tryparsamide to which the parasites were exposed. The optimum concentration of drug for this purpose was found to be the highest employed which failed to destroy all the trypanosomes in the suspension exposed to the drug. By this means a strain of trypanosomes was quickly produced which was at least 500 times as resistant to reduced tryparsamide as was the original strain. The use of lower concentrations of drug likewise sufficed for the production of a resistant strain of trypanosomes, but the process was much slower and the degree of resistance resulting was much less.

We have examined a considerable number of methods of making a strain of trypanosomes drug-resistant in the mouse, and found that the quickest and most certain method is to give daily such doses of the drug as just fail to clear the peripheral blood of parasites or at most do so for only a day or two. This is in accordance with the conclusions reached from the *in vitro* experiments—namely, that the optimum conditions for the production of drug resistance are attained when the trypanosomes are repeatedly exposed to the highest concentration of drug which just fails to destroy them all.

Although such a method cannot be adopted in the case of animals, like rabbits, in which trypanosomiasis is essentially an infection of the tissues, nevertheless the production of highly resistant strains in these animals is a matter of the greatest use. If, when a relapse occurs in a rabbit which has received a number of small sub-curative doses of atoxyl or tryparsamide the trypanosome is transferred to, and tested in, mice, it is almost certain to show a definite degree of resistance; and the resistance can rapidly be enhanced by continuing to treat the rabbit with rather larger doses of the drug.

As I have already pointed out, we do not yet know whether the failure to obtain cures in certain cases of human trypanosomiasis by atoxyl, tryparsamide, etc., is due to the fact that the treatment administered has resulted in the production of a resistant infection, or whether there is some other cause for the failure. Man is for obvious reasons a very unsatisfactory experimental animal, and in human trypanosomiasis the number of parasites in the peripheral blood is usually very small. These facts make it almost impossible to decide, by direct observation on man, whether or not the failure to cure in any particular case is due to development of drug resistance. From the analogy of our experiments in rabbits, it is highly probable that the production of a resistant strain in man is of frequent occurrence in practice, but, at the moment, that is as far as one is justified in going. However, the question is probably easy of solution by the procedure we adopted in the case of the rabbits—namely, by transferring the parasites to mice and testing their resistance to aromatic arsenicals in these animals.

If, as seems probable, a considerable number of cases of human trypanosomiasis treated with aromatic arsenicals do develop resistant infections, the fact is one of the greatest practical importance, because, when once a trypanosome strain has become drug-resistant, it retains the character apparently unimpaired for years, and because resistance to one of the aromatic arsenicals implies, broadly speaking, a resistance to all the aromatic compounds of arsenic and antimony.

Our experimental work has convinced us that when once an infection has developed a definite degree of resistance, it is hopeless to attempt to cure the animal by further administration of the aromatic arsenical or antimonial compounds; in fact, prolongation of treatment merely results in enhanced resistance. It is therefore a matter of great importance to ascertain beyond all doubt what part the development of drug resistance plays in the results of therapy of human trypanosomiasis, and the

particular factors which conduce to its development. Our experimental experience suggests that the development of drug resistance is slow to begin with—that is, there is no obvious change in the resistance of the trypanosomes in response to the first few doses of the drug, but when once resistance has begun to manifest itself it develops with great rapidity until a condition of complete resistance is reached, when further doses of the drug exercise not the slightest effect on the infection.

Furthermore, if human beings do, as the result of treatment, develop drug-resistant infection, the question whether the trypanosomes can retain that resistance in their passage through glossina becomes one of the utmost importance. It must, however, be borne in mind that because a patient is not cured by a course of treatment it does not necessarily follow that his infection has become drug-resistant. This is clearly shown by the fact that Chesterman and others record cures with tryparsamide in patients whom they had previously unsuccessfully attempted to cure with atoxyl. The failure to cure such cases with atoxyl could not have been due to the fact that the infections had become atoxyl-resistant, because atoxyl resistance implies also tryparsamide resistance. A reasonable explanation appears to be that in these cases there were foci of the infection which could be reached by tryparsamide, but not by atoxyl; and this hypothesis is supported by Chesterman's findings that cases which were not cured by the first course of tryparsamide cannot be cured by further dosage of that drug.

RECURRENT BOILS*

SOME POINTS RELATING TO AETIOLOGY, COMPLICATIONS, AND TREATMENT

BY

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There is a singular disposition to regard the individual suffering from a boil with a certain degree of levity, yet we have it on no less authority than the Bible that "Satan went forth from the presence of the Lord and smote Job with sore boils from the sole of his foot unto his crown." Those who have endured the extreme pain of a boil in the external auditory meatus must indeed be tempted to suppose that the same master hand was responsible for their affliction.

To Pasteur is due the honour of demonstrating that the boil is caused by the action of the *Staphylococcus aureus*—a micro-organism which he found also in pus from carbuncles and osteomyelitis—but we are well aware that mere contact between the skin and this organism is not necessarily followed by the development of a boil or carbuncle. The number, the virulence of the cocci, and the degree of resistance of the individual are the determining factors, as in the case of many other infections. Some investigators, amongst them Goldsmith¹ and Ferguson Smith,² hold that *Staphylococcus aureus* is not a normal habitant of the skin; others state that every man is a carrier of pyogenic cocci. Investigations of this nature must necessarily be incomplete, for it is impossible to include in the examination the whole skin surface or the contents of the follicles; neither is there at present a satisfactory means of distinguishing between virulent and non-virulent bacteria of the same species. We may, however, assume that most individuals, if not all, are frequent carriers of *Staphylococcus aureus*. The relative number will be influenced by such factors as personal cleanliness and occupation. The personnel of a hospital,

* Read in the Section of Dermatology at the Centenary Meeting of the British Medical Association, London, 1932.

for instance, must be constantly exposed to the infection. Trauma also plays a part in the aetiology—the equestrian is prone to suffer from boils on the buttocks. But it is the individual receptivity, the individual skin resistance to the staphylococcus, which is of supreme importance in determining whether a person will suffer from furunculosis. Curiously enough, the age of greatest vigour is that most susceptible to the infection. This is borne out by the following analysis of 163 cases.

Age	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80
Number of cases	7	37	49	33	22	13	1	2

Trauma is no doubt responsible to a certain extent for the selection of the second, third, and fourth decades. On the other hand, children during the school age are subjected to much trauma, yet the incidence at this age is low, while practical experience teaches us also that sedentary workers are frequently the victims.

Another peculiarity, difficult to explain, is the relative infrequency of recurrent boils in the female. In the series already quoted only 18 per cent. were females. In this respect the investigations of Hidaka³ are of considerable interest, for he found paucity of bacteria on the skin of women and children (see Table).

Prevalence of Bacteria on the Skin

Cases Examined	Average Number per 0.1 c.mm. of Skin		
	Face	Buttock	Thigh
Males (34)	707	240	173
Females (34)	103	65	42
Children (4)	3	2	29

The difference in environment and habits of the sexes is hardly sufficient to explain these facts. It therefore appears that the female skin offers a less suitable habitat for the bacteria.

SOME CONTRIBUTORY CAUSES

Some observers maintain that the first boil is the result of an accidental infection, and that subsequent boils are merely consequent infection of the follicles. But boils are not a common complication of other pyogenic diseases, such as sycosis and chronic osteomyelitis, where the skin of the whole body is subject to constant contamination with the *Staphylococcus aureus*. Again, it is notable that persons suffering from furunculosis will often give a history of having had previous attacks of the condition, with intervals of a year or more between. This shows that their follicular resistance to the invasion of the staphylococcus is low. Unfortunately we know little of the immune biological character of the skin. It is true, we are aware, that boils and carbuncles are relatively frequent in diabetes, yet glycosuria is met with in a very small percentage only of those suffering from furunculosis, and although Pick claims an almost consistent hyperglycaemia, Rost's most exacting tests do not confirm his statement.⁴ Nevertheless, an unusual partiality for sweets is sometimes admitted by the victims of the complaint, and a drastic reduction in the consumption of sugar is of great service in the treatment of many cases. A more important aetiological factor which has not received the attention it deserves is the frequent presence, in cases of recurrent boils, of an intercurrent infection on the skin. This occurred in 31 out of 98 consecutive cases examined from this point of view. Thus: 11 were found to be suffering from pruritus ani, 9 from scabies, 4 from impetigo, 2 from pediculosis corporis, 1 from otitis

media, 1 from whitlow, 1 from abscess, 1 from oil acne, 1 from perlèche.

It is conceivable that any of these coexisting lesions may have been acting as a focus for the staphylococcal infection of the skin. Their recognition is therefore of obvious importance. Another fruitful source of folliculitis and boils is the application of fomentations to suppurating wounds of the skin, the furunculosis often persisting long after the original wound is healed. To avoid this complication it is advisable to restrict the wet dressings to the smallest dimensions. A 1/2 per cent. silver nitrate solution may be employed with advantage, for it does not have the tendency to produce a folliculitis of the surrounding skin.

Fortunately the sufferers from furunculosis are usually unaware of the complications which may assail them, yet there are probably more fatalities arising from it than from any other skin disease. At one institution with which I am associated there were, during 1931, four deaths which could undoubtedly be attributed to boils. Of these cases, a girl aged 17 and a man aged 47 succumbed to a boil on the upper lip, a boy aged 16 and a man aged 57 to a carbuncle on the neck. The face and neck are recognized as a danger zone, but, in addition, surgeons meet with perineal and prostatic abscess and osteomyelitis following one or more boils. Any prophylactic measures which may prevent further boils are therefore of very definite importance.

PROPHYLAXIS AND TREATMENT

One of the most original methods of prophylaxis is quoted by Clement Simon in his interesting *Lettres*. A French military surgeon is alleged to have flamed the buttocks of his cavalry-men as a preventive. One learns with relief that the flame was held at a respectable distance!

The advisability of a reduction in carbohydrates has already been insisted upon. That the skin should be kept as dry as possible is a maxim which is supported both by clinical and by experimental evidence. The self-disinfecting power of the skin is influenced by the amount of moisture present. Norton and Novg,⁵ in their experiments with *B. prodigiosus*, found that these organisms when applied to the skin diminished rapidly in number, particularly during the first ten minutes. Similar results were obtained when cultures were placed on inert material, such as glass, paper, and hide. The rate of disappearance in all instances was governed almost directly by the amount of moisture present, and the experiments failed to indicate any inherent germicidal power of the skin. These findings are of the utmost importance in view of the fact that the fomentation still reigns supreme as a dressing for boils. Admittedly it is comforting, and also reduces the pain, but at the same time it cannot be too strongly emphasized that it is a common cause of the recurrence—the purulent discharge soaks into the dressing and staphylococci are spread to the neighbouring follicles, where they are encouraged to multiply under the optimum conditions of heat and moisture. My own practice is to recommend the frequent cleansing of the surrounding skin with spirit and the direct application of pads of gauze soaked in spirit as a covering to the boil.

Under the heading of prophylaxis must be considered the advisability of using such measures as vaccine therapy, chemotherapy, yeast, purgatives, etc. There is a wide divergence of opinion concerning these measures. For instance, Sabouraud⁶ states that staphylococcal vaccine, prepared according to his technique, rarely fails in subjects less than 50 years of age, and he concludes with the slogan, "One can, and one must, vaccinate against furunculosis." On the other hand, his fellow-countryman, Clement Simon, holds the opinion (with which I

concur) that vaccines in recurrent boils do not live up to their reputation. Brocq was equally dogmatic in testifying to the virtues of fresh yeast for the malady, for he referred to it as a specific of the same value as mercury for syphilis and quinine for malaria. The yeast he employed may be different to the variety used by brewers in this country; certainly an extensive trial of the latter convinced me that it is useless for the purpose.

It is impossible to discuss the innumerable remedies which have been sponsored, but I feel that my remarks would be incomplete if I did not refer to colloidal manganese hydroxide, the remedy introduced by Mr. J. E. R. McDonagh. I have given it an extensive trial over many years, and I am convinced of its utility. As regards the local treatment, most writers refer to the possibility of averting a boil in its early follicular stage. Puncture with the galvano-cautery, injection of pure carbolic acid, and painting with iodine, each has its advocates, but although some favourable results may be obtained success is by no means the rule.

The treatment of the fully developed boil is also a debatable subject. Whilst some advocate either excision or incision, others, more conservative in their ideas, allow Nature to take its own course. In either case it is the prophylactic measures taken to prevent reinfection of the skin which are of greater importance.

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- ⁶ Sabouraud: *Entretien*, 1922, p. 254.

Memoranda

MEDICAL, SURGICAL, OBSTETRICAL

SUDDEN DEATH FROM CYCLIC VOMITING

On June 5th I was called to see a girl, aged 7½ years, who had died shortly before my arrival.

She had been a nervous child, suffering from frequent attacks of "biliousness." There were four other children, all well. There was no hereditary taint, nor had the child taken food of a kind different from that of the other children in the family.

Thirty-six hours before death there had been an onset of lassitude and vomiting, accompanied by abdominal pains and constipation. (No doctor was called, as the mother was accustomed to these attacks, which usually passed over, with relief of constipation by castor oil.) At frequent intervals fluid nourishment was taken and immediately rejected. Death took place quite suddenly.

Post mortem nothing abnormal was found in any organ, but there was a persistent thymus, weight 1½ ounces, and hyperplasia of lymphatic tissues, particularly of the tonsils. Urine, taken from the bladder after death, showed the presence of much acetone, both by Rothera's and by Gerhardt's tests. The post-mortem appearance of the stomach and intestines was quite normal. They were free from any inflammation, and no irritating particles of food were present. The possibility of worms and acute pancreatitis was excluded, as was any abnormal condition of the brain.

In view of the absence of all other possible causes, after the most careful post-mortem search, one must conclude that this was a case of death from cyclic vomiting, which is here recorded owing to the rarity with which children die suddenly in these circumstances. The moral of such

a case as this suggests the advisability of giving glucose in any similar case of vomiting in children accompanied by acetonaemia, and where the diagnosis remains obscure.

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A CASE OF ABORTUS FEVER IN HERTFORDSHIRE

Abortus fever has now been recorded from a number of counties in Great Britain. Recently, two cases have been reported from Hertfordshire, and I wish to present my experience of another one. Although this fever has many features in common with undulant fever originating in the Near East, the main points of distinction appear to be the shorter duration of the fever in *abortus* infection and the comparative mildness of the symptoms. The total length of the fever in this case was about three months. The debility which results from *abortus* fever is of longer duration and is a factor which has to be taken into consideration in after-care.

CASE RECORD

The patient, a civil servant aged 36, first consulted me on February 25th, 1932, when he complained of headache—pain behind eyeballs—cough, and night sweats. His temperature was 102° F. At this period I was attending a number of patients suffering from influenza, and at the time I considered that this was the correct diagnosis in his case. He did not make a good recovery, but returned to duty on March 7th. I then lost sight of him until May 10th, when he again consulted me. I found that he had a temperature of 102° F., and sent him to bed. On going very carefully into his history, I discovered that since returning to his work he had never really been a fit man. There were periods of apparent improvement, followed by a relapse, when the main symptoms were cough, headache, shivering fits, extreme fatigue after the day's work, irritability, and heavy night sweats. The latter was a very marked feature—so much so as to cause rusting of the spring mattress of the bed. It became clear from the history that one was dealing with a condition which had been in progress since February.

On examination, nothing was found in the heart or lungs, but the tip of the spleen was palpable. Otherwise there was nothing of note in the abdomen. The tongue was clean at the tip and sides, but the posterior half was covered with a slight fur. The bowels were regular and the urine was normal. A sample of blood was sent for the Widal reaction and this gave a partial agglutination to *B. typhosus* and *paratyphosus* A and B in a dilution of 1 in 10. All higher dilutions were negative. A further specimen of blood was submitted to Dr. P. Manson-Bahr, and this was found to agglutinate an emulsion of *Br. abortus* in dilutions up to 1 in 160. The diagnosis thus became clear.

There was no history of contact with infected animals, but the patient is a consumer of raw milk. A mixed milk sample from the herd of cows at the farm supplying his household was submitted for examination. The report stated that the agglutination reaction for *Br. abortus* was negative both macroscopically and microscopically in dilutions of from 1 in 6.5 to 1 in 125. The cows, ten in number, were examined on June 3rd. One had an indurated hind-quarter of the udder: milk from this showed nothing abnormal except a few pus cells. The remaining cows were all healthy. The owner states that two or three were given to slipping their calves about two years ago, most probably the result of contagious abortion. These cows have since been difficult to get in calf, possibly owing to some lesion of that disease remaining in the uterus.

There is every reason to suppose that the fever started on February 22nd, 1932—that is, three days prior to the patient's first consultation with me. The temperature finally settled on May 21st, 1932, and it still remains normal. No treatment was given in this case other than rest in bed on a light nourishing diet.

I wish to thank Dr. Manson-Bahr for kindly allowing the serum tests to be carried out in his laboratory.

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