institutions which for years previously had been completely free from this disease, probably owing to the fact that most of the children are recruited from unaffected rural districts, we found that immunity was practically non-existent. And so, unfortunately, the building up of a sufficient degree of immunity proved a matter of no little difficulty, requiring indeed, as eventually became evident, a time interval more lengthy than previously observed. It remains to be seen whether the response to immunization work in scarlet fever will be found to run on similar lines. It is, I think, as yet hardly possible to estimate what may eventually prove to be its precise value as compared with immunization against diphtheria. As a matter of fact, so far as is at present known, attainment of anything like complete immunity by means of inoculation methods appears to be decidedly more difficult of accomplishment in scarlet fever than is the case with diphtheria. Moreover, there is, unfortunately, reason for believing that immunity thus produced is by no means permanent.

MEASLES.

As in diphtheria and scarlet fever, so also in the case of measles, infants appear to inherit some temporary immunity from their mothers, which is said to last until the fifth or sixth month of extrauterine life. From this period onwards, however, up to the age of 5 years, mortality from measles is high (from 13 to 15 per cent.), mainly owing to its complications—a fact which renders desirable some more effective method than “the careful nursing of each case” which at present, as we are told, constitutes “the only possible way of reducing its mortality.” It is therefore of interest to realize that a method of immunization has been worked out recently which has been reported by many observers to be of value in this connexion. The method consists, in its original form, of the subcutaneous administration of small doses of serum obtained from patients recently convalescent from the disease. If required, advantage may be taken of the fact that antibodies are also present, although in smaller quantity, in the serum of adults who have had measles.

It is of interest to note that as long ago as the year 1758 Francis Home of Edinburgh introduced a method of active immunization against measles which had been suggested by Alexander Monro in the previous year. About forty years ago Hugh Thompson, a vaccinator appointed by the Faculty of Physicians and Surgeons of Glasgow, devised a method of blistering measles convalescents and vaccinating contacts with the serum, for which he claimed good results. In this connexion, as in so many others, it is curious to note how history has a habit of repeating itself, as illustrated by the fact that only last year Professor Karl Leiner of Vienna introduced a similar method, the employment of which, however, he discontinued in consequence of a campaign of opposition from the daily press.

As in the case of scarlet fever, progress in regard to immunization against measles has been greatly hampered owing to want of knowledge as regards the specific virus of measles, although various micro-organisms have been incriminated from time to time. But, pending more definite knowledge as to the bacteriology of measles, the method of immunization by means of “convalescent serum” to which I have already referred is obviously one which demands our serious consideration. This was first employed by Nicolle and Conseil during a small epidemic of measles in Tunis in 1916, and has subsequently been employed extensively by Park and Zingher and by Richardson and Connor in America, by Degkwitz in Munich, and by Debré in Paris. Various workers have since modified the original methods of Nicolle and Conseil, and the production of active immunity has been attempted, apparently with some measure of success.

To achieve passive immunity the following methods of employing the serum are feasible: (1) Injection of convalescent serum into healthy contacts; in this case an immunity which lasts about a month is produced. (2) Injection during the first five or six days of the incubation period, when, as Degkwitz and others have shown, the patient will not develop measles; although the later it is injected the larger will have to be the dose.

If the serum be injected *after the sixth and before the ninth day*, measles will, nevertheless, develop; but the attack will be modified in the length of its invasion period, and by the absence of catarrhal symptoms, Koplik spots, and high temperature. The eruption also, if present, is less confluent, and the macules are smaller.

Injection at the beginning of the period of invasion (about the tenth day) will result only in *local* inhibition of the rash—the phenomenon of Debré—as regards which it should perhaps be mentioned that it is not, as has been suggested, comparable with the Schultz-Charlton reaction in scarlet fever.

With regard to the production of *active* immunity, besides the method mentioned of inducing a modified attack, Nicolle has suggested that the child it is desired to protect be given 10 c.cm. of convalescent serum, and, twenty-four hours later, 1 c.cm. of blood from an early case of measles. If the injection of blood be repeated, it is stated that the immunity produced is likely to be permanent. This method is probably reproduced in Nature when serum is given to a very early case.

The results obtained by the majority of workers who have used the earlier methods referred to have been decidedly favourable, as, indeed, is evidenced by the fact that municipal collecting and distributing centres for the serum have been established in connexion with hospitals in Germany, France, and America.

No original work on the subject had been published in this country prior to a paper by Dr. W. S. C. Copeman,¹ recording successful results obtained by him in face of a somewhat exceptionally severe epidemic of the disease which prevailed during the period February to July, 1925, at the Children's Hospital in Paris; and it will be of interest to members of the Harrogate Division to recall the fact that Drs. Smith and Miller, working on similar lines, recorded some successful results in a communication to the Pathological Society of Great Britain and Ireland in January, 1927.

In view of the importance of lessening, if possible, the mortality from measles in this country, we shall doubtless all agree that it is eminently desirable that investigation of the whole subject should be officially undertaken as speedily as possible, perhaps somewhat on the lines of that recently initiated in connexion with the work of the departmental committee on scarlet fever.

Meanwhile, it is encouraging to learn from Sir George Newman that the Ministry of Health, in conjunction with the Medical Research Council, is maintaining close observation upon the important investigations of Dr. Degkwitz, especially concerning the use of a sheep serum introduced by him, and the prophylaxis of measles generally.

REFERENCE.

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FUNGUS INFECTIONS OF THE HANDS AND FEET.

BY

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THE diseases to which I wish to draw attention are deeply situated in the epidermis and are very refractory to treatment. Many varieties of fungi may be pathogenic and provoke changes in the skin. Their classification is complicated, but broadly they may be divided into (1) the ringworms (*Gymnosaceae*), (2) the yeasts (*Saccharomyces*), and (3) some members of the order *Hyphomycetes* such as *monilia*. The reactions of the skin may be to all appearances identical, and the same species of fungus is able to produce lesions which differ clinically. The subject is still further complicated because many moulds and fungi are saprophytic, occurring on normal skin without producing any reaction, but both the yeasts and the ringworm *mycelia* have been found consistently invading the layers of the epidermis in the same type of skin lesion; in addition, the lesions have also been produced successfully by rubbing

the culture growth into scarified skin. Experimental work in this branch of dermatology is limited, for animals have a high degree of immunity to some of the species. Koch's postulate is therefore difficult to verify; but there is sufficient evidence that certain forms of skin disease are the response of the skin to the action of fungi which are pathogenic. Clinically they may be divided into (1) infection of the interdigital clefts; (2) acute vesicular eruption of the hands and feet; (3) infection of the nails.

Infection of the Interdigital Clefts.

In many patients the fungus responsible is the epidermophyton; this is the same parasite which attacks the upper third of the thigh and the groins, and causes the so-called dhobi itch or *tinea cruris*. It was first described clinically by Hebra under the name of "*eczema marginatum*" so long ago as 1860. Afterwards the parasitic nature of the malady was recognized, but it was not until fifty years later that Whitfield¹ in this country, and Sabouraud in France, called attention to parasitic lesions occurring on the feet, which were shown by Sabouraud to be due to the same fungus as the circular or polycyclic lesions of the groin.

Sabouraud's classic studies of the cultural characteristics of the pathogenic fungi known at that time established on a sound basis the importance of these diseases and led to an immense amount of research. It has since been proved that it is possible for the fungous elements to be carried by the blood stream, and to give rise to a generalized rash polymorphic in character (Arzt and Fuchs,² Ambrosoli³). In 1918 V. Graffenried⁴ successfully inoculated two human subjects with the epidermophyton. Bloch⁵ had previously shown that these fungi had the property of producing an allergic or sensitized state of the skin, but not always an immunity in the true sense of the word. He infected himself with the trichophyton and afterwards grafted a piece of his skin on to a patient suffering from a leg ulcer; the grafted skin alone was shown to be sensitized to the toxin of the fungus, thus demonstrating that the sensitiveness is a cellular phenomenon.

Some individuals are more susceptible than others, and it is not uncommon for one partner of a marriage to remain free from the infection although the other has suffered from it for many years. We must note also that different fungi have a predilection for various parts of the body. The interdigital infection, whether it be due to the epidermophyton or other fungus, may be present for years without the patient experiencing anything more than an occasional slight discomfort; yet it may flare up suddenly and rapidly spread to the axilla, the gluteal cleft, the sub-mammary folds, and elsewhere, not only causing considerable distress, but incapacitating the patient from following his or her occupation.

In an overwhelming proportion of the patients the disease is first noticed in the interspace between the fourth and fifth toes of one or both feet. If the toes are separated a white macerated epidermis is observed, which can be detached by forceps; small vesicles may be present at the edge or under the sodden skin, and not infrequently a fissure is to be found at the apex of the cleft. If the macerated skin is removed the exposed surface is seen to be of a bright red colour. The same condition may be present between all the toes, or may be limited to one or more clefts on one foot for years. In many cases if the plantar surface of the infected toes is examined it will be seen that this too is infected and fissured. The disease is inclined to spread along the sole, causing eczematous lesions together with increased cornification and painful fissuring. In addition, a dermatitis of the anterior surface of the legs is often present, and also in the hands one or both palms will sometimes be found to be fissured. It should be noted that the infection may occur on the instep without the toes being involved. As already stated, the axillae and groins may be affected, giving rise to circular or polycyclic patches of red inflamed skin. The following cases serve to illustrate the above description.

A married woman suffered from solid oedema of both ears and post-auricular fissures, with maceration and inflammation of the skin of the upper gluteal cleft. Maceration and fissures occurred between the toes of both feet, and mycelia were found in the

epidermic scales from between the toes. The patient had been aware of the cracks between the toes for six years; the other lesions had been present for two years, and were thought to be seborrhoeic eczema.

A man complained of pruritus ani of ten years' duration. He had had various treatments, including innumerable ointments, ultra-violet light, and x rays. Examination revealed extensive dermatitis of the perineum and buttocks, with the characteristic fissures between all the toes. Mycelia were present in the scales from the toes. The patient stated that the toes had been sore for more than ten years, and that the complaint was thought to be a manifestation of gout.

Two patients had dermatitis on the forehead and the upper lids, together with mycosis of the toes, verified by microscopical examination.

With reference to the second patient mentioned, it is interesting to note that A. Castellani⁶ drew attention to the fact that pruritus ani might be associated with a fungous infection. He found either the epidermophyton or trichophyton present in 11 out of the 54 cases he examined. Some of the skin complications are probably due to sensitization phenomena, and are not caused by the local growth of the fungous elements; for although it is possible to recover the fungus from the accompanying lesions between the toes, repeated examination fails to find it in other situations.

There is no doubt that the disease is more common in the middle classes than among the manual workers, and in my experience during the war groin ringworm was more frequently met with among the officers than amongst the men. Outbreaks of a serious nature have occurred in some public schools. The incidence is relatively high among young men; this is probably explained by the infection taking place through the medium of bathroom floors, towels, etc. Experiments show that the epidermophyton will live for at least a year in a dry state, and it has been recovered from infected boots four months after they were discarded. The incubation period is thought to be about twelve days.

Microscopical examination is essential for establishing the diagnosis, and may have to be repeated several times before the true nature of the disease is detected. The actual technique is simple, but requires some practice before the mycelia can be recognized. Epidermic scrapings should be taken preferably from the edge of the toe lesion, teased in liquor potassae, and then examined with a 1/6 in. objective. The mycelia are long, slender, highly refractile threads. Exact identification can only be achieved by culture on special media, but description of this process is outside the scope of this paper.

Treatment to be successful necessitates meticulous care on the part of the patient and his medical attendant. This is easily comprehensible when it is realized that the fungus occurs deep in the epidermis, is buried in all the nooks and crannies around the nails, is hidden in socks and boots, and in many cases is found to be growing in the nail substance itself. It is very resistant to moist heat, but according to Schamberg and Kolmer⁷ is killed when boiled for ten minutes. The same authors found that the epidermophyton is also easily destroyed by weak antiseptics.

Unfortunately it is no easy task to destroy these fungi in the living subject. In order to do so the exfoliating sodden epidermis must be thoroughly removed daily with a curette, and the toenails must be pared and scraped. As it is difficult for the average patient to perform the contortions necessary, it is advisable that this part of the treatment should be allotted to a third person.

There is a wide choice of remedial applications, the most noted of which is an ointment recommended by Whitfield, which now has a world-wide reputation. It consists of benzoic acid 5 per cent., salicylic acid 3 per cent., in a base of coco-nut oil and vaseline. Although the fungicidal property of the ingredients does not appear to be very high, yet in many of the cases an application of the ointment brings about a rapid improvement. Other remedies are tincture of iodine diluted with ten volumes of spirit, a 2 per cent. aqueous solution of mercurochrome-220, and 5 per cent. chrysorobin ointment. In my experience the first and the last named are the most serviceable, but whichever is chosen will fail unless the preliminary cleansing is carried out with exacting care. The feet should be washed daily. Socks should be of cotton, and

boiled for ten minutes daily; boots and shoes require dusting inside with an antiseptic powder such as boric acid. The treatment should be continued for at least a month after all signs of the disease have disappeared, and infected boots and clothing should then be destroyed. Surrounding dermatitis of the feet, if present, should be treated by the same remedies, but a fractional dose of x rays will greatly assist in its disappearance.

In 1908 Ciarocchi⁸ described a dermatitis limited to the webs of the fingers; this closely resembles in appearance the affection in the clefts of the toes mentioned above, but it is caused by other species of fungus—monilia or a member of the yeast group. It is curiously selective in position, for in the majority of patients its habitat is the web between the ring and middle fingers, although other webs may be involved. It is much less common than the mycosis of the toes, and so far has only been met with in women, most of whom have an occupation necessitating the frequent immersion of the hands in water. Kaufmann-Wolff⁹ produced similar lesions of her own hand with a culture from a patient with the disease. This disease is refractory and should be treated on the same lines as the mycosis of the toes.

Vesicular eruption on toes. A pure yeast culture was obtained from the vesicles.

Cheirpompholyx.

The cheirpompholyx of Hutchinson or the dysidrosis of Tilbury Fox has recently been the subject of research and discussion, and the consensus of opinion is that this vesicular eruption of the hands should in no small proportion of cases be regarded as a mycosis. Kaufmann-Wolff demonstrated a fungus in the vesicles in 30 per cent. of her cases. Darier¹⁰ stated that, excluding trauma and pyogenic infections, most cases (80 per cent.) were of mycotic origin. I have made a practice of examining the cases occurring in this district, and have found mycelia present in comparatively few. It is likely, however, that a more prolonged search would reveal a larger percentage of positive cases. The trichophyton appears to be the most frequent aggressor, but members of the yeast group are also responsible. The complaint is prone to recur, and is most common in young people, particularly women.

Although the hands suffer more frequently than the feet, it is by no means unusual to find vesicles in both situations during the same attack. The eruption is preceded by burning and itching. Small deeply situated vesicles then appear, the favourite position being the borders of the fingers and the palms. It is almost invariably symmetrical, and, should it be present on the feet, the vesicles are less numerous than on the hands. As the vesicles are deeply situated they do not rupture easily, but they may be secondarily infected, when they increase in size, coalesce, and rupture. Oedema of the hands accompanied by lymphangitis and pain is a further complication. Unless the pustules are incised and the whole of the exfoliating epidermis removed, the pus tends to burrow under the surrounding epidermis.

Such patients are usually of the hospital class, attending for the first time. They are often in a pitiable state; the hands are bathed in pus, under which is a dirty sodden skin, buttonholed in numerous places by the rupture of some of the pustules. It is astonishing how rapidly these patients improve if all the dead overhanging epidermis is removed daily, and a wet dressing of 1 per cent. solution of silver nitrate is applied three or four times a day. The oedema disappears, fissures heal, and, although the skin is covered with the black stain of silver oxide, it is soon apparent that the disease is under control. At this stage a fractional x-ray exposure materially hastens recovery. If the patient is spared the pyogenic infection, the vesicles dry and the skin exfoliates in about fourteen days. In such a case a protection by boiled cotton gloves or sterile gauze will suffice.

A girl, aged 10, was admitted to Sheffield Royal Infirmary suffering from vesicular eruption on all her toes. A pure yeast culture was obtained from the vesicles on three successive examinations. This case is interesting as she had previously been admitted to Firvale Hospital for the same complaint. A few weeks later she was discharged quite healed; but the vesicles returned within a few days—reinfection from her boots probably accounted for the recurrence.

Paronychia of the fingers and thumb. Culture showed growth of a cryptococcus.

Fungous Infection of the Nails.

Trichophyton infection of the nails has been recognized for many years. It may be present without any other manifestation of the disease, or may be associated with an affection of the beard or any other part of the body. Recently, however, cases have been described in England and abroad which are due to a yeast—*Oospora (Oidium) albicans* (Avid Scott,¹¹ Shelmire,¹² Kumer¹³).

When the disease is confined to the nail itself it commences at the free border, which becomes irregular, brittle, and of a dirty grey colour. This change gradually extends towards the lunula. In certain cases, and particularly when the "thrush fungus" is responsible, the changes in the nail are accompanied by paronychia. The appearance is then as follows: The soft tissue bordering the nail is oedematous, red, and raised. When gently massaged a sero-purulent fluid may be pressed from under the margins. There is often some crusting at the bottom of the nails, and if this be removed the nail fold is found to be detached from the nail. The free margin of the nail is raised by a brownish-grey debris. It is at first localized to one nail, but after varying intervals others are involved. The hands are more commonly affected than the feet. Changes in the nails which closely resemble the above are met with as an accompaniment of other diseases, or may be due to infection with staphylococcus or *B. coli* (H. MacCormac¹⁴), but careful microscopical and cultural examinations reveal an invading fungus in an increasing proportion of cases examined.

The treatment of the affliction is difficult, whichever variety of fungus is concerned. Perhaps the most successful procedure is avulsion of the nails, but even this drastic

remedy cannot always be relied upon to accomplish the desired result, for a recurrence may follow when the nail grows again. A more simple method is to pare and scrape the nails to the utmost limit of the patient's endurance, and then apply a 2 per cent. solution of silver nitrate or Fehling's solution. It is essential to keep the fingers dry, for the disease is most common in those whose occupation entails the immersion of the hands in water. It is also advisable to continue the treatment with a weaker solution after the disease is apparently cured.

In conclusion, I would emphasize the point that these diseases are more common than is generally supposed; they are of sufficient medical and social importance to deserve recognition and study by medical practitioners.

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Report

ON

THE TREATMENT OF MALIGNANT DISEASE BY COLLOIDAL LEAD.

BY

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IN view of the success claimed in the treatment of malignant disease by means of injections of colloidal lead I visited Liverpool in April, 1926, and, with Professor Blair Bell's permission, saw some of the patients who had there been submitted to the treatment, and observed the technique of the process. Although I was unimpressed by the results which were shown it was considered necessary by the Cancer Hospital that the method should be fully investigated. Dr. Lorna King was therefore appointed to assist me, and together we have treated a total of 88 patients in this way. Of these, however, 32 were given a preparation of colloidal lead hydroxide, and I omit details of them for three reasons—namely: (1) the preparation differs from that used by Professor Blair Bell in that all the lead has been converted to hydroxide, whereas in the latter only a variable and unknown proportion is in that form; (2) it is extremely toxic—ill effects so frequently follow its use, and are so marked, that I consider its employment unjustified; (3) no evidence of benefit was obtained in any case. Moreover, it has often been emphasized that satisfactory results could be obtained only if the lead be prepared in a particular manner, and if its pharmacological effects be closely watched in each patient. That much importance need be attached to such a statement is more than doubtful—the method used in Liverpool for preparing the metal has been many times changed, and there is no evidence whatever that one method is more successful therapeutically than another—but it was obvious that, in the first place, the original technique must be strictly followed.

Fifty-six cases were treated strictly by the Liverpool method—namely, 35 at the Cancer Hospital, 18 at St. James's Hospital, S.W., and 3 privately. In describing the results no differentiation is made between these series.

Method of Preparing the Colloidal Lead.

When this work was commenced it was impossible to obtain colloidal lead except by preparing it for oneself. The necessary apparatus was erected by Mr. C. E. Phillips, consulting physicist to the Cancer Hospital, and consisted essentially of a circuit containing a voltmeter and an ammeter together with an adjustable resistance, such that a current of 70 volts and 10 amperes passed when an arc was established between two pure lead electrodes immersed in distilled water. The water was placed in a porcelain

bowl with a few small lead shot. One electrode was then fastened so that its lower end was in contact with the shot, which were constantly stirred with the other electrode while the current passed. In twenty minutes a colloid suspension of lead (about 0.5 per cent.) was obtained. Its concentration was estimated by a modification of Nessler's method—a not very accurate one for such quantities, but the most practicable in the circumstances. For use, the suspension was diluted to exactly 0.5 per cent., and 0.4 per cent. gelatin, 2 per cent. sodium chloride, 0.05 per cent. potassium chloride, and 0.027 per cent. calcium chloride were added. The preparation is very unstable, sedimentation quickly occurs, and oxygen is rapidly absorbed from the air with the formation of very toxic lead hydroxide. It must consequently be used at once, and cannot be prepared in bulk for use at a later date.

From time to time certain slight modifications were made. First, 4.0 per cent. of gelatin was added instead of 0.4 per cent., so that the preparation was solid at ordinary temperatures. In this condition it could be stored in sealed ampoules, and remained stable for several months. Then iso-electric gelatin was substituted for the ordinary substance, and had the same stabilizing effect without becoming solid. Sometimes a trace of a reducing agent was added to hinder the formation of hydroxide. Finally, we reverted to the original preparation.

All these preparations are essentially the same, and there is no reason to suppose that their therapeutic action differs.

Type of Patient Treated.

Most types of malignant disease have been treated—epithelioma, carcinoma, and sarcoma. In every case the disease was inoperable when first seen, or was recurrent after operation. Many of them were in an advanced stage of the disease. To obtain suitable patients for such work is far more difficult than appears on the face of it. A large majority of the inoperable patients admitted to hospital are having, or have had, some other form of treatment (for example, radiation), and are therefore unsuitable for this, since any change observed could not be certainly attributed to either method. If the patient be not already under some form of treatment he or she is generally too near the end for any form. Another difficulty is that very often the patient refuses to remain long enough in hospital to give the method a chance. No patient in this series had received any but surgical treatment.

Dosage.

In deciding on the dose to be given an attempt was made to give the maximum amount of lead which did not endanger life, and to keep the patient as long as possible under the influence of this quantity. With six exceptions the initial dose was 0.08 to 0.1 gram. In one case this was repeated after seven days, with the result that the patient became very ill; there were several rigors, repeated vomiting, and marked jaundice. From these effects she eventually recovered, and survived about seven months, but it was not considered justifiable in any other case to repeat the dose at so short an interval. In seven cases the second dose was given a fortnight after the first, but again the reaction which followed was generally intense, so intense that it was decided to allow an even longer interval. In six cases an initial dose of 0.05 gram was given, and repeated in approximately a week. While these showed no better therapeutic results than the others, the reaction following each injection was reduced to a minimum, and never amounted to much. For the remainder an initial dose of 0.1 gram was followed by the same dose at the end of three weeks. Even after this interval some reaction was almost invariable, but was in no case serious.

Subsequent doses must depend, both as to the quantity and interval, upon the reaction of the individual patient. Our aim has been to administer a total of 0.6 gram to each patient, and we commenced by repeating the original dose of 0.1 gram at intervals of three weeks to six doses. This proved disastrous, for the only two patients who were so treated (one with five and the other with six doses) both died of uraemia within eleven days of the last dose. We therefore changed the procedure and gave three doses of 0.1 gram at intervals of three weeks, and then continued