In even a brief discussion the serological aspect cannot be omitted. The spinal fluid picture which we have found to be almost constant is a normal or slightly increased cell count, a normal protein content, a negative Wassermann reaction, and a positive reaction to colloidal gold.¹⁵ This latter test, in conjunction with a negative Wassermann reaction, is, in my opinion, of undoubted value in the recognition of early cases of the disease.

Symptomatology.

As regards the symptomatology of disseminated sclerosis, I would like to emphasize one of the earlier manifestations. Retrobulbar neuritis is specially worthy of investigation and experimental research. In one of my cases of frank disseminated sclerosis in a woman aged 37 I obtained the following history. Fifteen years prior to the onset of gross symptoms she had suffered for a short time from bilateral retrobulbar neuritis, but in the interval had appeared to be in good health. Here we would appear to have a latency of infection comparable with syphilis. The occurrence of so-called idiopathic retrobulbar neuritis in a young and otherwise healthy adult should always be carefully investigated as a potential early manifestation of disseminated sclerosis.

Occupational Incidence.

So far I have referred chiefly to laboratory methods in the investigation of this disease. There are other channels into which inquiry may be profitably directed. It is of great importance not merely to study the natural history of a disease, but especially to investigate the circumstances under which the earliest manifestations appeared. The following observations are based on my personal experience of cases in the West of Scotland, and may be governed by conditions peculiar to the district. The majority of the patients I have seen with disseminated sclerosis come from the country, as opposed to the town. The incidence of the disease in this respect would appear to be in direct contrast to that of neuro-syphilis. The typical picture is that of a young adult, usually of good physique and with a healthy family history. It is excessively rare to find two cases occurring in the same family or in the same household—a fact which would point either to special personal susceptibility or to special exposure to infection. In this connexion the theory of insect transmission is worthy of investigation. Such a view has already received the support of Dreyfus¹⁶ in a published paper and Kuhn in a personal conversation. The occupations which seem to me to render the individual most liable to infection are farming, woodworking, game-keeping, gardening, byre-keeping, etc. Persons so employed are essentially earning their living in the open air in country districts. It is not only in these individuals that the disease seems specially liable to occur, but also in various members of their families. Recently McAlpine¹⁷ has referred to the desirability of investigating this occupational incidence of the disease.

Admittedly such a history cannot be obtained in a proportion of cases, but when one realizes the apparent latency of infection, to which reference has already been made, the difficulties of ascertaining when and where the infection occurred will be immediately apparent.

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ON CERTAIN ADRENALINE EFFECTS AT THE MENOPAUSE AND THEIR SIGNIFICANCE.

(Preliminary Communication.)

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In two theses read by myself at Cambridge dealing with the causation and treatment of "flushing" at the menopause, and in a recently published monograph on the same subject (1), I have drawn attention to certain adrenaline effects observed during my researches.

Flushing Produced by Adrenaline.

Intravenous injections of 10 minims of a 1 in 1,000 solution of adrenaline chloride, in women complaining of flushing at the menopause, gave rise, in all cases, to an immediate attack of flushing which was in all respects identical with the attacks which occurred spontaneously.

In order to exclude the possibility of this experimental flushing being caused by an increase in blood pressure, or the painful stimulus of an injection, control injections were made of pituitrin and normal saline; in no instance did the control injections give rise to an attack of flushing. It would appear, therefore, that the production of flushing at the menopause by the intravenous injection of adrenaline is due to the specific action of this substance.

A consideration of the results obtained by observers, such as Petzetakis, on the effects of intravenous injections of adrenaline in normal individuals yields no evidence of the production of flushing by adrenaline in such individuals.

Increased Tonus at the Menopause.

Loewi's reaction—namely, dilatation of the pupil following instillation of adrenaline into the conjunctival sac—occurred in 40 per cent. of those women at the menopause upon whom the experiment was tried; the reaction was constant on eight consecutive days; only women who complained of flushing were selected for this experiment.

If adrenaline be instilled into the conjunctival sac of a normal individual no dilatation of the pupil occurs, owing to the destruction of the adrenaline (Dixon). In some diseases of the pancreas, however, where there is impairment of the secretory cells, certain adrenaline effects become more pronounced and dilatation of the pupil occurs; this phenomenon being caused, according to Loewi, by the absence of the restraining influence of the pancreas on the suprarenal glands, these glands being physiological antagonists. Bearing in mind, therefore, that pancreatic disease might be present in some of my cases, an examination of the urine was undertaken in those cases where the pupil reaction was positive; in no instance was evidence of glycosuria obtainable.

From my experiments it would appear that the sympathetic nervous system of women, who at the menopause complain of flushing, is in a condition of increased tonus. The menopause is, we know, associated with ovarian atrophy and loss of the Graafian follicles; furthermore, removal of both ovaries will produce a syndrome closely resembling the natural process: my research, therefore, would seem to indicate that the internal secretion of the ovaries and that of the suprarenal glands (medullary portion) are physiological antagonists.

The ovarian extracts which are available at the present time are unsatisfactory, but I have had some success in the treatment of flushing at the menopause by the subcutaneous administration of an extract of the whole ovary in combination with a dry extract of the corpus luteum, orally (2). In two of my cases, Loewi's pupil reaction has disappeared under ovarian substitution therapy.

The Significance of Adrenal Sensitiveness at the Menopause.

It would appear from my research that the flushings of the menopause are due to an increase in the tonus of the sympathetic nervous system at this time, this increase being caused by the absence of or deficiency in the restraining influence of the internal secretion of the ovaries on the

suprarenal glands. It would also seem possible that this sympathicotonicity may account for some of the many symptoms, such as headache and sensations of tingling and numbness in the extremities, which make up the menopausal syndrome.

The use of Thyroid Extract at the Menopause.

Thyroid extract is frequently used at the menopause. As I have shown elsewhere (3), the intensity of the attacks of flushing at the menopause is increased by the administration of thyroid extract at this time; this phenomenon is to be expected if, as has been suggested by Goetsch, the internal secretion of the thyroid gland sensitizes the body cells to the action of adrenaline.

In my opinion, therefore, thyroid extract should not be given, as a routine, to women at the menopause.

The Use of Chloroform as an Anaesthetic at the Menopause.

There is considerable evidence that the syncope which occurs during the induction of chloroform anaesthesia is associated with fibrillation of the cardiac ventricles, and is caused by abnormal irritability of the heart muscle, in which the sympathetic nerve supply is involved. Cushny says that this ventricular fibrillation is possibly caused by reflexes through the accelerator apparatus, or by an increased secretion of the suprarenal glands. If, as I have shown, women at the menopause are sympathetictonic, chloroform should be avoided as an anaesthetic at this time.

Following a suggestion made to me by Dr. W. E. Dixon, I have endeavoured to ascertain if women at the menopause are particularly susceptible to chloroform syncope; owing to the infrequency with which chloroform is administered in these days and the comparatively few cases of chloroform syncope which have been recorded with details of the

menstrual history at the time of the accident, my researches into this question have hitherto been unsatisfactory. It is interesting, however, to remember that pregnant women, in whom the ovaries are present in a condition of increased activity, are extremely tolerant to chloroform.

The preparation of the active hormone or hormones of the ovary is attended with many technical difficulties, and I know of no satisfactory product at present on the market. I am satisfied, however, that some of the ovarian extracts which are available are effective to a limited and varying extent; but until an active substance, of standardized potency, is available, the clinical value of my observations must remain inconclusive.

Summary.

1. The tonus of the sympathetic nervous system of women at the menopause is increased.
2. The increase in tonus of the sympathetic nervous system is responsible for the vasomotor phenomena and, possibly, for some of the other symptoms which make up the menopausal syndrome.
3. The increase in tonus of the sympathetic nervous system at the menopause is caused by the unrestrained action of the suprarenal glands, the internal secretion of the ovaries being deficient or absent.
4. Thyroid extract should not be administered at the menopause, owing to its adrenal sensitizing action.
5. Chloroform should not be used as an anaesthetic in women at the menopause.

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Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

RUPTURE OF THE HEART.

An edentulous man, aged 71, was given a large cup of hot meat extract at 11 p.m., followed an hour later by a large cup of hot cocoa. He was found dead in bed at 1 a.m. At the *post-mortem* examination I found a rupture, 1 in. long, in the anterior wall of the left ventricle. The muscle was pale, flabby, and fibrotic. The stomach was enormously distended with air. I concluded that in sipping the hot liquids he had swallowed this air, and the consequent distension of the stomach embarrassed the heart sufficiently to tear it.

In the interesting paper by Drs. Strickland Goodall and Weir (May 7th, p. 834) there is a history of recently ingested food or fluid in seven out of fourteen cases; one would like to know the condition of the stomach in these cases, and whether flatulent distension was a contributory factor to the rupture.

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HEREDITARY DEFORMITY OF THE FINGERS.

A MAN, aged 22, presenting the following abnormality of the fingers, was admitted to Addenbrooke's Hospital in November, 1926, suffering from renal calculus.

The middle and terminal phalanges are shortened, the fingers being of the average breadth for an adult man. The body of each finger-nail is double. The two parts are separated by almost normal skin, which runs distally over the dorsum of the terminal phalanx and is continuous with the skin covering the tip of the finger. On either side of this median strip of skin nail tissue appears, of the normal texture and elasticity. The cuticle is present on each side and overlaps the nails in the usual fashion. The intermediate central part is harder than normal skin and bears longitudinal striations; it is, however, quite distinct from the nails. At the distal end there is the usual shallow transverse groove, where the free end of the nail should be. The little finger of the left hand approaches the nearest to

normal. There is here a nail occupying three-fifths of the width of a normal nail. The man used to scratch this finger when a boy in order to make the nail grow.

The thumbs show this peculiarity in the highest degree. The nail bed on each side is represented by areas 2 mm. in width and 4 mm. in length, each containing a tiny nail. The nails all grow slowly, and seldom require cutting. The feet are normal.

The man stated that several members of his family have hands similar to his own. In the following table the persons marked with a cross are those who exhibit this deformity.

The patient could not trace his family further back than the grandfather, nor could he state whether the abnormality had ever been transmitted through one of the female members of the family.

I am indebted to Dr. J. Aldren Wright for permission to publish details of this case.

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AN UNRECOGNIZED CASE OF FRACTURE OF A CERVICAL VERTEBRA.

THE following case presents some points which may be of interest:

A man, aged 38, was admitted to the Chester Infirmary in May, 1926, during the general strike, after being run over by a railway lorry, which crushed his chest. No fracture of the ribs could be found, and, as he had apparently quite recovered, he was discharged after a short stay in hospital.