CENT. | REACTION WITH LITMUS. |
|-------------------------|--|-----------------------|
| ENGLISH.                |  |                       |
| 1. Invert sugar ... ..  | Nil                                      | Acid.                 |
| 2. " " " " " "          | "  | Neutral.              |
| 3. " " " " " "          | 0'03                                     | Acid.                 |
| 4. " " " " " "          | 0'03                                     | "                     |
| 5. " " " " " "          | 0'04                                     | "                     |
| 6. Glucose... ..        | Nil                                      | "                     |
| 7. " (for stout) ... .. | "  | "                     |
| 8. " " " " " "          | "  | "                     |
| 9. " " " " " "          | 0'04                                     | "                     |
| 10. " " " " " "         | 0'05                                     | "                     |
| 11. " " " " " "         | 0'05                                     | "                     |
| AMERICAN.               |  |                       |
| 12. Glucose... ..       | Nil                                      | Faintly acid.         |
| 13. " " " " " "         | "  | Neutral.              |
| 14. " " " " " "         | "  | "                     |
| 15. " " " " " "         | "  | "                     |
| 16. " " " " " "         | "  | "                     |
| 17. " " " " " "         | "  | "                     |
| 18. " " " " " "         | "  | "                     |
| 19. " " " " " "         | "  | "                     |
| 20. " " " " " "         | "  | "                     |
| 21. " " " " " "         | "  | "                     |
| UNKNOWN ORIGIN.         |  |                       |
| 22. Glucose... ..       | Nil                                      | Acid.                 |
| 23. " " " " " "         | "  | "                     |
| 24. " " " " " "         | Faintest trace                           | "                     |
| 25. " " " " " "         | "  | "                     |
| 26. " " " " " "         | "  | "                     |

The proportion of sugar used for displacing malt varies within very wide limits. Some brewers do not exceed 5 lb.

\* Valentin, W. J. : *Journ. Soc. Arts*, xxiv. 404.

of sugar per barrel of 36 gallons; this quantity represents about 10 per cent. of malt. Others, however, use very much more, displacing as much as 30 or 40 per cent. of malt. In one instance we have found as much as 50 per cent. of the malt to be substituted by sugar. Beer No. 12 was brewed from produce of these proportions. Arsenical glucose, containing 0.04 per cent. of arsenious oxide, was used; the quantity of beer produced at the gravity stated by the brewer indicated that it contained the soluble matter of  $\frac{3}{4}$  lb. of sugar per gallon—equivalent to 2 gr. of arsenious oxide. From the table it will be seen that analysis only discovered about three-quarters of this quantity. It is extremely likely that the yeast is responsible for some of the deficiency as well as the brewing plant, which has certainly been found to contaminate subsequent brews made with arsenic-free ingredients.

The retention of the arsenic in the sugar suggested the testing of the different kinds of sugar as to their reaction with litmus. If in the manufacture of the sugar the acid were completely neutralised, it would be almost safe to infer that calcium arsenate would be precipitated, otherwise, as already mentioned, it is possible it remains in solution in the acid liquid. Although we have not had an opportunity of making any investigation on these lines, it is very significant that all the arsenical sugars have a marked acid reaction. It is also noteworthy that the American samples, with one exception, are neutral.

That arsenical glucose is not a new danger is apparent from the following note by Blyth.\* 'M. Ritter found:

|                    |     | 'Grm.  |         |     |             |
|--------------------|-----|--------|---------|-----|-------------|
| ' In white glucose | ... | 0.0105 | arsenic | per | kilogramme. |
| „ yellow           | „   | 0.0170 | „       | „   | „           |
| „ black            | „   | 0.1094 | „       | „   | „           |

Clouet, in the examination of a very large number of arsenical glucoses found as a minimum 0.0025 grm., as a

\* Blyth, A. W.: 'Foods: their Composition and Analysis.' London, 1896.

maximum 0.0070 grm., and as a mean 0.0051 grm. metallic arsenic per kilogramme (T. Clouet, Du glucose arsenical. Ann. d'Hygiène Publique, xlix., January, 1878). Assuming Ritter to mean arsenious oxide by 'arsenic,' it will be seen that between his maximum (0.01 per cent.) and the maximum obtained by Clouet (0.001 per cent. [ $7 \text{ As} = 10 \text{ As}_4\text{O}_6$ ]) there is a very considerable difference. But even Ritter's highest figure is only one-third to one-fifth of the quantities found during the present epidemic of arsenical poisoning. It should be pointed out that although some of the arsenical glucoses appeared at first to be of different origin, further inquiries, persistently made, ultimately elicited the fact that the samples which came into our hands emanated from one firm only.

Among other articles we have examined are malt,\* hops, gypsum, caramels of different kinds, finings, 'bisulphite of lime,' 'monocalcic sulphite,' potassium meta-bisulphite, cane-sugar, etc., but in none of these substances is there arsenic sufficient to account for the excessive amount which has been discovered in many beers.

### Sulphuric Acid.

The very general use in this country of sulphuric acid for the conversion of starch into glucose, and the general practice now prevailing of using arsenical pyrites for the manufacture of sulphuric acid, give great importance to the question of the possible arsenic content of sulphuric acid. Unfortunately, we were not able to secure a specimen of the acid which was inculpated in the manufacture of the poisonous glucose. We have observed, however, that Professor Harold Dixon† stated it contained 'more than

\* Minute traces of arsenic have been detected in samples of malt. This is hardly a matter for surprise because of the method often adopted for kilning the malt. A portion of the products of combustion of the fuel will come into contact with the grain, and thus contaminate it. Macadam (*Pharm. Journ.* [3], ix. 538) in 1878 found soot to contain as an average quantity 0.1 per cent. of arsenious oxide.

† *Lancet*, December 1, 1900, 1602.

1·4 per cent. by weight of arsenious acid.' A journal\* which is more than usually well informed upon matters connected with the sulphuric acid industry says: 'Sulphuric acid made from Tharsis pyrites seldom contains more than 0·21 per cent. by weight of arsenious acid, and that from Rio Tinto pyrites seldom exceeds 0·41 per cent. of the same constituent.' Dott† found 0·17 per cent. of arsenious oxide in commercial sulphuric acid, and Buchner‡ determined the proportion in a sample of English oil of vitriol, and found it to be 0·13 per cent. The excessive quantity present in the incriminated acid demands some other explanation than that furnished by the very meagre literature on the subject. As long ago as 1887 Dr. Clark§ pointed out the danger there was of manufacturers of sulphuric acid accepting pyrites as free from arsenic, while really they contained a considerable quantity. He gave an instance in which a specimen of pyrites had been certified 'by a well-known French chemist as free from arsenic'; this he (Dr. Clark) found to contain 0·149 per cent. of arsenic. Increased attention to the material from which the acid is made is a certain consequence of the present calamity.

### Excretion of the Arsenic.

In twelve cases we have examined the urine of patients with negative results. The urine of one patient has been examined on four occasions, and each time distinct evidence of the presence of arsenic was obtained. Three other cases also exhibited traces of the poison. We have been very fortunate in being able to test on two occasions the milk of a suckling mother suffering from arsenical neuritis, but were unable to detect the faintest trace of arsenic. The desquamated skin of a patient—collected at one gathering—amounted to 2·605 grammes; this was carefully dried and submitted to distillation with concentrated hydrochloric acid.

\* *Chemical Trade Journal*, December, 1900, 444.

† *Pharm. Journ.* (3), xxi. 475.

‡ *Chem. Zeitung*, xv. 13.

§ *Journ. Soc. Chem. Ind.*, 1887, vi. 352.



On submitting a portion of the acid distillate to Marsh's test, a very dense mirror was obtained in a very short time. The actual proportion of arsenic to be found in the skin is a matter claiming further investigation.

### Dosage.

The variations in the arsenic contents of the contaminated beers has been so great as to make it impossible to ascertain the amount of poison inhibited by an individual. Taking as a basis for calculation a beer, partaken of by a patient, in which was found 0·14 grain of arsenious acid per gallon, and supposing a half-pint to be the quantity consumed at one time, it appears that approximately  $\frac{1}{100}$  of a grain is the dose of arsenic taken. The average medicinal dose of the drug may be accepted as  $\frac{1}{30}$  of a grain ( $\frac{1}{80}$  to  $\frac{1}{15}$  is the official dosage), so that an average medicinal dose will be inhibited in three glasses of beer. The actual quantity of beer consumed by some of the patients seen must reach at least a gallon per diem; and this is quite frequently exceeded. In such cases the daily dose will be about  $\frac{1}{6}$  of a grain, which would generally be considered to be likely to produce toxic results. But it must be remembered that many beers have been examined containing decidedly more arsenic than the one mentioned, and in one in particular ten times this quantity was found. There is, therefore, no reason to doubt that the beer has been an efficient cause in the production of the recent epidemic of peripheral neuritis.

In connection with the question of dosage, it is of clinical interest to remember that peripheral neuritis may occur from the medicinal administration of arsenic. Dr. Railton\* has shown that an aggregate quantity of 6·3 grains administered in the form of Fowler's solution, 10 drops three times a day after food, and continued for three weeks, is capable of producing peripheral neuritis in a girl of twelve.

Dr. Raw has recorded an interesting observation regarding the length of time necessary to produce the symptoms of

\* Railton, T. C.: 'Cases of Peripheral Neuritis following Chorea treated with Arsenic.' *Medical Chronicle*, 1899-1900, 3 S., vol. ii., 315.

arsenical neuritis. A man was admitted to the Mill Road Infirmary, Liverpool, on December 1. He had been a teetotaler for six months until Sunday, November 24. He drank 36 pints of beer in three days, and then stopped; forty-eight hours afterwards he was seized suddenly with pain in the stomach, intense itching of the skin, tingling of the feet and hands, and general malaise. Arsenic was found in his urine the day after admission, and the next day. The symptoms soon subsided, and he was discharged recovered in a week.

### Summary.

The cases investigated presented in various degrees the characteristic manifestations of chronic arsenical poisoning. Arsenic was found in the secretions and the tissues of the affected persons.

In the beer partaken of by the patients was found sufficient of the poison to account for all the symptoms exhibited. Such beer was traced to the breweries, and further investigation made clear by what means the arsenic found entrance into the beverage, and the glucose thus incriminated proved to contain quantities of arsenic quite sufficient to account for all the poison found in the beers.

A consideration of these facts will show that no great difficulty should be experienced in obviating a repetition of the recent alarming and distressing epidemic. This may be done (1) by the adoption of a standard test for arsenic to which all samples of beer must conform, and (2) by a regulation being promulgated by the sanitary or other authorities providing that no sulphuric acid shall be allowed to enter into the composition of any food or drink unless it is found to be arsenic-free as tested by a standard test.

PART IV  
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With the Overseas Experiments









