Post-Graduate Medical Journal

LONDON, JUNE 1944

NEUROLOGICAL DISORDERS IN RELATION TO PREGNANCY

By H. G. MILLER, M.D., M.R.C.P., D.P.M.

(Late Medical Registrar to the Royal Victoria Infirmary, Newcastle-on-Tyne)

The fields of contact of different branches of science are often interesting and illuminating, and this is certainly true of obstetric neurology. Although the conditions discussed are rare, they are of considerable interest, and may present difficult problems in diagnosis and treatment. The relative infrequency of these complications is shown by an analysis of 23,000 obstetric cases in Edinburgh by Russell (1), which included twenty-nine cases of chorea, nine cerebral vascular accidents, and four subjects with polyneuritis.

POLYNEURITIS

Complaints of peripheral numbness and tingling are not uncommon during pregnancy. Polyneuritis may occur at any period of cyesis or in the puerperium, and is commonest in first and second pregnancies. Ironside (1) has defined two main groups of cases. The first type is relatively mild, is sometimes associated with evident dietary deficiency, bears no relation to toxæmia, and has a gradual onset most commonly about midterm. Paraesthesiae, numbness, cramps, and progressive weakness affect the lower limbs first and maximally, though the arms are often involved later. There is wasting, impairment of tone and power, with absent tendon reflexes, tender calves, and patchy sensory loss most marked peripherally. Sometimes there is associated mental confusion and disorientation. Although the disability may be severe, many of these cases show marked recovery even during pregnancy, with rest and treatment, and the more obstinate respond well after delivery. The frequency of this condition varies widely, and whilst the incidence quoted above may be taken as average for British experience, a Frankfurt investigator found the condition in approximately one out of every 300 pregnant wives of unemployed workers in 1937.

The second type, rarer, and more severe, follows hyperemesis gravidarum often with emaciation and jaundice, and sometimes with anaemia (2). The onset is sudden, occurring sometimes a few weeks after the cessation of vomiting, at the third to fourth month, sometimes later. There is a severe flaccid muscular palsy, generalised, though again maximal in the lower limbs, and occasionally so acute as to produce a Landry syndrome. Tachycardia is present and achlorhydria frequent, while cranial nerve involvement may be shown by facial palsies, nystagmus, nerve deafness, or retrobulbar neuritis. Foetal death and spontaneous abortion may occur. Mental changes are usual in these severe cases, and may vary in degree from mild confusion to a fully developed Korsakow's psychosis, with disorientation, drowsy confusion, amnesia with pseudo-reminiscences, ophthalmoplegia, retinal haemorrhages and coma. These cerebral symptoms are associated with symmetrical haemorrhagic lesions in the vicinity of the aqueduct and the walls of the third and fourth ventricles, known as Wernicke's encephalopathy (3), and they frequently lead to death within seven days. Recovery may occur, however, even in severe cases with marked mental changes. Some respond rapidly to treatment, others clearing slowly over a period up to two years. The condition may progress despite emptying the uterus, although this is often advised in the severe cases. Residual dementia occurs uncommonly. The mortality of gestational polyneuritis varies widely in different series, and milder cases are often undiagnosed, but it would appear that more than a third of the severe cases die. If infective and toxic causes are excluded, differential diagnosis is not difficult, hysteria or general weakness being precluded by the organic neurological signs, and particularly by the disappearance of knee and ankle jerks.

Whilst many points in the aetiology of these conditions remains obscure and laboratory studies are not conclusive, there is strong presumptive evidence of the importance of nutritional factors, and in particular of the vitamin B complex. The variable incidence of the condition under differing economic circumstances, the not infrequent history of dietary deficiency or of conditions interfering with absorption, the high incidence in communities where beri-beri is endemic, the trebled demand for vitamin B₁ known to accompany pregnancy, the frequent

response to therapy directed along these lines, and the occurrence of coincident cerebral changes similar to those produced experimentally by B deficiency, are all in favour of such a relationship as is the known tendency of beri-beri to begin during pregnancy.

The occurrence of gestational polyneuritis in cases without a history of evident dietary deficiency or failure of absorption is perhaps comparable to the incidence of macrocytic anaemia of pregnancy under such circumstances, although both conditions are commonly associated with such a history. It is also of interest to note that peripheral paraesthesiae are frequent in this type of anaemia, and that associated confusional states have been recorded. Failure of gestational polyneuritis to respond to vitamin B therapy may be related to inadequate dosage, to the presence of multiple or secondary deficiencies, or to other complicating factors, and is, seen also in beri-beri. Nutritional deficiencies in man are frequently multiple, and the symptoms produced are the result of the interaction of the deficiency and the constitutional peculiarities of the affected individual. Gastric acidity is one of the more obvious of such possible constitutional factors, and there must be others less immediately evident but also conducive to clinical variability. In this connection it is of interest that familial incidence (4) and later recurrence of polyneuritis both during and independent of subsequent pregnancy (5) have been recorded.

Treatment consists in rest in bed with careful immobilisation to prevent stretching of paralysed muscles, a full mixed diet despite the frequent anorexia, and Thiamin 50 mg. daily intravenously or intramuscularly, with $\frac{1}{2}$ –1 oz. of baker's yeast and marmite by mouth in addition. The injected dose may be gradually reduced after the first weeks. In severe cases the use of the respirator may be necessary.

Mononeuritis is not uncommon during pregnancy, and any nerve may be involved. Some of the reported cases of retrobulbar neuritis may be initial indications of disseminated sclerosis, but others, occurring particularly in association with hyperemesis, may leave severe and permanent visual defect. Where vomiting and choked disc are thus associated, the differential diagnosis from cerebral tumour may present difficulties (6).

CHOREA GRAVIDARUM

Chorea (7) may occur at any time during pregnancy or in the puerperium, but is commonest at about the third or fourth month in primigravidae, in the early twenties, with a previous history of chorea or rheumatism, and it may recur. Hubble (8) has recently stressed the role of emotional factors in the production of chorea in children, and the importance of this aspect has frequently been noted in cases occurring during pregnancy.

Most cases are mild and respond to rest and sedatives (calcium aspirin gr. 10 t.d.s., phenobarb gr. $\frac{1}{2}$ –1 t.d.s.), but in some the movements are of great and increasing violence, leading to sleeplessness, and finally to an unmanageable state of maniacal excitement. These cases present a difficult problem. Dehydration, exhaustion, and emaciation are rapid, and although the mortality as a whole is below 15 per cent, probably about half these severe cases die. Marked mental changes, persistent tachycardia, high pyrexia, active carditis and incontinence, are unfavourable signs. There is a high foetal mortality, and this event is usually without effect on the symptoms (9).

Absolute rest and isolation are essential, and every effort must be made to maintain nutrition, if necessary by tube feeding or intravenous glucose-saline. Phenobarbitone, large doses of chloral and bromide, rectal avertin or paraldehyde, are indicated. Termination of pregnancy is by no means certain to produce relief, but is often advised in the severer cases; if it is done it should be carried out before the patient's condition becomes desperate. Under such circumstances it has a very high maternal mortality.

CEREBRAL VASCULAR ACCIDENTS

Cerebral vascular accidents during pregnancy and the puerperium may of course result from syphilis, rupture of an intracranial aneurysm, from cerebral haemorrhage in chronic renal disease, or from an embolus from the left auricle in rheumatic heart disease, but the incidence of such lesions in the otherwise apparently uncomplicated puerperium has been recognised for many years, and is known to occur also in domestic animals (10).

Briefly, cerebral vascular accidents usually occur in multiparae during the first two weeks following delivery, with an onset often of dramatic suddenness, and frequently exhibiting hemiplegia with or without aphasia, hemianopia or amaurosis. The mode of onset, commonly with

convulsions and loss of consciousness is naturally suggestive of an embolic cause, but such an aetiology presents obvious difficulties, and sudden thrombosis related to sluggish blood flow and possible altered blood states has been suggested, as also the red herring of paradoxical embolism. A recent paper by Martin (11) provides an alternative and more convincing explanation of these cases. He describes the clinical picture of thrombosis of the superior longitudinal sinus occurring in the puerperium. This is associated with the sudden appearance of raised intracranial pressure due to impairment of the absorption of cerebro-spinal fluid and producing headache, vomiting, papilloedema, amaurosis, convulsions, and stupor or coma, and often hemiplegia.

The cerebro-spinal fluid may contain a little blood, but has an unchanged protein content. One of Martin's cases later developed a transverse spinal cord lesion. This picture usually occurs in multiparae with venous thrombosis elsewhere, and particularly in the femoral and pelvic veins, and this author quotes the anatomical findings of Batson (12) describing an anastomotic connection between the pelvic veins and the cerebral sinuses by way of the vertebral venous system. It has been shown experimentally in the monkey that if the blood flow through the inferior vena cava is impeded by abdominal pressure, as by a binder or in straining, blood may be shunted through this anastomotic system, and it is suggested that portions of thrombus may find their way to the cerebral sinuses by this route and produce the above syndrome, forming a nucleus for further thrombosis in the superior longitudinal sinus. By the same process of retrograde embolisation some particles may pass directly into the cortical veins producing a more localised loss of function. It is evident that this mechanism also provides a possible aetiology for some cases of transverse spinal cord lesions in the puerperium usually described as transverse myelitis. These also may show a marked tendency to recovery, though some leave paraplegia of varying severity.

The localised vascular accidents are not very uncommon and in general the prognosis is good. The vascular tree in these patients is healthier than in the usual subjects of hemiplegia, and recovery of function is often excellent except for the finer hand movements.

The cases of longitudinal sinus thrombosis are more serious, and the condition is an occasional cause of death in coma during the puerperium. Nevertheless it would appear that many cases recover often without gross residual disability.

If the suggested view of the aetiology of these conditions is accepted, prophylaxis consists in the avoidance of tight binders and excessive straining in patients with manifest venous thrombosis, who should be kept propped up. Treatment of established sinus thrombosis consists in repeated lumbar puncture to control the intracranial pressure and intravenous or intramuscular soluble phenobarbitone to allay fits.

VISUAL DISTURBANCES

Transient visual disturbances of cortical type with visual agnosia or failure of localisation, during the puerperium, have also been attributed to cortical thrombosis (Martin (1)). The attribution of field defects, and occasionally reported bitemporal hemianopia, during pregnancy to chiasmal pressure from physiological hyperplasia and hypertrophy of the pituitary, is considered doubtful by Traquair (13), who shows that the fields described indicate a functional rather than an organic visual impairment. Visual symptoms in toxæmia of pregnancy (14) may be associated with retinitis, often of a marked degree with sudden onset and tremendous exudation leading in some cases to retinal detachment. This retinitis does not imply the grave prognosis of similar changes occurring in chronic nephritis, is seen chiefly in later pregnancies, is not inclined to recur, and often recovers well. Vision may fail in eclampsia however, independently of retinal changes or uræmia, and may proceed to complete amaurosis. The light reflex is frequently retained and the changes attributed to cortical vasospasm, while complete recovery is usual. Post-haemorrhagic visual impairment may also follow post-partum haemorrhage, and such cases have recently been discussed by Tidy (15). One type follows immediately after a severe haemorrhage with syncope, recovers rapidly and completely, and is considered, due to retinal or cortical anaemia. Another, very rare variety occurs in patients in ill-health, particularly with chronic anaemia, and comes on some days after the haemorrhage with a bilateral partial or total loss of vision affecting chiefly the lower fields, and sometimes associated with swelling of the discs. The condition may become progressively worse for a few days and recovery may then ensue, rapidly at first but slowly later. Only a small proportion of cases of this type,

however, show complete recovery of vision, approximately a third remaining blind, and the remainder being left with severe and permanent visual defects and the appearance of primary or secondary optic atrophy. Ophthalmoplegias of unknown aetiology sometimes occur during pregnancy or in the puerperium. The abducens is most frequently involved, and recurrent cases have been described.

ECLAMPSIA

Toxaemic eclampsia and its relation to epilepsy are of considerable neurological interest. Fatal cases of toxæmia may show diffuse haemorrhagic lesions throughout the cerebrum. These findings are attributed to vasospasm, may occur independently of fits, and are absent in pregnant women dying in status epilepticus, which condition may be clinically distinguished from eclampsia by past history and the absence of albuminuria, hypertension, and the eclamptic tendency to abortion. Recent electro-encephalographic studies (16) indicate that eclamptic fits occur more frequently in those cases of toxæmia which show a positive family history of epilepsy and electro-encephalographic abnormalities, and brings toxæmia of pregnancy into line with other trigger mechanisms releasing a pre-existing convulsive tendency. It is suggested that the routine prophylactic administration of anti-convulsant drugs be considered in toxæmic cases showing such predisposing features.

PRESSURE SYMPTOMS

Muscular cramps in the legs during pregnancy are often attributed to foetal pressure on the lumbo-sacral plexuses, but since they often occur elsewhere in the body, some more general cause, such as calcium deficiency, appears likely. The results of continued pressure are infrequently seen under modern obstetric conditions, but unilateral or bilateral sciatica of any degree, from transient paraesthesiae or shooting pains in the course of the nerve to severe paralysis, may occur in primiparae or multiparae from pressure, instrumental delivery or traction on the foetal leg. Although unilateral or bilateral foot-drop occasionally seen after delivery is sometimes attributed to such causes, some cases may be due to anaesthetic pressure paralyses, and Ironside (1) has suggested, to unrecognised polyneuritis which may show a mononeuritic onset or asymmetrical nervous involvement. Pressure cases, as elsewhere, show good recovery when the cause is relieved.

PREGNANCY AND PRE-EXISTING NERVOUS DISEASE

The incidence of most organic nervous diseases during the reproductive age-period is such that few observers have wide experience of pregnancy occurring during the course of these diseases, and knowledge is based chiefly on reports of very small series of cases.

It is known that the reproductive functions of animals are little affected by gross disorganisation of the central nervous system, and that parturition can occur normally even after high spinal section. This is in keeping with repeated observations that even advanced nervous diseases usually interfere surprisingly little with pregnancy and parturition in the human subject. Repeated normal childbirths have been recorded in cases of severe paraplegia from a variety of causes, and in advanced disseminated sclerosis, postencephalitic Parkinsonian rigidity, myasthenia gravis, general paresis, poliomyelitis, and syringomyelia. Normal pregnancy may also continue unaffected by severe head injury.

The effect of changes in the internal environment associated with pregnancy, on pre-existing nervous diseases, is so variable that prognosis in the individual case is difficult. In epilepsy complete remission and aggravation of fits have both been recorded, by one observer in 28 per cent and 35 per cent of cases respectively (17), while some cases are unaffected. The onset of epilepsy may rarely occur during pregnancy, and this may take the form of status epilepticus (18). Epilepsy may even occur in pregnancy with a male but not with a female foetus (19). Needless to say, pregnancy is no indication for the cessation of treatment, nor epilepsy for the termination of pregnancy. Migraine is commonly relieved, and may entirely disappear during pregnancy.

While disseminated sclerosis may occasionally remit during pregnancy, such cases more commonly deteriorate, particularly in the puerperium, under which circumstances the condition may also first appear. In view of the similar age incidence of the two conditions it would appear that even in such cases pregnancy should be regarded as a provoking rather than as an aetiological agent. It is generally agreed that pregnancy should be avoided in the established

disease, though there appears to be little evidence that artificial termination is less harmful than spontaneous delivery, and rest throughout pregnancy and afterwards, with avoidance of breastfeeding, is indicated.

Myasthenia gravis may be unaffected by pregnancy and exacerbation has occasionally been recorded, but many cases remit surprisingly, particularly during the later months. Prostigmine treatment can be continued throughout pregnancy without risk (20).

General paralytics usually tolerate pregnancy well, and the onset of physical or mental deterioration under such circumstances is unusual (21).

Epidemic or sporadic acute encephalitis may occur in pregnancy (22) and shows no special features, though it may present a difficult differential diagnosis from chorea, pre-eclampsia, or the nervous complications of hyperemesis already described, and some authors consider that pregnancy is associated with a higher mortality. Post-encephalitic Parkinsonism, though providing no impediment to normal parturition, may deteriorate considerably during pregnancy and there is a tendency for the latter to be associated with the onset of Parkinsonian symptoms in recent subjects of the acute disease.

Narcolepsy also may be intensified by pregnancy, and it is interesting in considering hypothalamic and pituitary function, so closely related to vegetative and reproductive life, to note the tendency to ketosis and coma in the pregnant diabetic and the occasional incidence of transient or permanent diabetes insipidus at this time.

PITUITARY NECROSIS

The syndrome of massive anterior pituitary necrosis has recently been clarified by the important studies of Sheehan (23). This condition follows delivery associated with collapse and haemorrhage, the presenting symptoms being a complete failure of lactation, and amenorrhoea which may prove permanent. These are followed by signs of a general depression of endocrine function of varying severity and incidence. A picture showing increased sensitivity to cold, apathy, and some gain in weight with myxoedematous features is not uncommon. Super-involution of the uterus, loss of pubic hair, and hypoglycaemia may occur. Some cases simulate Addison's disease, and rarely, in older multiparae, the full picture of Simmond's cachexia is seen. The pituitary lesions indicate a coagulative necrosis with infarction, and thrombosis in the pituitary sinuses.

Whilst some cases are associated with thrombosis elsewhere, the constant relation of the syndrome to collapse at the time of delivery suggests that the pathological process has its origin at this time rather than at the puerperal period usually associated with the cases of sinus thrombosis already described.

Partial syndromes of this type are probably not very uncommon. Further pregnancy may be accompanied by regeneration of the gland and clinical improvement. Many cases, however, fail to become pregnant, and the results of attempts at direct substitution therapy with pituitary extract are not very encouraging.

NEUROSES AND PSYCHOSES IN PREGNANCY

Whilst any of the neuroses may arise in relation to the stresses of pregnancy, they present no distinctive features. It is not very uncommon for the chronic psychoneurotic to show considerable improvement while pregnant, but this is often followed by relapse after delivery. Many chronic neurotic symptoms actually date from the adaptive demands of pregnancy and childbirth, and every practitioner is familiar with the complaint, "I've never been well since the baby came." The past history of such cases will usually reveal pre-existing neurotic traits and symptoms, and they are a clear indication that pregnancy, like marriage and service in the Armed Forces, should never be advised in the hope of curing neuroses or other psychological abnormalities. These often have their origin in emotional conflicts unlikely to be resolved by such superficial therapeutic measures. In addition, "One neurotic makes many," and the child of neurotic parents only too often acquires their habits of mind.

The rare Korsakow's polyneuritic psychosis and chorea have already been mentioned. During pregnancy psychoses may result at any period from the unmasking of a latent constitutional reaction-type, such as schizophrenia or the manic-depressive cycle.

A typical psychosis of the puerperium is the organic toxic-exhaustive reaction, often manifested as a confusional state, and not infrequently followed by depression of varying dura-

tion. This may occur following first or later pregnancies, and shows no constant relation to toxæmia or any obstetric abnormality other than infection, which is often present. The principle of multiple aetiology in psychological illness is well illustrated in these cases. A family history of psychological disorder, previous personal nervous instability, fear of pregnancy, emotional stress in relation to the father or the child, anaemia, debility, and infection may all play a part. These states may occur at any time during pregnancy and lactation, but they are commonest in the puerperium. Initial symptoms are sleeplessness and terrifying dreams, followed by disorientation, delusions and hallucinations leading to suicidal or infanticidal attempts. Variable delusions usually of a persecutory nature and states of agitated depression, or more rarely of mild excitement, may occur. Early recognition is important to guard against the ever-present risk of the patient harming herself or the baby, and unless exceptional facilities are available, cases of any severity should be treated institutionally. Interference is generally considered unwise should the condition occur during pregnancy, as the baby usually goes to term and is normal, but the infant should be taken away after delivery.

The prognosis of these states is in general good. There is some mortality, but probably about three-quarters recover completely, the duration being on the average longer than in similar reactions unassociated with pregnancy. It is usually stated that cases occurring after the early puerperium have a worse prognosis, but this is in fact more probably related to the aetiological factors involved, and in particular to the respective roles of endogenous and exogenous influences. Acute cases associated with severe infection and pyrexia in the absence of a family history of psychological disorder and with a good prepsychotic personality may be expected to do best.

EUGENIC ASPECTS OF NERVOUS DISEASE

Eugenic advice is rarely sought by those who stand in greatest need of it, and still more rarely taken unless it coincides with the inclination of the enquirer. Much human genetic data is difficult of assessment, there is a good deal of hypothesis, and really confident prognostication is rarely possible. With these reservations it is reasonable to state the facts and probabilities, as far as they are known, to any patient seeking advice. Considerations in giving such advice are not purely medical. Not even the most enthusiastic eugenicist is likely to counsel abstinence from reproduction in an otherwise socially admirable menage in which a partner is affected by a minor disorder with a dominant familial tendency such as migraine, and similar considerations not infrequently arise in considering other neurological conditions. Indeed often the most valuable service in this direction to a patient is a reassurance that his fears of handing on a disability are exaggerated, which is not infrequently the case in the type of patient requesting advice.

Some general principles are that it is frequently a tendency rather than a disease that is inherited, and that often, as probably in epilepsy, additional non-genetic factors may be necessary to produce the clinical syndrome. Subclinical forms, as in the finding of the skeletal abnormalities of Friedreich's ataxia without neurological concomitants, may occur in apparently unaffected relatives, and these obscure elicitation of the full family history which is the first essential in investigating any case from the genetic point of view. This is particularly important in view of the fact that the same disease not infrequently shows a different mode of heredity in different families, sometimes dominant, sometimes recessive.

The situation is further involved by the fact that the complex and variable heredity of some conditions with a familial tendency has led to the postulation of separate dominant and recessive factors, the coincidence of which is necessary for the appearance of the disease.

Frequent familial recurrence of a disorder from generation to generation in the absence of consanguineous parentage usually indicates a dominant hereditary factor. An affected parent transmits the condition on the average to half of his or her offspring, and unaffected members of such a family can be reassured as to the unlikelihood of their transmitting the disease. Such a mode of heredity is often seen in migraine, neurofibromatosis, Lindau's disease, myotonia congenita and dystrophia myotonica, familial periodic paralysis, spina bifida, myelodysplasias, hereditary tremor, and Huntington's chorea. In the case of the latter disease the late post-reproductive onset renders eugenic measures difficult, and all children of an affected parent would probably be well advised to avoid reproduction.

Recessive disorders, on the other hand, are characterised by a relatively infrequent familial

incidence with cases often arising from cousin marriages of unaffected members, who can be given no assurance that they will not transmit the disorder. On an average one of every four children will be affected. Peroneal muscular atrophy, the cerebromacular degenerations, torsion spasm, albinism, hepatolenticular degeneration, and some myopathies may show this mode of heredity.

Leber's optic atrophy is amongst the disorders which show a sex-linked recessive tendency, being chiefly found in male members of affected families. When not sex-linked, it tends to appear in early adult life in males, but near the menopause in female subjects.

Epilepsy follows no regular genetic pattern, although a positive family history of fits is not infrequent if carefully looked for, and this can be correlated with a high incidence of electroencephalographic abnormalities in the families of epileptics. Additional non-genetic factors undoubtedly play an important part in the actual production of epilepsy. Russell Brain (24), whose review of the genetics of neurological disorders is a mine of valuable information freely drawn on above, states that approximately one in ten of the children of an epileptic is affected by the disorder. In the absence, however, of a family history of fits, the risk of direct transmission appears to be statistically small, though again probably raised by consanguineous parentage.

REFERENCES

- (1) RUSSELL, W. R., IRONSIDE, R., MARTIN, J. P., *et al.* (1939), *Pro. Roy. Soc. Med.* **32**, 865.
- (2) STRAUSS, M. B., and McDONALD, W. J. (1933), *J.A.M.A.* **100**, 132.
- (3) CAMPBELL, A. C. P., and BIGGART, J. H. (1939), *J. Path. and Bact.* **48**, 245.
- (4) UNGLEY, C. C. (1933), *J. Neurol. and Psychopath.* **14**, 15.
- (5) PAKOZOY, K. (1929), *Deutsch. Med. Wchnschr.* **55**, 1509.
- (6) ALPERS, B. J., and PALMER, H. D. (1929), *Journ. Nerv. and Ment. Dis.* **70**, 465.
- (7) WILLSON, P., and PREECE, A. A. D. (1932), *Arch. Int. Med.* **49**, 471.
- (8) HUBBLE, D. (1943), *B.M.J.* **1**, 121.
- (9) BROWNE, F. J. (1942), *Antenatal and Postnatal Care* (London).
- (10) WILSON, S. A. K. (1940), *Neurology* (London).
- (11) MARTIN, J. P. (1941), *B.M.J.* **2**, 537.
- (12) BATSON, O. V. (1940), *Ann. Surgery.* **112**, 138.
- (13) TRAQUAIR, H. M. (1942), *Clinical Perimetry* (London).
- (14) MOORE, R. F. (1925), *Medical Ophthalmology* (London).
- (15) TIDY, L. (1941), *B.M.J.* **1**, 774.
- (16) ROSENBAUM, M., and MALTBY, G. L. (1943), *Archiv. Neurol. and Psych.* **49**, 204.
- (17) NERRLINGER (1889), *Inaug. Dissert.* (Strasbourg).
- (18) TURNER, W. A. (1907), *Epilepsy, a study* (London).
- (19) MUSKENS, L. J. J. (1928), *Epilepsy, Comparative Pathogenesis, Symptoms and Treatment* (London).
- (20) VIETS, H. R., *et al.* (1942), *J.A.M.A.* **62**, 122.
- (21) NAYRAC, P., GERNEZ, L., DUVAL, R. (1939), *Gaz. des Hop.* **112**, 493.
- (22) ROQUES, F. (1928), *Journ. Obst. and Gyn. Brit. Emp.* **35**, 1.
- (23) SHEEHAN, H. L. (1939), *Quart. Journ. Med.* **8**, 277.
- (24) BRAIN, R. (1934), in *Chances of Morbid Inheritance*, ed. C. P. Blacker (London).

DISORDERS OF THE ENDOCRINE GLANDS IN RELATION TO PREGNANCY

By S. L. SIMPSON, M.D., F.R.C.P.

(Physician, Willesden General Hospital, with charge of Diabetic Clinic; Physician, Princess Louise Kensington Hospital for Children; Consulting Physician, Soho Hospital for Women.)

Pregnancy should not be thought of as a condition affecting only the reproductive glands and organs, even when it is entirely physiological and uncomplicated by disease. Through the interrelationship of the endocrine glands, changes are probably produced in all the endocrine glands, the effects being only temporary in many cases, but in others a residual degree of change persists. The extent of this physiological change depends on what I have termed "the endocrine constitution" of the individual. The reality of such an "endocrine constitution" can be appreciated by observing familial endocrine tendencies, or stigmata, as variants of so-called normality, and more specifically by studying, for example, the effects of bilateral ovariectomy.