Summary

Functional uterine bleeding is defined as bleeding from the cavity of the uterus for which no cause can be found by general or local clinical examination, or by curettage of the cavity. Post-menopausal bleeding is considered to be of a different character. The diagnosis is made after full physical examination, both general and local, with study of the vaginal smears by the Papanicolaou method, and confirmed by curettage and microscopy of the endometrium. The cases are initially divided into age groups.

Treatment is considered under four headings—symptomatic, surgical, radiotherapeutic, and hormonal—and the indications briefly discussed. The importance of conservative measures in adolescents and in women under the age of 40 is emphasized.

It is claimed that the vaginal smear is a valuable method of assessing ovarian function and of diagnosing variations from the normal, thereby providing a rational basis for hormonal therapy. Such therapy should be controlled by a planned series of smears.

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CONTRIBUTIONS OF NEURO-ANATOMY AND NEUROPATHOLOGY TO PSYCHIATRY*

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It is sometimes forgotten, amidst the luxuriance of the psycho-analytic jungle, that the roots of our knowledge lie embedded in the soil of the basic sciences. This soil is often alleged to be an extremely inhospitable medium for the growing plant of psychiatry to flourish in, and there has been, particularly in the American continent, such a shift away from these basic sciences as to be quite alarming. It is my contention, and it will be my aim, to show that neuro-anatomy and neuropathology have contributed at least as much as any of the other basic sciences to our present understanding of mental disorder. For such a vast field a review such as this can either be all-embracing and panoramic or, on the other hand, can select certain topics for critical consideration. It is this latter method I have chosen, the topics being schizophrenia, the anatomical problems of leucotomy, the epilepsies, and the senile and presenile dementias.

Before we consider these groups in general, it is proper to consider the techniques which are now available for their investigation. Unfortunately the revolutionary developments in physical science have not, as yet, had their fullest application to anatomy and pathology. The basic methods of microscopical work remain very much unchanged. Sections are stained by a variety of new stains, it is true, but the microscope remains the

chief tool. Both anatomy and pathology have, however, become more functional, in the sense that descriptive studies are more and more closely integrated with studies of function. The direction which these two sciences are taking is toward a greater understanding of function in its relation to structure, and as a result there is a considerable use of techniques derived from other fields. Physiological neuronography, for instance, has added a great deal to our knowledge of brain anatomy, whilst histochemistry is developing our understanding of cell structure in terms of biochemistry. It seems proper, therefore, to outline briefly some of these new techniques before passing on to consider the results of their application.

New Techniques

Of the more orthodox methods, the use of specialized silver impregnation methods has been most rewarding. The advantage of these stains is that the actual axis cylinders, and particularly their terminal arborizations, can be determined, irrespective of the degree of myelination. M. Meyer (1949), for instance, was able to trace a direct pathway from the dorsal frontal convexity (approximately areas 8 and 6 of Brodmann) to the mammillary bodies and other parts of the posterior hypothalamus. The development of histochemistry will soon have important repercussions in these two sciences. Lison (1936), in France, may be regarded as the first to organize knowledge in this field, and since then there have been rapid advances. A known chemical reaction is used in order to identify substances within a histological preparation, but certain physical properties of substances are also made use of, such as fluorescence, ultra-violet or x-ray spectrography, and tracer techniques. The chemical substances in the tissue must first be immobilized in the situations where they occur during life, and the freeze-drying technique has therefore been extensively used. In addition, the chemical reaction or physical method used in order to identify the substances within the section must not interfere with tissue structure, and must produce a reasonably stable result and, preferably, a highly insoluble and deeply coloured precipitate.

In the nervous system enzymatic activity in relation to normal and diseased tissue is clearly an important field for work. Naidoo and Pratt (1954) have traced the development of adenosine 5'-phosphatase activity in the rat cerebral cortex during maturation, and have shown that there is an increase in enzyme activity which is greatest between 15 and 80 days of life. This activity appears to arise in nerve fibres, and may be related to myelination. They have also (Naidoo and Pratt, 1955) shown that in chickens deficient in vitamin B₁ there is a significant increase in the thiamine pyrophosphatase and alkaline phosphatase activity in the optic tectum, but no change in the acid phosphatase activity. The effects of physical treatments such as leptazol can be investigated experimentally, and the method is full of promise both for neuro-anatomy and for neuropathology.

At the other end there have been advances in microscopy which are perhaps not as well known as they should be. The phase contrast, the reflecting microscope, and the electron microscope have all their individual advantages over orthodox microscopy. To date, however, technical difficulties in dealing with biological specimens have hindered progress, and, to the best of my knowledge, the contributions to our specialty have been negligible.

Schizophrenia

Of the topics which I have chosen for special consideration, that of schizophrenia presents the most difficult problems. In spite of this, anatomical and pathological research into schizophrenia has indirectly opened up new vistas in our understanding of neuro-anatomy. The study of post-leucotomy brains at the Maudsley Hospital by Professor Meyer and his associates has added an impressive chapter

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to our knowledge both of the disease and of the human brain. And the work is in many ways still in its infancy. Josephy (1930) reviewed the literature on the histological changes in the brain of schizophrenics, beginning with the communications of Alzheimer (1897, 1913), Buscaino (1920, 1929), and numerous others. The gist of this work was that characteristic changes were found in the brains of schizophrenic patients. These consisted of focal areas of neuronal loss (the so-called *Lückenfelder*), and of a variety of nerve-cell changes in the neurones of the cerebral cortex, ranging from loss of Nissl bodies to alveolar degeneration and fatty degeneration. Buscaino, moreover, described peculiar areas of demyelination (*zolle di disintegrazione a grappola*) in the white matter of schizophrenic brains, and has up to the present time repeatedly maintained that these are produced by an intoxication. He claims that schizophrenia is the result of an "aminic" toxicosis arising from disorder of the gastro-intestinal tract or the liver.

These findings, however, did not remain unquestioned. Spielmeyer (1930) thought that no characteristic neuropathological changes could be established, and his pupil Peters (1938) published an excellent paper on the subject. By using as control material non-psychotic executed criminals, Peters showed that all the changes which had been described for schizophrenia were also to be seen in his control material. In other words, they were non-specific, and most probably post-mortem artifacts. Wolf and Cowen (1952), using biopsy material, arrived at similar conclusions. However, the controversy has still continued, and in 1952 a symposium was held on the subject at the First International Congress of Neuropathology. Of the seven distinguished workers who delivered communications on this problem, only the voice of Professor Meyer (1952) was raised to point out that there is still no irrefutable evidence of neuropathological change in schizophrenia.

The whole tenor of the communications is that schizophrenia is associated with characteristic changes in the nervous system. The Vogts (1948, 1952), for instance, considered that schizophrenic symptoms were the result of nerve-cell disease, and not the result of loss of nerve cells. By serial sections of the brains of schizophrenics they were able to find a cyto-architectural alteration, with minimal vascular and glial reactions. But, in addition to cortical changes, other parts of the brain are involved. The hypothalamus is always intact, but the medial nucleus of the thalamus is often affected. Anatomically the greatest alterations are in the prefrontal gyrus, the anterior cingulate gyrus, the ventral temporal region, and the anterior and mesial nuclei of the thalamus. By a careful clinico-pathological correlation these authors aspire eventually to finding a specific localization for every symptom.

Walter Bruetsch (1952), of Indianapolis, drew attention to the occurrence of rheumatic occlusive endarteritis of the small meningeal and cortical arteries in about 9% of schizophrenic brains. He pointed out that classical cases of schizophrenia, in which no organic disorder has been suspected during life, may on coming to necropsy reveal severe cerebral disease such as diffuse and extensive demyelination of Schilder type, multiple sclerosis, or brain tumour. The problem of schizophrenia remains, therefore, the problem of establishing various pathological states by new techniques. The fact that in many cases of schizophrenia the brain is normal means only that our techniques are inadequate. "The substratum of schizophrenia," he writes, "is at present too subtle for demonstration by present techniques. The majority of instances of schizophrenia appear to be due to an organic process."

Two-way Approach

These are challenging statements, and demand investigation. Professor Meyer (1952) has approached the problem in two ways. In answer to those who see a specific anatomical localization, he has pointed out that, in all the leucotomized brains of non-schizophrenic subjects with bilateral frontal lobe damage and degeneration of the dorso-

medial nucleus of the thalami as a result of the operation, no schizophrenic symptoms have been seen. Nor, indeed, have they been observed with the wide variety of anatomical changes often seen at such operations. Secondly, he carried out a clinico-pathological analysis of 42 cases of "functional psychosis," using both post-mortem and biopsy material. Schizophrenic, depressive, and obsessional patients were all included. Very careful attention was paid to the question of artifact. Meyer remarks, for instance, that the two types of nerve cell which Hyden and Hartelius (1948) regarded as characteristic of schizophrenic brains, and with ultra-violet microscopy as indicative of a lack of nucleotides, can in fact be seen in biopsy specimens from the brains of normal humans and animals. Many of the changes in nerve cells and glia can be correlated with the admission of the two physical treatments—electric shock and insulin coma—whilst the effect of age and systemic disease has also been insufficiently reckoned with. Careful studies such as this are being further implemented at the present time, using a much larger case material and matched controls.

Although neuropathology has on the whole contributed so little to our knowledge of schizophrenia, there is no good reason to despair for the future. For instance, individual cyto-architectonic variations and the maturation processes of the brain in relation to disease have as yet hardly been investigated, whilst neuropathological techniques remain in their infancy. On the other hand, the advance in our knowledge of neuro-anatomy as a result of leucotomy has been astounding. And springing from this knowledge have come the various modifications in neurosurgical procedures.

Anatomical Problems of Leucotomy

In his Henderson lecture, for 1953, Professor Meyer summarized the anatomical results of these operations. The principal afferent fibres passing to the frontal lobes arise in the thalamus, running from the dorso-medial nucleus to areas of granular frontal cortex and from the anterior nucleus to the cingulate region. The thalamo-frontal projection is systematically organized—and the thalamic nuclei concerned are in turn linked with the hypothalamus. In animals, fibres passing along the cingulate fasciculus connect with the hypothalamus, thus forming a circuit linking frontal lobe, cingulate gyrus, and hypothalamus. The afferent projections to Brodmann areas 32 and 12 and to the agranular frontal cortex have not yet been adequately identified, whilst the so-called diffuse thalamic projection system has been the subject of much speculation. Here electro-physiological work on animals has outstripped the work on human material, and still awaits anatomical verification in man.

The facts concerning this diffuse thalamic projection system are of such importance as to require consideration here, in view of the later discussion of the problem of epilepsy. Lorente de Nó (1943) described two types of cortical afferent, one ending in a brush-like arborization in the fourth cortical layer, and the other an "unspecific afferent terminating in all cortical layers, giving rise to many collateral branches. The specific fibres ending in the fourth layer came from the thalamic nuclei, whilst the unspecific ones were either from undetermined regions of the thalamus other than the specific thalamic nuclei, or from transcortical or transcallosal association fibres. At the same time, Morison and Dempsey (1942) were investigating the effect of electrical stimulation of the intralaminar parts of the thalamus, and had observed that cortical electrical activity over a wide area was greatly influenced by stimulation of these areas. Moreover, the effect was quite different from that following stimulation of specific thalamic nuclei. Since then the diffuse thalamic system has attracted great attention, and Jasper (1949, 1954) and Hanbery and Jasper (1953) have demonstrated that, in addition, characteristic wave-and-spike activity of three cycles per second, of the type seen in petit mal, could be evoked from the intralaminar portion of the cat thalamus.

The efferent pathways from the frontal lobe have been more difficult to elucidate, owing to the peculiar fact that retrograde degeneration within the frontal lobe anterior to the leucotomy cut is not usually found. Special silver techniques are therefore needed. However, it has now been established that the frontal lobe sends fibres to the thalamus, hypothalamus, red nucleus, substantia nigra, corpus striatum, corpus luyi, and pons. The ventro-medial nucleus of the thalamus seems to be the most important end-station, and this nucleus, at least in the monkey, also receives fibres from the amygdaloid nucleus and the tip of the temporal pole.

More recently, Elisabeth Beck (1950), who carried out a masterly study of the prefronto-pontine pathway, has shown that a transneuronal degeneration of granular and Purkinje cells occurs in the cerebellum with lesions of the fronto-pontine tract. The long association tracts (superior longitudinal tract, uncinate, angular and subcallosal fasciculi) are also the subject of investigation at the Maudsley Hospital.

These studies in man show that the frontal lobes are connected with thalamus, hypothalamus, and, indirectly, with rhinencephalic centres. They have led to a greater understanding of personality and enabled clinicians to refine their technique. For instance, whilst improvement is related to the amount of white matter involved in the cut, there is some evidence that a regional localization is important in mental functions. Improvement occurs more often with cuts involving the mid-central, orbital, and cingulate sections of white matter than with cuts involving the dorsal and dorso-lateral sectors. With lesions in this latter situation personality changes are often severe. Fulton (1951) has related the effectiveness of orbital and cingulate cuts to involvement of the visceral brain, whilst Professor Meyer (1954) has suggested that owing to the position of the thalamo-frontal projections in these situations it will almost certainly be severed in operations on these areas. Numerous problems of great significance for clinical psychiatry are at last being illumined by facts and not by speculation.

The Epilepsies

Interestingly enough, these anatomical advances have greatly influenced another field of great concern to the psychiatrist. I refer to the problem of epilepsy. Here the combined neuropathological and anatomical investigation of the brain in epileptics has led directly to the relief of suffering. We have seen that anatomical and physiological studies have gone hand in hand, and that the thalamus and basal nuclei have been the main foci of interest. The dramatic effects of stimulation of intralaminar systems in the thalamus on cortical activity, and the production of 3 c./sec. wave-and-spike activity, had immediate repercussions in clinical work on epilepsy. Penfield (1952) had postulated the presence of a centrencephalic system regulating consciousness, and the anatomical data suggested that this might be located in the intralaminar systems of the thalamus, the reticular formation of the brain stem, and the non-specific projection systems.

Anatomical research into this brain-stem system has been carried out by Olszewski and Baxter (1954), whilst the pathological anatomy of epilepsy has been re-examined. For more than a century sclerosis of the cornu ammonis has been recognized in the brains of chronic epileptics. Spielmeyer (1927) noted that it occurred in 80% of 126 epileptic brains which he investigated. He and his pupils, in particular Scholz (1938) and Meyer (1939), have elucidated the pathological changes occurring in epilepsy with great thoroughness.

Marginal sclerosis and Ammon's horn sclerosis, particularly involving the Sommer sector, are common, as is a degeneration of the Purkinje cells of the cerebellum. The cerebral cortex is also affected, particularly the occipital cortex, and then follow the thalamus, dentate, and olives,

in order of frequency. These changes are usually slight, but more severe lesions may be seen, and Scholz (1951) has suggested that in some cases of lobar atrophy, or infantile diplegia with epilepsy, the fits may have been responsible for the severe cerebral lesions. The German school has considered, and still believes, that these lesions which I have mentioned are the results of anoxia, and are due to the repeated anoxic insults which occur during recurrent epileptic attacks. The localization of the lesions is related to special factors of vulnerability, such as rates of tissue oxygenation, vascular supply, or susceptibility to the effects of cerebral herniation.

It remained for Penfield, through his work on temporal lobe excision, to bring the whole problem into focus. Penfield and his collaborators (Earle *et al.*, 1953) have suggested that an incisural sclerosis is the commonest cause of temporal lobe epilepsy. It is the result of a herniation of the temporal lobe into the tentorial opening during the head-moulding process of birth. Compression of the anterior choroidal, posterior, and middle cerebral arteries occurs, with a subsequent anoxia. The whole of the temporal lobe may be involved, but the inner and lower parts of the lobe—that is, the uncus and hippocampal gyrus—were most commonly affected. There are, of course, many cases of temporal lobe epilepsy in which a post-natal pathology is found—such as tumours, abscess, or traumatic lesions, but the commonest cause of temporal lobe epilepsy is birth trauma.

This challenging theory of incisural herniation was fundamentally different from that of the German school, which saw the cerebral lesion as the result, and not the cause, of the epileptic attacks. Meyer, Falconer, and Beck (1954) have critically examined both theories on a material consisting of 18 excised temporal lobes. All were cases with a unilateral E.E.G. focus in the temporal lobe and no evidence of a space-occupying lesion. Apart from four cases in which small tumours or post-traumatic lesions were found, the main group of 14 lobes showed a variety of changes ranging from a laminary atrophy of the third cortical layer, or a generalized cortical atrophy, to sclerosis of the cornu ammonis, meningeal fibrosis, marginal glia, and gliosis of the white matter of the lobe. These observations are more in line with the findings and theories propounded by Scholz (1951).

Birth trauma may be one factor, but it certainly is not an exclusive cause of temporal lobe epilepsy, and Meyer, Falconer, and Beck (1954) have put forward convincing reasons for a more comprehensive approach to the problem. In a more recent paper (Meyer and Beck, 1955) he has also drawn attention to the lesions of the amygdaloid nucleus which he has found in certain cases of temporal lobe epilepsy. The anatomical and physiological implications of these findings are of great interest, for the uncus, the amygdaloid, and the transitional cortex of the anterior insula, posterior orbital, and anterior cingular regions make up what the physiologists call the visceral brain. And if it is true that psychiatry is more concerned with feelings than with cognition, then this is the head ganglion, to use Sherrington's words, of the "feeling system."

The Presenile Dementias

Since 1892, when Arnold Pick first described that peculiar disorder of the presenium since named after him, anatomy and pathology have steadily extended our knowledge of these presenile dementias. Inextricably linked with their study is the problem of ageing in general, and the whole field of senile and presenile disease is potentially one of the most fruitful for research. Clinical differentiation, largely as a result of the particular form assumed by the symptoms and signs of these disorders, has only led a certain distance. It has remained for neuropathology to clarify many of the problems. In a sense, it has perhaps been unfortunate that presenile and senile dementias have been associated, for

certainly it is only in Alzheimer's disease and related conditions that the similarity bears examination. The clinical and pathological changes in Alzheimer's disease are identical with those found in the brains both of senile demented and of "normal" old people. But in all the remaining "presenile dementias," to the best of my knowledge, the pathological processes bear no relationship to ageing. The problem therefore has been twofold—the recognition of new clinico-pathological syndromes, and the question of ageing, senile dementia, and Alzheimer's disease.

Even though Alzheimer's and Pick's diseases have been recognized for half a century it is only in the last two decades that serious attempts have been made to differentiate them clinico-pathologically. The neuropathological appearances are characteristic, but, even so, some unusual conditions have come to light during these studies. Worster-Drought *et al.* (1940) described an unusual form of familial presenile dementia associated with spastic paralysis, whilst other authors, from a somewhat different standpoint, had reported similar cases (van Bogaert *et al.*, 1940; Lüers, 1947). In these patients there was an unusual histological picture in that the presence of senile plaques with the neurofibrillary tangles seen in Alzheimer's disease was associated with a change in the media of the blood vessels consisting of a hyalinization and a deposition of amyloid. This change in the blood vessels had already been described by Scholz (1938) in the brains of old people and called by him *drusige Entartung* (plaque-like degeneration). The senile plaques were also unusual in their prominence and their morphology. Divry (1947) had already shown that the central core of many senile plaques with histochemical techniques behaved like amyloid, and that this was also the case with the neurofibrillary tangles. Here, then, was a condition where the changes of Alzheimer's disease were found together with an amyloid change in the blood vessels. Moreover, similar changes occur in the elderly brain. Corsellis and Brierley (1954) have described two further examples of this condition and reviewed the literature. Here is a link between the ageing process and a particular disease which may be of some theoretical importance.

Divry (1947) considers that these amyloid changes represent a change in the physical state of the brain—a colloidal precipitation, with the transformation of a sol to a gel. If this be true, then some of the morphological peculiarities of the senile brain can be better understood; for instance, the different appearances of senile plaques in different sites of the brain.

Jakob-Creutzfeldt Syndrome

There is another group of presenile dementias in which slow but steady progression is being made solely as a result of neuropathological work. Under the name of the Jakob-Creutzfeldt syndrome have been clustered together a heterogeneous collection of disorders. In 1920 Creutzfeldt reported the case of a young woman of 27 dying from a condition characterized by a progressive dementia and signs of bilateral pyramidal disorder. Jakob (1921, 1923) described five cases which he considered essentially similar to the original case of Creutzfeldt. The clinical picture was one of a combination of extrapyramidal, pyramidal, and bulbar or spinal amyotrophic signs, together with mental disturbance. Pathologically, degenerative lesions in the nerve cells of the cerebral cortex, basal ganglia, brain stem, and spinal cord were associated with a glial overgrowth in these situations. To such a clinico-pathological syndrome the eponym Jakob-Creutzfeldt has been applied. Twenty-six further cases have since been reported, chiefly in the German literature, and attempts have been made to establish the validity of the syndrome.

Generally speaking, the pathological diagnosis depends more on negative than on positive findings—largely by exclusion of one or other of the well-recognized presenile dementias. What is left is a picture of widespread degenerative change in nerve cells, with a certain degree of

systematization. Thus there is a group of cases in which dementia and the signs of motor neurone disease are associated with extrapyramidal features; another in which dementia alone occurs; and a third, recently the subject of a paper by Meyer, Leigh, and Bagg (1954), in which cortical blindness and dementia go hand in hand. The problem is whether in fact these widely varying conditions are members of a homogeneous group, or whether the Jakob-Creutzfeldt syndrome is a hotchpotch of disease, having in common only their relative unclassifiability.

The interesting theoretical status of this alleged syndrome is that the neuronal degeneration and glial overgrowth is also found in most of the senile and presenile dementias, in Huntington's disease, and in most systemic degenerations. It is also encountered in physiological ageing, and Gellerstedt (1933) has pointed out that the larger motor neurones are usually the first to be affected by the ageing process, together with the olives, dentate nuclei, and dorso-medial nucleus of the thalamus. It is in these areas that changes are to be found in cases of Jakob-Creutzfeldt disease. It is tempting to suggest that it represents an exaggerated and premature ageing in wider areas of the central nervous system than is usually involved in system degenerations. The whole question of dementia in such conditions as the hereditary ataxias and cerebellar degenerations is still *sub judice*, and the complex relationships of one disorder to another are still a rewarding field for study.

Conclusions

Nothing is more salutary for the clinician than to review at certain periods of his life the general trends of his specialty. He is often absorbed in clinical work with its loose and humanistic approach, and a reappraisal of the scientific principles on which his work is based is vitally necessary. My own interests have passed through neurology and neuropathology to psychiatry, and in particular to the so-called dynamic psychiatry in relation to psychosomatic medicine. The contributions of anatomy and pathology to psychiatry, as I see it, are of fundamental importance. Psychopathology may be useful for descriptive and perhaps therapeutic purposes, but further advances in understanding will not come other than through the basic sciences. What progress has been made in the past twenty years owes more, I suggest, to anatomy and pathology than to any other of the basic sciences.

Summary

Although technical advances in neuro-anatomy and neuropathology have not kept pace with advances in the physical sciences, a wealth of new information has sprung from these two sciences over the past twenty years. The study of schizophrenia has both directly and indirectly contributed to our knowledge of the anatomy of the brain and of its mechanisms, in health and disease. Although opinions differ, present techniques have not revealed a neuropathology of schizophrenia. Leucotomy, however, has provided a human experiment whereby the relationship of the frontal lobes and basal grey masses has been clarified. Out of this knowledge has developed the concept of the visceral brain, with all its far-reaching implications. Dovetailing with this research, and again largely as a result of neurosurgical work with patients, epilepsy is yielding up some of its mysteries. The temporal lobe is under extensive anatomical scrutiny, as is the neuropathology of epilepsy.

Lastly, neuro-anatomy and neuropathology are seen as playing a more important part in the unravelling of the problems of ageing, and of the presenile dementias. The development of new techniques, particularly histochemical techniques, is full of promise, and already some of the enzymatic processes of nervous tissue have been

elucidated. It is concluded that these two sciences have, in fact, entered upon a new phase of usefulness in the study of psychiatric disorders.

My thanks are due to Professor Alfred Meyer for his continued interest in the problems of a clinician.

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The American Embassy in London has issued details of United States pre- and post-doctoral training programmes on the peaceful uses of atomic energy. The courses are open to foreign nationals and last one to two years. The subjects are industrial medicine, industrial hygiene, and radiological physics (radiation protection). Excluding travel, the cost of participation is estimated at a minimum of \$2,800 per student for each of the first two courses, and over \$4,000 for the last. At present there are no United States funds available to assist foreign students, and it is assumed that the costs will be met by the foreign government or other foreign sponsor. A memorandum giving further details of these courses may be obtained from Mr. P. J. SEARBY, Atomic Energy Office, 1, Richmond Terrace, Whitehall, London, S.W.1.

ANAEMIA OF PREGNANCY IN AFRICANS OF LAGOS

BY

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Severe anaemia is a common complication of pregnancy in all tropical countries (Fairley *et al.*, 1938; Napier, 1940; Russell, 1941). It is one of the most important causes of maternal and infant mortality and one of the most difficult to treat. Experience in Lagos, as elsewhere, has shown that these patients respond poorly to treatment. It has been the custom to put all severely anaemic patients on treatment with iron, liver, and folic acid from the moment they are admitted to hospital rather than wait for the result of blood investigations. Even so, the majority of these patients have shown little response and pregnancy commonly terminates in abortion.

An attempt has been made to investigate these anaemias in some detail, and this paper is a review of 30 patients seen over a period of eighteen months. These were taken at random from the large number of women admitted to hospital for treatment of anaemia. None had had any form of treatment before the first blood and marrow specimens had been examined. Thirteen were subsequently treated with vitamin B₁₂, and their response is described.

Local Geography and Background of Patients

Lagos, the capital of Nigeria, is a busy town and seaport on the coast of West Africa within 10 degrees of the Equator. In this region of high forest, swamps, and lagoons the humidity is high, and although the shade temperature rarely exceeds 90° F. (32.2° C.) the climate is oppressive and encourages a state of torpor in European and African alike.

Though a Yoruba town, Africans of many other tribes are seen, and the population is continually being increased not only by Yorubas from other parts of the western region of Nigeria but also by Ibos from the east and Hausas from the north, attracted to Lagos by the prospect of higher wages. Many of these live in conditions of poor sanitation and gross overcrowding. The cost of living is high, and few Africans can afford the more expensive foodstuffs. Consequently most Southern Nigerians are vegetarian by necessity; meat is too costly to be an important part of their diet. Meals are monotonous and starchy, consisting of stews prepared from cassava, yams, rice, maize, or guinea-corn, with plenty of palm oil or groundnut oil. This may be supplemented with fruit (oranges, bananas, and plantains) and white bread made of high-extraction American flour, which is becoming increasingly popular. Eggs are too expensive and milk is unobtainable.

Apart from the high price of food, many Nigerians (not only those in the poorer sections of the community) will not "waste" money in an attempt to improve their diets, but prefer to spend it on clothing, an important mark of social distinction. The possession of a wife is another indication of prosperity. It is still the custom for the groom to pay his future father-in-law a sum of money, often very considerable, for his bride. This