(a) syringes intended for human use or (b) filter candles. We have carried out a few experiments with trypsin, but, even after prolonged digestion, traces of tuberculin or tuberculo-protein were frequently detected in subsequent washings with saline or B.B.S. The difficulties encountered in removing tuberculo-protein, which contains no glycerin, from syringes and pipettes, suggests that the "tenacity" of old tuberculin to glassware is not a function of its high glycerin content.

Since this work was carried out, Professor E. R. Long, who has recently visited this country, has informed us that he and Dr. F. B. Seibert had also noticed the property of tuberculin of adhering to glassware, and insist on the use of separate syringes for tuberculin and control fluids. More recently our attention has been drawn to a paper by Zieler (1911), who anticipated us by many years in describing this dangerous "tenacity" of tuberculin. This publication seems to have also escaped the attention of the writers of textbooks.

Summary

Tuberculin adheres to apparatus with exceptional tenacity and is extraordinarily heat-stable; every trace of tuberculin is not removed by thorough washing and autoclaving. A simple but reliable method of removing traces of tuberculin, applicable to the ward side-room, has yet to be found.

All glassware and filter candles used for handling tuberculin should be clearly marked and restricted to that purpose. Tuberculin should, in fact, be kept most rigorously apart from all other products, including control fluids, in all stages of preparation and injection.

Separate syringes should be reserved for different dilutions of tuberculin.

It is a pleasure to acknowledge our indebtedness to our colleague Miss E. E. Whatley for her assistance in connexion with this work.

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PALATAL PARALYSIS IN EXTRA-FAUCIAL DIPHTHERIA

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The theory that diphtheritic paralysis is the result of an ascending neuritis has several exponents among the leading French authorities. One of the arguments advanced in its favour is the assertion that paralysis of the palate is not met with in extra-faucial diphtheria. "Comme l'avait remarqué Trousseau, en pareil cas, la paralysie débute sur le membre, ou sur la partie du corps primitivement touchée, et les paralysies vélopalatines font défaut" (Lereboullet). This supposition concerning the palate is also a premise of Walshe's interesting conception of the pathogenesis of the condition. In 1918 and 1919 he described a number of cases of faucial and extra-faucial diphtheria, but unfortunately only a few of them could be followed throughout their entire course. As he himself pointed out, some of his observations "remain inconclusive." Nevertheless, his contribution is a valuable one, and although his views have not secured any general acceptance by fever clinicians, they are frequently quoted in neurological works.

A full discussion of the whole subject of diphtherial paresis would be outside the scope of the present paper. We merely seek to demonstrate that the occurrence of palatal palsy is certainly not restricted to the faucial variety of the disease. The establishment of this point is important, because it would refute the hypothesis that the impairment of palatal function is necessarily the result of an involvement of the medullary nuclei by toxin which travels from the fauces via the perineural lymphatics.

Instances of extra-faucial diphtheria are common enough, but the site of infection is usually the nose, larynx, ear, or conjunctiva. Unless faucial infection co-exists, paresis is very exceptional in this group. On the other hand, paresis may sometimes be associated with wound diphtheria, and, as might be expected, the war period furnished a number of examples. Modern surgical methods have almost completely banished such cases from hospital practice. In recent years medical literature has made few references to their occurrence; the very occasional examples which have been recorded seem to have responded well to serum therapy and to have had no parietic sequelae. A case of this kind was under treatment in the South-Eastern Hospital in January, 1933, and mention might be made of the cases reported by Dixon (1921) and Anderson (1931). In June, 1933, we were fortunate enough to admit a second case, which was complicated by extensive paresis. The following are the clinical details.

Case Report of Wound Diphtheria

A male, aged 25, was transferred to the South-Eastern Hospital on May 18th, 1933. He had a history of an abscess of the right thigh, which was opened on February 26th at his first hospital; the resulting wound broke down extensively, leaving a large indolent ulcer. About the middle of April he found himself unable to read on account of blurring of the print. His vision for distant objects was normal. This paresis of accommodation lasted for some two weeks, and in the first week of May it was noted that his voice was distinctly nasal in character. He now complained of numbness of the fingers and toes, and shortly before transfer to the South-Eastern Hospital there was an increasing weakness of both arms and legs, but the palatal paresis was improving. This sequence aroused suspicion of a diphtheritic origin of the paresis, and on May 15th a culture of the wound showed the presence of Klebs-Loeffler bacilli. Two cultures of the throat gave negative results.

On admission the patient was thin and cachectic. There was a large granulating ulcer with shelving edges on the outer surface of the upper aspect of the right thigh, which in its largest diameter measured $3\frac{1}{2}$ inches and extended towards the gluteal region. The surface was covered by a thin layer of purulent debris, but no membranous exudate was present at this stage. There was marked wasting of the muscles of the right leg, and tenderness of the calves of both legs. The tendon reflexes were absent. The throat was clean and uninjected; there was no evidence of rhinitis. Movement of the right side of the palate was impaired and the voice was slightly nasal. The right lower facial segment was parietic. No ocular symptoms were discovered. Muscular power of the limbs was poor; the grip of the right hand was weaker than that of the left. Sensation was impaired; below the elbows and knees light touch was not perceptible, and appreciation of a pin-prick was diminished. Formication was complained of over the fingers and toes. Astereognosis was marked, and ataxy was a notable feature. Neck and trunk muscles were then unaffected. The heart sounds were indicative of myocardial weakness; the first sound was abrupt and occasionally reduplicated, and there were frequent extrasystoles. Blood pressure was 110/80. Cultures were taken from the throat, nose, and wound. The throat and nose were negative for diphtheria, but polar staining organisms were found in the wound culture. Subsequent laboratory investigations showed them to be saccharose fermenters, and animal inoculation tests proved them to be avirulent. A Schick test was negative. An intramuscular injection of

48,000 units A.T. serum was given. On May 20th the condition was unchanged and the serum injection was repeated. By May 25th the wound had begun to show signs of healing and the general condition was much improved. A second wound culture was taken, with the same result as the first.

The wound was granulating well on June 1st. The peripheral neuritis remained unaltered. There was some wasting of the serratus magnus. During the next three weeks the heart sounds became normal in character; the palatal paresis passed off; the wound continued to heal, though not so rapidly as at first; there was no improvement in sensation or muscular power—indeed, the latter showed a decrease. Until the sixth week after admission the patient was unable to feed himself. On June 29th the wound had almost completely healed. Sensation had returned and muscular power was much improved; paresis of the deltoid and serratus magnus was still obvious. All pareses had passed off by July 20th, although a small sinus persisted at the edge of the wound area. The patient was transferred back to his original hospital on August 8th, from which he was discharged home about fourteen days later. He was then able to walk, and felt quite well.

This is an example of a palatal paralysis in extra-faucial diphtheria. The paretic syndrome is so typical that the diagnosis hardly required bacteriological confirmation, but such data as we were able to secure are fully in accord with what the work of previous writers had led us to expect. The results of the virulence tests suggest that the organisms then investigated were not the toxin-producers which were originally present in the wound. Both virulent and avirulent bacilli coexisted in a case of wound diphtheria that was treated in this hospital in 1925. A number of French workers have shown that untreated cases which develop extensive paresis possess considerable antitoxic immunity at the time of the appearance of paretic symptoms. The negative Schick test was therefore the most probable finding. It would be idle to speculate at any length on the origin of the infection. It was hardly likely to have been the throat or nose. Our necessarily belated cultural examinations of these areas may not entirely exclude the possibility, but the clinical details lend no support to such a contention, and the alternative of a "healthy carrier" who infected his own wound scarcely merits discussion.

Cases in the Literature

Commenting on the rarity of similar cases, the Medical Research Council's monograph states that considerable difficulty was experienced in tracing them "in the very scattered literature." In the course of a somewhat prolonged search we found that the majority of examples of extra-faucial diphtheria seem to have been recorded on account of the aberrant nature of the infected site, and only a few writers have reported cases because of the interest attaching to the paresis. This is not surprising if we remember that in the pre-aseptic period, when wound and cutaneous diphtherias were less uncommon than they are to-day, the then authorities believed that the same palsies might be met with in any form of the disease. Until comparatively recently this view, which was subscribed to by no less an authority than Baginsky, was not seriously challenged, so that no particular reason existed for the recording of cases which were not regarded as anomalous.

Since attention has been directed to the subject clinicians have lacked some of the opportunities which used to present themselves to the older physicians. Reviewers of the literature have also to contend with the fact that it is exceptional to come across a paper that affords any bibliographical assistance. C. B. Ker declined to accept the assertion that the palate was never involved

in the paresis of extra-faucial diphtheria. Though he gives no actual case details he states that he had seen examples of "palatal selection." As far back as 1893 we find Gowers alluding to palatal palsy in wound diphtheria. Gayton (1894) published an account of a case of vaginal diphtheria in which palatal paresis and strabismus occurred. No evidence could be obtained of any co-existing faucial lesion. Cochrane (1921) saw a very interesting example of a diphtherial infection of the penis. The paralyses, which included the palate, resembled those met with in faucial diphtheria. Diphtheria bacilli were present in the genital lesion, but the absence of any other infective focus was proved both clinically and bacteriologically. In another case, described by Leendertz, a primary diphtheria of the vagina was followed by paresis of the bladder, rectum, and later of the palate. There was no history or any sign of a faucial infection.

A case which had some features of resemblance to our own was reported by Emrys-Roberts (1923); this was a diphtheritic infection of the right foot in a young adult. The specific organism was cultured from the infected area, and healing rapidly followed the injection of antitoxin. Paralysis of accommodation was the earliest form of nervous involvement. Peripheral neuritis was a later feature, and special mention is made of a weakness of the right hand. No reference is made to an examination of the palate, but nasal voice is noted. As the patient was the son of a medical man it may be assumed that the intonation was the result of palatal paresis and not merely indicative of a habitual peculiarity of speech.

Two of Walshe's cases would appear to be examples of palatal paresis in non-faucial diphtheria. The author argued in favour of the applicability of the term "double infection," but the patients gave no history of sore throat and no evidence could be adduced to the contrary. Anschütz and Kisskalt saw 140 cases of wound diphtheria in German military hospitals. The writers were surgeons who were more particularly interested in the local lesions, and their allusions to paresis are not accompanied by precise details. That palatal palsy figured in the series may be gathered from their references to "Schluck und Akommodations-lahmung" as points in the retrospective diagnosis of late cases.

Diphtheria of the umbilicus in infants may be complicated by paralysis of the palate, as was observed in a case recorded by Prausnitz (1919). In his commentary on an example of wound diphtheria, C. Saggau pays special attention to the occurrence of ciliary paresis, and quotes Scheby-Buch as stating that three out of thirty-eight instances of this complication were seen in extra-faucial cases. Saggau's patient did not have a palatal involvement, but two out of five similar cases, which he found in the works of the older writers, had both forms of palsy. Many of these writers refer to the death of Griesinger in 1868. They attribute the fatality to a multiple paralysis, including palate, which followed the diphtheritic infection of a laparotomy wound. As diagnosis in this period was necessarily entirely clinical, further quotations from these writers would be superfluous.

In more modern times we find that Guthrie (1894), Flesch (1895), Deutchlander (1912), and Rieder (1923) allude to palatal palsy in non-faucial diphtheria. Some of their cases were probably quite authentic, but in the absence of certain confirmatory particulars we do not propose to describe them. At a meeting of the Section of Dermatology of the British Medical Association in 1910 Dawson read a paper on cutaneous diphtheria, and gave an account of three cases. He mentions seven other cases which he had found in the literature, but, unfortunately for our purpose, paresis is not referred to. In the course of the subsequent discussion one of the speakers

(G. Pernet) stated that he had seen a fatal case which was complicated by palsy of the palate. Four deaths occurred among the ten cases cited by Dawson, and it is significant to note that these were the youngest patients in the series.

From these and other records we have been impressed by the fact that, in young subjects, cutaneous lesions seem to be even more serious than faucial. A comparative infrequency of paretic sequelae is probably due to the severity of the toxæmia, which leads to a fatal issue before paresis has an opportunity of manifesting itself. An unusually severe toxæmia may result from the diphtheritic infection of varicella lesions. Instances of this grave association have been reported by Warren and Sutton, and by Joe. In one of these cases the patient succumbed shortly after infection, despite the fact that a negative Schick test proved that the child possessed a certain degree of natural resistance to diphtheria.

Interesting Clinical Data from Recorded Cases

The cases we have quoted have been selected mainly because of their relation to our subject, but they are a minority of the recorded examples of extra-faucial diphtheria. The patients in many cases that we have not mentioned had forms of paresis other than palatal, while a not inconsiderable number recovered without complications. Apart from the maintenance of our thesis our study has yielded some interesting clinical data. Multiple paresis is met with in both faucial and extra-faucial diphtheria, and, on the question of symptomatology, the view of the older writers is correct. Whether the toxic spread is from the throat or elsewhere the same pareses may occur. There are, however, important differences in the relative frequency and in the order of occurrence. In the extra-faucial type paralysis of accommodation is by far the most frequent and usually the earliest in onset, while palatal paralysis tends to develop at a later stage of the disease. The order and relative frequency of these palsies is therefore the reverse of what obtains in faucial diphtheria. Peripheral neuritis is the latest form of nervous involvement in all diphtheritic lesions.

Though our observations are based on an analysis of the clinical details of cases of natural diphtheria, their correctness receives confirmation from the records of certain accidental injections of toxic solutions. In England diphtheria immunization has always been safe and effective, but in some foreign countries there were occasional mishaps in the early days of this procedure. These incidents are, happily, of the past, but from them we have learned something of the effects of the parenteral injection of diphtheria toxin. Palatal paralysis figured in each series of cases concerning which information is available. Its usual time of onset was in the third or fourth week, and the order and form of the other pareses corresponded closely to what we have described in respect of the natural varieties of non-faucial diphtheria.

Conclusions

Palatal paralysis undoubtedly occurs in extra-faucial diphtheria, and theories of pathogenesis which postulate a contrary assumption are untenable. In the non-faucial varieties of diphtheria palatal paresis is less common, and tends to be met with at a later date than in faucial diphtheria. Paresis of accommodation is the most frequent, and usually the earliest paretic sequel of extra-faucial diphtheria.

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TREATMENT OF LYMPHATIC LEUKAEMIA

WITH SPECIAL REFERENCE TO THE USE OF IODINE

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A recent edition of a popular textbook of medicine¹ states that in chronic lymphatic leukaemia "symptomatic relief has followed the use of Lugol's iodine solution in doses of about 10 minims thrice daily." The rationale of this treatment is based upon the resemblance that has been traced by certain authors between lymphatic leukaemia and hyperthyroidism. It is well known (Du Bois²) that the metabolic rate is increased in both these conditions, and there may be a number of common symptoms such as loss of weight, a warm, moist skin, increased sweating, and tolerance for cold. Minot and Means³ noted that the common symptoms were those which could be ascribed to the increased metabolic rate, while those that were more characteristic of hyperthyroidism, such as nervousness, tremor of the hands, insomnia, and exophthalmos, were not seen in leukaemia.

Friedgood⁴ thought that the parallelism between these two conditions was much closer than Minot and Means had described, the differences being chiefly quantitative. He argued from this that as Lugol's iodine was of proved benefit in Graves's disease, it might also be expected to be of use in lymphatic leukaemia. He treated ten cases of chronic lymphatic leukaemia with doses of Lugol's iodine solution of 30 to 45 minims daily for prolonged periods. The results were somewhat conflicting. Martin⁵ had previously been unable to detect any effect on the basal metabolic rate, using smaller doses of Lugol's iodine in such cases, although Friedgood claimed large decreases in some of his cases (half of which had had previous x-ray therapy).

With regard to the blood picture, in four cases the white cell count was reduced, often very considerably (for example, from 200,000 per c.mm. to 94,000 per c.mm.); in three there was some increase; and in three the results were indefinite. It was noted that when the iodine had any influence the maximum change occurred in about a fortnight, and thereafter conditions tended to return to their previous state; this compared well with the effect of iodine in Graves's disease. Similar beneficial effects