before she had left her bed, severe pain occurred in the right hypochondrium. She herself soon afterwards felt a "lump" in that region which was tender to pressure, and she drew her doctor's attention to it. During August and September she had repeated attacks of most severe pain in this swelling. They were accompanied by vomiting and profuse perspirations, but there were no rigors. She did not suffer from jaundice or notice any alteration in the colour of the stools. She stated that during each attack of pain the tumour in the abdomen increased markedly in size.

On examination, it was easy to make out a tense pyriform tumour in the situation of the gall bladder, which extended down almost to the level of the umbilicus, and was very tender on pressure. She was kept in bed for several weeks, and, by rest, great improvement occurred, so that all her pain subsided and the tumour diminished so as to be only doubtfully perceptible on palpation. When she was allowed again to be up and to walk about relapse quickly occurred. On December 10th I operated, opening the inflamed and somewhat thickened gall bladder, stitching it to the abdominal wall and inserting a drainage tube. It contained a quantity of muco-pus and inspissated bile, but no gall stones. Then and on several subsequent occasions cultures of the fluid were made, and yielded a pure growth of *Bacillus typhosus*. In January, 1908, the typhoid bacillus was no longer found in the discharge, but a very short Gram-negative bacillus was present. On February 3rd the drainage tube was removed, and on March 10th the patient went home. She was then in good health and free from all pain, but the sinus still furnished some glairy discharge. She continued well, except on occasions when the discharge was retained by a temporary closure of the fistula; and in November, 1908 (seven months after leaving hospital) the fistula healed securely. About the same time she became pregnant. She enjoyed excellent health throughout her pregnancy, having no trouble whatever with the gall bladder. The child, which was her twelfth, was born on August 20th, 1909, after an easy labour. She remained well until the middle of October, when pain and the former tense swelling were once more felt in the right hypochondrium; and after several recurring attacks of the pain and vomiting she came back under my care. I reopened the sinus without much difficulty and reintroduced a small drainage tube. A pure culture of *Bacillus typhosus* was again obtained from the discharge on four different occasions. In December bile began to flow freely from the tube and the typhoid bacillus was still in pure culture. Dr. Carl Browning, who conducted the bacteriological investigations, has referred to the case in a lately published paper entitled "Latent and Chronic Infections with Typhoid Bacillus" (*Glasgow Medical Journal*, August, 1910), and from that paper I may quote what is to be said further regarding the bacteriology of the case.

"Subsequently there was found," he writes, "in addition to *Bacillus typhosus*, *Bacillus proteus* and a very short Gram-negative bacillus. On the last examination, in January, 1910, typhoid bacilli were still present. *Bacillus coli* was not found in the discharge from the gall bladder at any time. The typhoid bacillus from this case gave all the typical reactions and was agglutinated to the limit (1 in 8,000) by an antityphoid immune serum from a rabbit. The urine was examined on three occasions during November to December, 1909, but *Bacillus typhosus* was never found. Thus, in this case, typhoid bacilli are still present in the bile passages two and three-quarter years after the acute illness. The patient's serum was tested on several occasions from October to December, 1909, with her own strain of *Bacillus typhosus* as well as with the laboratory culture. The Widal reaction was positive, but not markedly so (agglutination in forty minutes with a dilution of 1 in 40) at room temperature."

She was dismissed on February 12th, 1910, in good health, but with discharge still escaping from the sinus. Within the last few days her doctor kindly sent a reply to a note of inquiry regarding her present condition which I had addressed to him, and in that reply he writes as follows, under date February 10th, 1911:

"I saw Mrs. H. yesterday. After leaving the hospital a year ago the sinus continued open till August, when it closed and remained so until January of this year. Then there occurred once more a great swelling of the gall bladder. With hot fomentations constantly applied the sinus opened up again, and the swelling subsided. She is now once more going about as usual, there being a little discharge daily from the wound."

Probably the bacilli still persist. The question of treatment in such a case is one of some difficulty. If the organisms were altogether confined to the gall bladder its entire removal might be contemplated. But no doubt they are present throughout the biliary passages generally, and in these circumstances removal of the gall bladder would prove futile.

I shall conclude my clinical illustration of this subject by detailing shortly the main facts of a case of amoebic abscess of the liver, the only example of the disease which I have ever had occasion to treat.

CASE VIII.—*Amoebic Abscess of the Liver occurring more than Six Years after Recovery from an attack of Dysentery.*

On April 30th, 1910, N. M., aged 27, a soldier, was admitted into the Western Infirmary under my care. He had served in the army for four years, and two of those years were spent in

South Africa (1902-1904). While there he suffered from a severe attack of dysentery, and was in hospital for some months. His recovery, however, was complete and satisfactory, and in the summer of 1904, as his own battalion had been recalled to this country while he was ill in hospital, he was attached to another, and found himself able for all his work. He was, after a time, sent to this country, and rejoined his old battalion at Maryhill Barracks, Glasgow, where it was then quartered. After serving there for another year, his time of service expired, and he went back to work as a baker, the trade which he had learnt before joining the army. He continued to enjoy excellent health and worked uninterruptedly as a baker until his present illness began. Ten weeks before his admission into hospital he one day felt ill, and was seized with shivering. He was laid up, and a week later began to suffer pain in the right hypochondrium. This continued for a week, and then seemed to alter its position, becoming localized about the level of the fourth interspace on the right side and being only felt on deep inspiration. Soon, however, the pain became generalized over the side and gradually increased, but varied in intensity from time to time. About a fortnight before admission swelling became obvious, bulging the lower ribs on the right side outwards; and it was said that for a week the pain had been very severe, almost entirely preventing sleep. The patient looked extremely ill and exhausted, complained of great weakness, and frequently moaned on account of pain. All over the right chest, front, side and back, about as high as the fifth intercostal space, and also over a considerable area in the right hypochondrium there was dullness on percussion. Over the bulging part of his side distinct fluctuation could be made out in the intercostal spaces, in spite of the fact that the slightest pressure elicited loud complaints of pain. There seemed to be no doubt that the abscess was there adherent to the chest wall.

The operation proved a very simple one. I made an incision in the sixth interspace at a point where fluctuation was very distinct, and before cutting through the whole thickness of muscle the contents of the abscess began to flow. Having extended the opening, I introduced a large and long drainage tube, drawing off nearly a pint of reddish-brown fluid. Some of this was received in a sterile tube and sent to the laboratory for examination. On the following day the patient was very well although weak; he was free from pain and had enjoyed some sleep. He progressed most satisfactorily. On May 13th it is noted: "The drainage tube has been removed and a smaller and shorter one inserted. The discharge is decreasing and becoming serous in character." It was soon trifling in amount and entirely serous, while the patient rapidly gained flesh and strength. On June 3rd, the wound having been absolutely healed for some days, he was allowed out of bed, and on June 10th was sent to the convalescent home. Dr. Carl Browning reported as follows regarding the discharge:

"Amoebae, containing red corpuscles, were seen in the pus. Cultures yielded no growth of any kind."

This tropical abscess of the liver, therefore, was solely due to the protozoal organism, being sterile so far as *Bacillus coli* and cocci were concerned. This is, I believe, in accordance with what is usual. It seems marvellous that the amoebae of a dysentery contracted and satisfactorily recovered from in South Africa should remain in this soldier's liver and put his life once more in danger in Glasgow six years afterwards by the sudden development of hepatic abscess, that well-known sequel of dysenteric disease. But the fact is one beyond any possibility of dispute.

SALVARSAN ("606") AND ARSENIC CANCER.

BY

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It is now known that the active agent in the so-called "606" is arsenic, and as it has gained wide popularity, it becomes a duty to examine and record the facts which concern its possible drawbacks.

I have been myself through a long professional life a zealous, not to say enthusiastic, advocate for the two minerals—arsenic and mercury. They have been, indeed, my sheet anchors in practice, compared with which all the rest of the *Pharmacopoeia* has seemed almost useless. They are remedies concerning which definite assertions may be made, and from which definite results may be always expected. They are tools concerning which all that has seemed necessary was that we should know how to use them.

My faith in their efficiency remains, after more than sixty years' experience, unshaken, but, as I very much regret to say, regarding one of them, I have been obliged of late years to feel that there are drawbacks which almost forbid its use. In former years I regarded arsenic

when employed in medicinal doses, as curative in a large proportion of the chronic diseases of the skin and of benefit in many of those of the nervous system and the blood. I knew of no important drawbacks and believed that it might be used with impunity and usually with great benefit to the general health.

I had learnt the use of arsenic from the writings of Dr. Hunt and from the practice of the late Mr. James Startin, whose junior colleague I was for many years at the Blackfriars Hospital for Skin Diseases.

In the year 1850 a collective investigation was instituted by the British Medical Association (then the Provincial Medical and Surgical Association) to determine whether the practice of prescribing arsenic for various affections, which was then becoming common, was really safe. The conclusions reached after the collection and consideration of much valuable evidence were affirmative.*

During the middle period of the last century probably there were few practitioners who used arsenic more freely than I did, for I was a pluralist with a very large field of observation, as I held appointments at several large institutions, and I had no serious misgivings as to the drug.

About 1880 it occurred to me to observe that common herpes zoster frequently followed arsenic, and I soon became convinced that they were cause and effect, and ventured to state this conclusion repeatedly in my clinical lectures. My friends at first assured me that I was attaching undue importance to what were mere coincidences. This, however, did not last long, for arsenical zoster was tolerably common and came within the experience of many, and it is, I suppose, now accepted as one of the best established facts in reference to the use of drugs. It was, indeed, the frequency with which zoster occurred which led to the identification of arsenic as the cause of the epidemic in connexion with poisoned beer a few years ago.

Not very long after the observation of the association between the use of arsenic and herpes zoster another and much more serious revelation took place. A succession of facts convinced me that the use of arsenic might be not only responsible for a comparatively unimportant eruption on the skin—the transitory neurosis known as “herpes zoster”—but could give proclivity to cancer. The importance of this fact—first made public, I believe, about the year 1887—is, I am assured, now widely acknowledged. I cannot claim that it is universally so. Facts have, however, accumulated both at home and abroad, and so long ago as 1902 a distinguished French authority—M. Darier—whose opinion, I believe, records the experience of many others, expressed himself as follows (*Semaine médicale*, December 10th, 1902):

I now show you a man, aged 47, whom I first saw in 1890. At that time his face and neck showed confluent patches of pigmented lenticular spots and vascular maculae, while his hands and feet were the seat of diffuse hyperkeratosis associated with numbers of warty outgrowths. I lost sight of him for some twelve years, but in the spring of the present year, 1902, he came to see me again. The pigmentary and telangiectatic conditions had diminished, but the warty condition remained. Four of the growths, one on the neck and three on the hands, had become transformed into true epitheliomata, a fact which was confirmed by histological examination after their removal by the curette. At the present time a new epithelioma can be seen in process of development at the angle of one of his eyes. The origin of these cutaneous lesions is explained by the fact that this patient (by way of treatment of a chronic bronchitis accompanied by induration of the pulmonary apices) took for ten years (between 1886 and 1896) a daily dose of 12 drops of Fowler's solution on twelve days of each month and 7 drops for seven days of each month during the following five years (1896 to 1901).

We are aware that in 1887 J. Hutchinson put forward a view that there was an arsenical form of cancer; it was received with some scepticism, but has since been confirmed by a certain number of observations. The case now before you appears to afford his belief very material support.

Since then M. Dubreuilh, the distinguished surgeon of Bordeaux, has published an excellent summary of the whole subject, and has drawn up a table of 19 cases of arsenical cancer (see *Annales de Dermatoses*, February, 1910).

I must not trouble the reader with my own narratives of cases; many are given in some detail, and with several pictorial illustrations, in one of the more recent fasciculi of the New Sydenham Society's Atlas.

* A summary of these conclusions was given by myself in one of the early volumes of my *Archives of Surgery*.

I may, however, just mention briefly one of the most recent facts which has been brought under my notice in this connexion, since there are social reasons for its delayed publication in detail. I am informed of a young married lady who has become the subject of multiple epithelial cancer concerning which her surgeon writes to me:

It is a typical example of what you have described as “arsenic cancer.” The case will, I believe, soon be published.

The patient took arsenic for long periods for the cure of psoriasis in girlhood, and is now, after her first confinement, the subject of epithelial cancer in several different situations.

I think, therefore, that I am justified in stating that it is proved that the use of arsenic may create a proclivity towards malignant forms of growth. These are not by any means always the same; most conspicuous and frequent are epitheliomata, but they are by no means the only ones, for various forms of sarcomata and probably endotheliomata occur in the same connexion, and possibly in the same individual.

It would appear that this most powerful drug can give tendency to aberrant forms of nutrition in various directions. I must confess that I have felt somewhat astonished that the facts which appear to justify this conclusion have claimed so little attention from recent writers on cancer. They appear to me to be of the very first importance in reference to our creed as to the possible causation of these neoplasms. The term “arsenic cancer” is somewhat misleading, since it is apt to concentrate attention upon certain cases, unquestionably rare, in which the evidence appears to show that the direct and efficient cause of a peculiar form of cancer is arsenic. These are probably only very exaggerated forms of what in minor degrees is very common.

What we ought to understand is that arsenic originates, or intensifies if already present, a general proclivity to this mode of growth; nor ought it to be hastily assumed that prolonged use of the drug is necessary to this effect. Many of the well-known results of the medicinal use of arsenic occur not after very prolonged courses, but after comparatively short ones, and it is well known that an almost indefinite length of interval may occur between the use of the drug and its manifestation. It is to these facts that it is due that so much has been overlooked in the past and is probably still overlooked in reference to this most potent drug.

I must not, however, write a dissertation upon them. My object in the present paper is simply to invite the attention of those who may be inclined to prescribe this newly vaunted remedy for syphilis without due recognition of its possible danger. For myself, since I became aware that arsenic gives proclivity to cancer I have almost abstained from its employment, and would now advocate its use only in cases which very specially demand it.

Another part of my subject must be left for the present; if I ever enter upon it on another occasion it will be to show that but little has been alleged respecting the new remedy which is not equally true of mercury and the iodides when properly and boldly used.

If it be asked how arsenic acts in giving proclivity to cancer, it may be suggested that it is as a depressant of growth power rather than as stimulating it. By diminishing the vigour of the forces which favour normal animal organization it permits remotely and after an interval of degraded types of growth more nearly allied to those of vegetation.

I wish, however, to advance no theories, but to confine myself to showing evidence of the clinical fact.

At the recent annual meeting of the International Medical Association for the Suppression of War (Rue des Mathurins 25, Paris) Dr. J. A. Rivière was unanimously re-elected President, and it was decided that the congress in Paris this year should be held at the end of October instead of in September. The subjects for discussion thereat were also selected. Only one is of a distinctly medical character—namely, international hygiene. The rest deal with differences in language, weights and measures, and monetary systems, and other analogous matters deemed by the society to obstruct the road towards universal and enduring peace.