LOCALIZATION OF FUNCTION

While it is undoubtedly true that certain portions of the cerebral cortex seem to specialize in particular functions, the conception of brain centres obtained from most textbooks of medicine is extremely misleading; and Broca's area, still unhappily described as the speech centre, forms an example of the persistence of an antiquated ignorance of cerebral function. Speech probably involves many portions of the cortex and myriads of cells in all layers. Notwithstanding this, certain portions of brain cortex do have specialized functions, as is proved by the findings of cyto-architectonics. Brodman, Campbell, Marinesco, Betz, and many others, divide the cortex, from the known arrangement of its cells, into as many as upwards of a hundred areas. It suffices to say, with von Economo, that there are at least five main structural types of cortical cell construction and lamination. Thus the area known generally as the Rolandic motor area is largely devoid of granule cells, which it does not need, because it is concerned with outgoing cerebral impulses. This comparative absence of granule cells enables us to recognize such portions of the cerebral cortex under the microscope with considerable facility, and von Economo calls these areas the agranular cortex. Areas, on the other hand, which are primarily concerned with the receipt of impulses from the chief exteroceptive senses, such as sight, hearing, taste, and touch in all its forms, will be particularly rich in granule cells, thus forming easily recognizable cortical areas, termed granular cortex. With these exceptions, the rest of the cortex is mainly made up of slight, but recognizable, variants of the five or six cellular layers. Correlating these facts with clinical conditions the Viennese and other Continental schools find that mental disorder is rarely associated with area lesions, but shows a predilection for certain laminae in one or other of the five types of cortex.

PATHOLOGICAL CHANGES

With the recognition of these five or six cortical layers of the brain there has subsequently accrued, especially as the result of English work, a considerable knowledge of their pathological alterations in association with certain mental disorders, especially in mental deficiency. It is now well established that mental deficiency results from a lack of development of the cells of either or both of the pyramidal and fusiform cortical layers, with a consequent diminution in their numbers, a disordered structural formation, a consequent microcephaly, and disordered psychological reactions to the environment best summed up, perhaps, by a single word, unsanity. Bolton, in his classic work on *The Brain in Health and Disease*, extended and applied our knowledge of cortical lamination to both the amentias and the dementias; and von Economo has been able to go even further in applying it to both psychology and psychiatry.

The agranular cortex, for example, shows no change in general paralysis, which chiefly affects some of the cell laminae in the anterior frontal lobe of the brain, parts of the parietal and temporal lobes, and certain other sites. According to Jakob, the majority of organic mental diseases do not attack areas of the brain, but show a widespread affection of the cortex with a predilection for certain regions. In demential psychotic disturbances of the personality, von Economo finds that the chief lesions are in the third cortical layer. On the other hand, those diseases which primarily affect the capacity for expression and motility show a particular affinity for the cells of the fifth and sixth layers. In those cases of senile dementia which show a striking extrapyramidal muscular rigidity, in addition to their psychic symptoms, von Economo finds a marked affection of the cells of the fifth and sixth

laminae. In many other cases of dementia there is not only a destruction of cortical cells, but also a proliferation of the glial cells, as instanced by von Economo, and also found in a case now under examination from a recent post-mortem at Stoke Park Colony. Mental deficiency, on the other hand, does not result so much from a dissolution of brain cells, as from their inherent inability to develop, many of them remaining in the neuroblastic condition; and feeble-mindedness is, according to Hammarberg, a closely allied condition of inhibition of proper cell development.

FIG. 2.—Cortical areas of von Economo. 1. Agranular cortex, chiefly confined to motor areas. 5. Granular cortex, chiefly found in sensory areas. 2. Frontal type. 3. Parietal type. 4. Polar type. Nos. 2 to 4 variants of the type illustrated in Fig. 1. No. 3 in the diagram corresponds to focal points of intelligence.

But cyto-architectonics is not of importance only to the psychiatrist. It promises results for the psychologist also, inasmuch as cellular studies of the cortex suggest that there are present richly receptive focal points of intelligence (von Economo) in both the prefrontal and parietal areas; but again the warning must be sounded that "for every kind of psychic expression the functioning of the entire cerebrum is necessary."

Thus does the apparently dulllest and most forbidding of subjects, cyto-architectonics, hold out the greatest hope for the future of mental science in all its branches. And indeed it cannot now be long before the brain gives up the last of its secrets—the fashioning of mind out of the functions of neurones and their synapses.

ACIDOSIS AND SEBORRHOEA

BY

JOHN T. INGRAM, M.D., M.R.C.P.

PHYSICIAN IN CHARGE OF THE SKIN DEPARTMENT, GENERAL INFIRMARY, LEEDS; LECTURER ON DISEASES OF THE SKIN, UNIVERSITY OF LEEDS

AND

F. S. FOWWEATHER, M.Sc., M.D., D.P.H.

CHEMICAL PATHOLOGIST TO THE GENERAL INFIRMARY, LEEDS; READER IN CLINICAL CHEMICAL PATHOLOGY, UNIVERSITY OF LEEDS

The problem of seborrhoea is one of great importance and complexity. The minor manifestations of this disorder are so common as to be almost universal, while the major dermatoses of this group form a very large part of all skin cases seen in private and hospital practice. The subject is therefore one of interest to the general practitioner as well as to the dermatologist, and merits investigation from more than one point of view. MacLeod¹ and Dowling² have added much to our knowledge of the organisms concerned in the production of some of these disorders, but the seborrhoeic diathesis has received little attention, except from the clinician.

Three factors play a part in the production of most seborrhoeic affections—namely, a constitutional, an infective, and a precipitating factor. A brief explanation of each of these features is necessary.

THE CONSTITUTIONAL FACTOR

In a seborrhoeic subject the whole organism, as well as each separate organ or system, is abnormal to some appreciable extent. Outstanding among these variations is the functional instability of the skin, particularly with reference to its secretory functions, but also manifest in hypersensitivity to external or internal irritants, in vasomotor instability, and in diminished resistance to infection. In like manner the mucous membranes, especially those lining the mouth and upper respiratory passages, show secretory disturbances, diminished resistance to infection, and general hypersensitivity. There is commonly evidence of endocrine imbalance, a feature recognized by all authorities and sufficiently shown in the high incidence of seborrhoeic affections about the time of puberty and the menopause. Seborrhoeics are prone to dyspepsias and other functional disorders of the alimentary system. According to some authors they usually secrete a hyperacid urine³; if this is true, it may only be the result of some disorder of the secretory mechanism of the kidney. They are subject to vasomotor disturbances and to functional disorders of the cardio-vascular system. They appear to be more prone to the minor affections of the respiratory organs; and they are commonly the subject of nervous and emotional instability.

The seborrhoeic constitution, it would seem, can be summed up as one of general functional instability, and the question arises whether this feature is dependent upon a primary nervous instability, or upon endocrine imbalance, or whether the syndrome is the result of some unrecognized biochemical abnormality. The problem is probably most easily explained upon the basis of a primary nervous disorder; this is supported by the incidence of seborrhoea in the course of, and as the result of, epidemic encephalitis lethargica.⁴ Whatever the basic factor may be, there can be no doubt that constitutional predisposition is the essential consideration in the elucidation of this group of disorders.

THE INFECTIVE FACTOR

The organisms chiefly concerned in provoking seborrhoeic manifestations—the *Staphylococcus epidermidis albus*, the seborrhoeic or acne bacillus, and (most important of all) the bottle bacillus or pityrosporon of Malassez, the nature of which has been recently demonstrated by MacLeod¹ and Dowling²—are harmless saprophytes on the normal skin, but may provoke inflammatory reactions in the skin of the seborrhoeic subject. These organisms assume chief importance in the minor manifestations of seborrhoea, as scurf of the scalp, simple pityriasis corporis, and, to some extent, in acne affections, all of which are readily amenable to treatment. The infective organisms of seborrhoea play only an insignificant part, however, in the grosser and more chronic seborrhoeic affections—chronic seborrhoeic dermatitis and eczema, gross acne and rosacea, which are most resistant to treatment and present the dermatologist with some of his most difficult problems.

THE PRECIPITATING FACTOR

Probably every seborrhoeic disorder is dependent at its onset on some precipitating cause acting upon the unstable constitution of the subject, and so reducing resistance to infection or disturbing functional activity of the skin. Such jars may take the form of infective or toxic injuries, physical or chemical trauma, occupational hazards, environmental changes, psychological disturbances, puberty, menopause—indeed, any change affecting the constitution as a whole. It is not our purpose to discuss further this aspect, but to confine ourselves to a consideration of the constitutional factor upon which seborrhoeic disorders must arise.

NATURE AND RESULTS OF INVESTIGATION

We proposed to investigate the acid-base balance in the blood of seborrhoeic subjects, hoping to find some clue as to the character of the constitutional disability we have described.

Sabouraud⁵ in 1902 suggested that many seborrhoeics passed a hyperacid urine showing excess of chlorides and diminution of phosphates. In 1918 Barber and Semon,⁶ from their study of a large number of cases of seborrhoea among soldiers on active service, reaffirmed this finding as regards hyperacidity, and from certain therapeutic investigations concluded that the "status seborrhoeicus"—as they described the constitutional dyscrasia in seborrhoeics—was essentially a state of relative acidosis. It is widely held that treatment by alkalis is constantly beneficial in seborrhoeic affections (an impression which one of us has not been able to confirm from the clinical point of view) and the finding of a state of relative acidosis in the blood would put such a line of treatment on a rational basis. It seemed to us, therefore, that it would be of some value to examine the blood in various types of seborrhoeic affection from this point of view. Our investigation covered a series of patients of all ages, suffering from various types of the more marked constitutional seborrhoeic disorders.

To say that an acidosis is present in any condition does not carry us much further towards a real understanding of that condition, unless we know something of the mechanism by which the acidosis is produced. Beyond stating that chemical examination of the urine never revealed the presence of diacetic acid or β -oxybutyric acid, Barber and Semon offer no further evidence as to the nature of the acidosis which they believed to be present. As we shall show later, hyperacidity of the urine does not necessarily mean that there is an increase in the total excretion of acid. Further, even when there is an increased excretion of acid, it is not absolutely necessary to conclude that an acidosis is present; for if we assume that, in consequence of some functional disturbance of the kidneys, these organs excrete more acid than normally, while the production of acid within the body remains at its usual level, the result would be a *relatively* increased balance of alkali within the body—that is, we should have an alkalosis. We are not aware that such an alkalosis has ever been described, but its occurrence in this way is conceivable. A similar explanation has been advanced for the alkalosis which sometimes occurs in association with pyloric stenosis—namely, that excessive loss of hydrochloric acid from the stomach, due to vomiting, is the cause of the increased alkali reserve.

Barber and Semon found confirmation of their views regarding the presence of acidosis in seborrhoeics, in the results of tests for alkaline tolerance. It was claimed that these tests showed markedly increased tolerance in the majority of cases. But tests for alkaline tolerance (for example, Sellard's test) are not entirely free from objection as tests for acidosis, and, moreover, in recent work it has been shown that the limits of alkaline tolerance in normal individuals are much wider than was originally supposed. Sellard put the upper limit of alkali tolerance at 5 grams of sodium bicarbonate, while, more recently, Hawk and Bergeim⁷ put it at 30 grams.

EXAMINATION OF THE BLOOD

It seemed advisable to investigate acidosis in seborrhoeics having regard to the blood, rather than to the urine. In general, changes in the urine depend on and reflect changes occurring in the blood. An examination of the blood is therefore a more direct approach to the problem than an examination of the urine.

Acidosis is of two main types—namely, that concerned with volatile acid (that is, carbonic acid) and that con-

cerned with fixed acids. There is no reason whatever to assume that in seborrhoea we are dealing with the former type. On the contrary, it is to be inferred, from what has been written on the subject, that, in this condition, certain metabolic disturbances are supposed to be present which result in the production of fixed acids in increased amount, and these have to be dealt with by the blood and finally excreted in the urine. The first result of the pouring of increased amounts of fixed acids into the blood stream is the using up of increased amounts of the alkaline buffer salts (chiefly sodium bicarbonate) which are present in the blood to effect their neutralization; in short, a reduction of the alkali reserve of the blood. Changes in this alkali reserve are fairly well represented by changes in the sodium bicarbonate content, or of the carbon dioxide combining power. The determination of the latter is a fairly simple procedure, which is often employed in clinical investigations, and it is this determination which we have used in the present inquiry.

The normal range for the carbon dioxide combining power of the blood, as shown by Van Slyke, Stillman, and Cullen,⁸ is from 53 to 77 c.cm. of CO₂ per 100 c.cm. of plasma. The results which we have obtained in 26 cases of seborrhoea may be grouped as follows:

CO₂ combining power: Over 70 c.cm. per 100 c.cm. of plasma, 4 cases; 65 to 70 c.cm., 9 cases; 60 to 65 c.cm., 7 cases; 55 to 60 c.cm., 4 cases; less than 55 c.cm., 2 cases. The highest figure obtained was 77.7 c.cm., and the lowest 50.9 c.cm.

It will thus be seen that of our 26 cases, 16 give results between 60 and 70 c.cm.—that is, they fall well within the normal range; 4 cases give values above 70 c.cm., and so approach the upper normal limit—that is, alkalosis—while 5 cases give results between 53 and 60 c.cm., and so approach the normal lower limit, or acidosis. Only 1 case gave a result (50.9 c.cm.) which can be considered as outside the normal range. The values obtained and the range shown are almost exactly what would be expected from a similar number of normal individuals. It is clear that, in our cases, there is no evidence whatever of any general tendency towards a depletion of the alkali reserve, and, so far as the blood is concerned, there is no evidence of acidosis. These results were not according to our expectations, and during the latter part of the investigation we decided to make examinations of the urine as well as of the blood.

EXAMINATION OF THE URINE

Acidity of the urine is only very roughly gauged by its action on any single indicator. The degree of acidity is most accurately ascertained by determining its pH; for practical purposes this can usually be obtained with sufficient accuracy by noting the action of the urine on a series of indicators, or on a composite indicator which shows a number of colour changes over a fairly wide range. But the degree of acidity of urine is not an indication of the actual amount of acid present, since it depends very largely on the amount of buffer substances (chiefly phosphates) present in the urine, and also on the nature of the acids, as well as their quantity. It is obvious that, for the purpose of investigating acidosis, the amount of acid excreted offers more information than the degree of acidity of the urine, and this is best obtained by determining the titration acidity of the urine—that is, the amount of standard alkali required to neutralize the urine (with phenolphthalein as indicator). The most useful value is that obtained from the twenty-four-hour specimen, but, unless great care is taken in the collection and preservation of the urine, very considerable error may be introduced, owing to the liability of the urine to undergo fermentation, with the production of ammonia. As most of our patients were out-patients, we felt it unwise, there-

fore, to consider the results on twenty-four-hour specimens, and contented ourselves with single specimens passed at the time the blood specimens were taken, and analysed immediately after being passed. All specimens were taken about four hours after the patient's last meal.

The normal values for the titration acidity of urine vary considerably; they usually lie between 10 and 40 c.cm. of decinormal sodium hydroxide per 100 c.cm. of urine. Very much larger values are frequently obtained in acidosis. The urine of 15 of our cases has been examined in this way, with the following results:

Less than 10 c.cm., 5 cases; from 10 to 40 c.cm., 7 cases; over 40 c.cm., 3 cases.

These results are similar in general import to those obtained from examination of the blood, in that they show very wide variation, the majority being within the usual normal limits. They exhibit no recognizable tendency in any one direction, and thus give no support whatever to the view that acidosis is a definite feature in seborrhoeics.

While these figures fail to confirm the opinion that acid excretion in seborrhoeics is increased, they do not disprove the occurrence of hyperacidity—that is, increased degree of acidity as opposed to increased amount of acid—in the urine of such patients. This is a point we have not examined, but have reserved for future investigation, since our present concern is simply to obtain evidence as to the occurrence of true acidosis. But if hyperacidity of the urine is present along with normal quantitative excretion of acid, then the quantity of buffer substances excreted must be reduced. This may perhaps be the case, for, as we have already mentioned, Sabouraud found a diminution in phosphate along with hyperacidity. It is obvious, however, that on theoretical grounds, it is unjustifiable to accept hyperacidity of the urine as sufficient evidence of the presence of true acidosis, and our present results show that, even if hyperacidity does occur, there is, in fact, no evidence to indicate that acidosis is a constant feature, or even a common feature, in seborrhoeic subjects. As Barber and Semon point out, their subjects—soldiers on active service—were living in very unusual environmental conditions, and, particularly, were on a dietary likely to provoke some degree of acidosis. It seems possible to us that, in their series of cases, an acidosis may have been the precipitating factor in producing seborrhoeic manifestations, especially in view of the dramatic effects of alkaline therapy recorded by them.

The majority of the cases investigated by us were of acute and chronic seborrhoeic dermatitis and seborrhoeic eczema, with and without secondary impetiginization and septic folliculitis; some cases of severe acne vulgaris and rosacea were also included.

CONCLUSIONS

1. We have found no evidence to suggest the presence of acidosis in persons subject to seborrhoeic disorders.
2. We have found no evidence to suggest that there is increased excretion of acid in the urine of seborrhoeic subjects, but we have not investigated the question of their secreting a hyperacid urine.
3. We have found no evidence to support the alkaline treatment of seborrhoea, except where this may be indicated by the nature of the precipitating cause of the attack.

REFERENCES

- ¹ MacLeod, J. M. H.: *Brit. Journ. of Dermatol.*, xlii, 549.
- ² Dowling, G. B.: *Ibid.*, xlii, 562.
- ³ Barber, H. W.: *Lancet*, 1929, ii, 363.
- ⁴ Krestin, D.: *Quart. Journ. of Med.*, 1927, xxi, 177.
- ⁵ Sabouraud, R.: *Séborrhée, Acnés, Calvitie*, 1902.
- ⁶ Barber, H. W., and Semon, H. C.: *British Medical Journal*, 1918, ii, 245.
- ⁷ Hawk and Bergeim: *Practical Physiological Chemistry*, ninth edition, p. 439.
- ⁸ Van Slyke, D. D., Stillman, E., and Cullen, G. E.: *Journ. of Biol. Chem.*, 1917, xxx, 401.