tion of the opening. Therefore, the opening must always be made over those parts of the cortex which can be dispensed with by the patient with least inconvenience. In right-handed individuals the left side of the skull being that containing the educated association centres should not be chosen unless there is some very special reason for choosing that side.

I have seen in one case in which I made an opening over the left temporo-sphenoidal lobe in a right-handed individual aphasia develop simply from the centre in Broca's convolution having its function thrown into abeyance by being involved by the protrusion in the neighbourhood. Also proximity to the fissure of Rolando must be avoided, so as to save the motor areas in front of that fissure and their sensory representations behind, as hemiplegia would be a

very likely result of an opening in this position. A good area to choose is over the temporo-sphenoidal lobe, as Cushing points out; but this should be chosen on the right side in right-handed individuals only, and the left side, though also recommended by Cushing, should be avoided if possible in right-handed individuals, for the

reason of avoiding any interference with the neighbouring educated association centres. In left-handed individuals, of course, the reverse applies.

In the present case I chose the situation between the occipital and parietal lobes because there did not appear to be any chance of causing inconvenience to the patient by choosing this site.

Interference with the centre for vision or with the optic radiation from protrusion in the neighbourhood of the occipital lobe would result in hemianopsia in the event of sight being restored; but in this case this consideration was of no moment, for restoration of sight was out of the question. Such a restoration is one of the happiest events in these operations, and it is almost sure to follow if the operation is undertaken early enough, but in this patient the optic nerve had

Fig. 2.—Intracranial fibro-glioma, compressing pons, medulla, and right lobe of cerebellum

been destroyed. Therefore there was nothing to be lost by choosing this region as the site of the bone defect, and the opening in this region permitted the formation of a better hernia in a more convenient situation, and the result was that he was not in any way incommoded by any damage to the cortex which resulted from the hernia cerebri.

THE CULTURAL CHARACTERISTICS OF THE MICROBACILLUS OF ACNE.

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THE object of the present research on the microbacillus of acne was to reconcile, if possible, those accounts of its biological and cultural properties which have been given by recent contributors to the subject, with those originally described by Sabouraud in 1897. Such work is rendered all the more necessary when it is realized how great are the differences in the pathogenic qualities ascribed to this bacillus by the various authors who have treated the subject.

In order to bring these discrepancies of opinion clearly before those interested in the subject it is necessary briefly to refer to the principal works dealing with the acne bacillus.

It was Unna¹ who in 1896 discovered this organism in the comedo, but who, being unable to cultivate it, drew, from purely histopathological data, the conclusion that it was the cause of the comedo and the subsequent suppuration. The classical work, however, upon the subject is that of Sabouraud,² who, studying the organisms both in the lesion and in culture, was able to speak more authoritatively on the subject. He assigns to the microbacillus the causative agency in the production of the comedo, but decides that the suppuration is due to the staphylococcus. This opinion he supports, first, on the histological grounds that the staphylococci are found in the phagocytes, while

he was never able to find microbacilli undergoing the process of phagocytosis in these cases; secondly, because he was never able to produce suppuration even by injecting huge quantities of microbacilli under the skin. For the cultivation of the microbacillus a special acid glycerine agar was required, and the details of its preparation will be found in his work. The inoculation was made with the central portion of a seborrhoeic filament, which, by the aid of a lance-headed needle, was carried into the medium to a depth of several centimetres. Incubation at 37° C. results in rapid growth of staphylococci of the non-liquefying variety, followed in four days by the appearance of a red-brown button, which gradually increases until it reaches the size of a small currant. This is the culture of microbacilli, which can be obtained pure by reinoculating after a month's growth, at which time the staphylococci are found to have died. He never succeeded in obtaining an ordinary stroke culture, but obtained subcultures by several other methods—for example, by inoculating and incubating eggs. These researches were performed at a time when anaerobic methods were very imperfect. Inoculation experiments on animals were uniformly negative in Sabouraud's hands.

These results were confirmed by Gilchrist,³ but it is extremely doubtful whether the organism he was dealing with was identical with that of Sabouraud. Cultures of his bacillus were fatal to guinea-pigs and white mice in some cases.

In this state the matter rested for some years, the conclusions of Sabouraud being fairly generally accepted in France and England.

Then followed in 1907 some work on the sebaceous

glands by Hallé and Civatte,⁴ who, in making anaërobic cultures from comedones, found constantly colonies of an anaërobic organism which corresponded very closely in microscopical characters with the organism seen in the comedo. This they pointed out to Sabouraud, who, with Hallé, compared the organisms obtained by both methods, and found by inoculating one of Sabouraud's cultures in a deep glucose-agar tube by the stroke method (which Hallé and Civatte, pupils of Veillon, used), that Sabouraud's organism grew only anaërobically. This is a surprising fact, the only explanation for which is that the microbacilli in the centre of the material used for inoculation in Sabouraud's cultures were so protected by the surrounding fatty material that the penetration of oxygen was insufficient to prevent growth. At the present moment Sabouraud has only modified his previous teaching in so far that he impresses the fact that the microbacillus is anaërobic in culture.

The next contribution to the subject was that of Fleming,⁵ who, in describing his cultural experiments, came to some conclusions at variance with those of Sabouraud. In the first place, he describes pure cultures of microbacilli by surface inoculation of pus from cases of acne, on a medium described by him in his work. This fact and the failure to grow staphylococci in all cases, led him to the opinion that the latter when present were only the result of accidental contamination. Accordingly he makes the microbacillus the cause of both comedo and pustulation—a conclusion supported by his success in obtaining a pustular eruption by rubbing a culture into the arm of a susceptible person. This Sabouraud had failed to obtain. Secondly, he described his cultures as being made by ordinary surface inoculation, by which method Sabouraud always failed to get growth. Results of calculation of opsonic indices and the therapeutic action of vaccines prepared from the organisms cultivated were also given in support of his views.

This paper evoked criticism from Whitfield,⁶ who maintained his previous opinion that suppuration in acne was due to staphylococci by reference to histological and cultural experiments, and could not agree that the results of opsonic work justified the conclusions drawn by Dr. Fleming.

Quite recently a paper by Südmersen and Thompson⁷ appeared recommending the use of a strongly acid agar with the addition of horse serum, but the most significant part of the work was their recommendation of anaërobic methods for the cultivation of the organism.

Thus as the matter stands at present the microbacillus is described as being aerobic and pyogenic by some, anaërobic and non-pyogenic by others, and a multitude of minor differences in characters morphological and cultural are disputed.

My own personal work consists of a series of primary cultures from cases of acne, now totalling over 30. The materials used for inoculation were generally comedones, sometimes seborrhoeic filaments and pus.

The medium employed for these cultures was simply 2 per cent. glucose agar in deep shake tubes or stab, or slopes incubated anaërobically. Personally I find the most convenient method for isolating pure cultures the deep shake method as recommended by Veillon. The agar is melted and allowed to cool to about 45° C., when a drop of an emulsion is added, made by crushing a comedo, or such material as is to be used, in a few drops of salt solution, mixing well and transferring to a second tube 3 or 4 drops from the first, and 10 to 20 drops from the second to a third. The agar is allowed to solidify and the tubes incubated at 37° C. By this method in the second and third tubes isolated colonies are obtained and can be easily picked out for subculture. This is most easily done by using a sterile Pasteur pipette drawn out to about 1.5 mm. in lumen. To this a rubber tube with a mouthpiece at one end is attached, and when the tube is held horizontally against the light the pipette can be pushed down to the colony, which then is sucked up into the lumen, withdrawn, emulsified, examined, and re-inoculated by a procedure exactly similar to that described above.

In cultures made from comedones or pus by this method staphylococcal colonies appear in a day or two, chiefly confined to the upper aerobic areas of the first tube; but after an interval of four days minute colonies appear in

myriads, confined to the anaërobic areas. These slowly increase in size, and when discrete assume a lenticular form or often a shape composed of regularly intersecting lenticular bodies; the colour of these colonies is greyish-white. Scattered amongst these white growths, especially if the material inoculated has been a comedo, are seen a few similarly shaped colonies, but red and larger in size.

On microscopic examination the organism found in the white colonies is seen to be a short plump Gram-positive bacillus, exactly corresponding in appearance with the organism seen in a smear of the comedo. The red colonies show coco-bacillary forms also Gram-positive, but not recalling the organism found in the comedo. Subcultures made by the shake method readily show the anaërobic character of both these organisms which only grow at a distance not less than 1 cm. from the surface.

Stab cultures made in the usual manner in glucose-agar tubes give growth in the deeper parts of the stab, but show no special characters. On slopes inoculated from a pure culture of the microbacillus, incubated in a Bulloch's apparatus or Buchner's tube, isolated whitish colonies or a continuous growth is obtained according as a dilute or thick seeding is made. By these surface inoculations one obtains longer and more diphtheroid organisms with occasional irregular forms, contrasting with the uniform short plump forms of the mother colony.

Cultures may also be obtained in glucose broth incubated anaërobically, but a large amount of material must be inoculated. On ordinary agar, and in ordinary broth, attempts were almost uniformly futile, or such an insignificant growth occurred that one doubted whether the seeding had increased at all. For a very long time attempts to obtain an aerobic culture failed, but finally, by using a very old strain frequently subcultivated, an aerobic growth was obtained. This is more likely to succeed when material from a slope culture is used than when a colony from a deep shake tube is inoculated.

Similar methods are successful in cultivating the organism growing in red colonies, but the colour production soon diminishes on subcultivation, and is not evident on slopes.

To compare this organism with a culture obtained from Sabouraud was the next step. In this I quite confirm the results obtained in Paris, an emulsion from Sabouraud's culture inoculated by the shake method growing only in the anaërobic areas. Also, I was able, after some difficulty owing to the lack of sticky coherence required for this method of inoculation, to transfer a colony from an original culture in a shake to Sabouraud's medium in the manner described by him. The mass increased and assumed a brownish hue as seen in Sabouraud's culture.

These cultures have been accepted by Sabouraud as identical with the organism described by him, but a culture of Fleming's organism when shown to him was not recognized as being identical with the microbacillus. With regard to animal inoculations made with the microbacillus, negative results with guinea-pigs were always obtained. The morphological and cultural characters of Gilchrist's bacillus, and its marked pathogenic qualities for guinea-pigs and white mice, lead one to think that his organism was more probably a form of streptothrix, and not the microbacillus of acne. In the human subject no result was obtained by rubbing in large quantities of the culture.

In comparing the organism isolated by anaërobic methods with two strains obtained from Dr. Fleming and a third obtained through Dr. Eyre of Guy's Hospital, a considerable number of important differences was found. First, and most important, it was found that Dr. Fleming's organism was strictly aerobic, growing only in the uppermost centimetre of a shake or stab culture, and never in the depths. On slopes incubated anaërobically no growth was obtained. Secondly, his organism grew quite readily, and appeared in about forty-eight hours on ordinary agar, and in ordinary broths, on which media the microbacillus, even under anaërobic conditions, is at least extremely difficult to cultivate. Even on glucose agar four days elapse before the colonies of microbacillus become evident. It was on these characters that cultures shown to Sabouraud were rejected by him.

About two months ago, however, I obtained a fourth strain from Dr. Fleming, and, much to my surprise, found that it grew anaërobically, being, in fact, exactly similar

to those growths obtained by educating the microbacillus to aerobic growth. This culture is undoubtedly different from the others, and is probably the true microbacillus.

In drawing conclusions from this work we are bound to consider, first, whether the organism cultivated by Dr. Fleming was identical with that grown by Sabouraud. I am forced to the opinion that this is not the case, since it is inconceivable that an organism really an anaërobe should be so changed in its characters by cultivation under anaërobic conditions as quite to lose the power of growing anaërobically. And even a very old strain of microbacilli which has been educated to aerobic conditions will, if transferred to anaërobic conditions, immediately reassert its preference. The early appearance of growth in Fleming's cultures, which is always less than the four days necessary for the first sign of microbacilli in cultures, is also a point against the identity. Again, the pustular eruption described by Fleming on inunction of a mass of his organisms into the arm of a susceptible person is not obtained by a similar experiment with Sabouraud's organism. Now, since it is admitted by all who have compared the two, that the organism seen in Sabouraud's cultures and that obtained by ordinary anaërobic methods are identical, there is no reason again to distinguish between Fleming's organism and the anaërobe.

The next question for consideration is, Which is the real microbacillus of acne?

In the first place, Fleming's organism is admittedly difficult to obtain, and a culture has not been forthcoming in my hands or in those of Dr. Whitfield, in spite of numerous essays. On the other hand, the colonies obtained by anaërobic cultivation are in myriads, as would be expected when one remembers the vast numbers of the organisms in the comedo. Again, Dr. Fleming does not mention a single instance of successful cultivation of his organism from comedo, all his cultures having apparently been made from pus, which is more liable to contamination and not so rich in the organism whose cultivation is sought as the comedo.

Most of Dr. Fleming's conclusions seem to have been based upon the opsonic indices of his patients to the organism cultivated. But it seems to me unjustifiable to pronounce an organism the cause of a particular lesion on these grounds. There are at least other possibilities.

With regard to inoculation experiments, at first sight the results published by Dr. Fleming appear more promising, but it is to be remembered that comedo formation and not suppuration is the essential lesion of acne vulgaris, and no account of a production of comedo is given in the description of his results. In addition, treatment with vaccines of Fleming's organism apparently caused increase of the amount of pustulation; but no mention is made of the disappearance of comedo under such treatment.

The inoculation experiments by inunction with the anaërobe are, it is true, unconvincing. But nearly everybody is at least seborrhoeic, and the liability of the subject to react to the presence of the organism by comedo production seems to be limited, in the vast majority of cases, to the age of puberty and early twenties, and then to certain well-defined localities—for example, face and back where inoculation results would be open to question. Those who have suffered from acne in their teens appear, as a rule, to become immune to the organism to the extent that the only reaction observed is a persistent excessive fat secretion.

Next, as to the causation of the pustulation, on only one occasion did I fail to find staphylococci in culture from pus, though it is only fair to acknowledge that Sabouraud in his vast experience has occasionally found cases which gave no staphylococci. It is true also that microbacilli can be cultivated in great numbers from the pus, but not more than might be expected considering the amount of comedo debris present in this material.

In conclusion, a great deal has been written about media for the cultivation of this organism. In my opinion the complicated agars recommended are quite unnecessary. The secret of success in cultivating the organism is the use of anaërobic methods. Under these conditions a simple and easily prepared medium like 2 per cent. glucose agar gives luxuriant growth. Sjödmersen and Thompson, who also used anaërobic conditions, recommend a highly acid medium (+ 40 to phenolphthalein). But even by reducing

the acidity to + 20, I was unable to obtain a material which was sufficiently stiff to be sloped.

Dr. Sabouraud still uses his special medium and method of inoculation, but for ease and rapidity of obtaining a pure culture from all sorts of material, I think it must be admitted the anaërobic methods are the most satisfactory.

In conclusion, I wish to express my gratitude to Dr. Ledingham at the Lister Institute for his goodness in controlling my work and advising lines of action; to Dr. Whitfield for the material he provided, and assistance throughout the work, and especially to Dr. Sabouraud for his kindness in furnishing me with the full literature on the subject, and in examining and identifying my cultures.

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ACHONDROPLASIA.

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ACHONDROPLASIA is described by Poynton¹ and others² as a rare disease. I recently saw five cases, three of which, it is true, were not quite typical, though, as I shall presently endeavour to show, they were undoubted cases. This morning I accidentally passed two more cases while walking in the streets of London within ten minutes' interval, making in all seven cases seen in three or four months. It would not, however, be fair to doubt the accuracy of the statement that the disease is rare on the strength of what may be an unusual experience, especially as five of the above cases were attached to a travelling company of dwarfs.

My remarks will be limited to three of these cases because they differ in some respects from the usual description. Two of them were sisters and the third was a daughter of one of them. Mother and daughter were 18 and about 40 years of age respectively. The aunt was about 42 years of age and a nulliparous widow.

These facts, of course, support the view that the disease may be hereditary, as has been recorded by Porak and others; but Drs. Rankin and Mackay³ appear to doubt the evidence for this. The transmission of the disease from parent to child is mentioned by Dr. Poynton. The diagnosis is easy in typical cases, and most authors lay stress on the pug-nose, which is so common as to be an almost invariable symptom; but in none of the three cases to which I now refer was this peculiarity present, nor was there anything in the appearance of the head or face to suggest any abnormality. Nevertheless, the great disproportion between the lengths of the four limbs as compared with the body (which was certainly small, as would be expected from imperfect ossification of the ribs and pelvic bones), the small stature, the characteristic appearance of the hands described as *main-en-trident*, the absence of rickety changes such as contracted chest, deformed ribs, curved spine, and bowed legs, leave, I think, no doubt of the nature of the disease. Moreover, the dentition did not appear to have been delayed, and the shortness of the limbs was noticed about the second year, when it is unusual to notice shortening from rickets. The history I was able to obtain may have been faulty, and I was only able to examine one of the two sisters clinically. Apparently this absence of the depression at the root of the nose, which is admitted to be due to a premature synostosis of the occipito-sphenoidal synchondrosis or os tribasillare, has been noticed by others, for Dr. Thomson⁴ says "there is usually an abrupt depression at the root of the nose," though he does not say definitely that there are other cases which might not show that peculiarity. The skin is described as