these may be given with advantage. The following letter from the parent of a child aged 18 months is instructive:

"A. lived on raw fruits, showing a marked preference for this kind of food. Lettuce leaves played a large part in his diet. Milk was given unboiled and cold, and he drank a quart daily. His appetite was poor at all times, but he would always eat raw fruit, and never objected to a drink of milk. The demand for repeated drinks was noticeable throughout his illness."

When the mouth is ulcerated cold foods will prove to be less painful than hot. A change from the city surroundings to the mountains or seaside is of the greatest benefit when the children begin to sleep better and their appetite improves. It should be emphasized, however, that during the worst months of the illness the parents are well advised to keep their children away from strangers and strange places. The resources of a nurse trained in the care of ill children are of great help if the anorexia is extreme. In some cases it may even be necessary to resort to tube feeding.

Drugs.—For insomnia occasionally a mixture containing bromides and chloral hydrate has been of help, but hypnotics are usually disappointing.

Prognosis

Under ideal conditions the mortality is low, most patients being restored to perfect health. Relapses are rare once the child begins to eat and sleep well and put on weight. Sequelae are unknown, and one attack apparently affords a permanent immunity. The complications that may appear during the prolonged course of

FIG. 3.—When cases of pink disease are treated in their own homes (A) the mortality is low (3 per cent.) compared with the results of hospital treatment both in Melbourne (B) (mortality 30 per cent.) and in Sydney (C) (mortality 29 per cent.).

but it must be admitted that the hospital group would naturally contain a higher percentage of severe cases. However, we consider that by diminishing the secondary infections of the skin and mouth, removing all possible sources of cross infection, and giving a well-balanced diet and plenty of fresh air the mortality rate of pink disease should be less than 5 per cent.

The length of the illness should be impressed upon the parent when the case is first diagnosed, otherwise the patient will pass from one medical attendant to another. After three or four months the child will be finally "cured" by some form of treatment which, if used at the beginning of the illness, would have failed to shorten the attack.

Summary

1. The early work on pink disease is described, and honour is paid to Selter.
2. The aetiology and pathology is discussed, with special reference to the part played by infection.
3. The symptomatology is described and the natural course of the disease is emphasized.
4. It is considered that no specific method of treatment has yet been established, but great benefit is obtained by attention to the details of symptomatic treatment.
5. The great danger of cross infection is stressed.

Our thanks are due to Dr. Reginald Webster, pathologist at the Children's Hospital, Melbourne, for his constructive criticism of this paper.

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PREVENTION AND PROGNOSIS OF THE LATE TOXAEMIAS OF PREGNANCY*

BY

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Definitions and Preliminary Observations

The "late" toxæmic manifestations exclude those arising before the twenty-eighth week, thus partially overcoming the difficulty of differentiating them from cases of chronic nephritis complicating pregnancy, in the large majority of which symptoms will have arisen earlier. It is not, however, so simple a matter to lay down what is or is not implied under the designation of the "toxæmias of pregnancy," as they form a group of disorders whose right to such a title, though justified on pathological grounds, has never been proved by the discovery of any definite toxin or toxins. Hence dependence for a definition of the conditions under consideration must be placed on their clinical features, of which a true albuminuria and raised blood pressure are the most consistently present. Associated therewith are others, such as oedema, headache, vomiting, insomnia, cramps, polyneuritis, jaundice, and ante-partum bleeding, in varying degrees of prominence and frequency. No useful purpose will be served by trying to do more than offer a syndrome of this kind for a well-recognized group of disorders, but the need for a period of observation before cases can be definitely placed in this category must be stressed. Albuminuria, for instance, even of proved renal origin, may mean much or little, and sometimes is late in appearance or even absent. I accept F. J. Browne's¹ conclusion, based on an analysis of 320 cases of so-called "pre-eclampsia," that the cause, whatever it may be, is capable of producing directly any one of the signs or symptoms ascribed to the condition.

* Read in opening a discussion in the Section of Obstetrics and Gynaecology at the Annual Meeting of the British Medical Association, Melbourne, 1935.

Prevention

Constructive Hygiene.—Ante-natal supervision being primarily a system of constructive hygiene, the crucial question in this part of our discussion is to determine how far it is possible to formulate a special hygiene for the expectant mother that may lessen the incidence of these conditions. Owing to our ignorance of their causal factors, a rational basis for a physiological system of this kind is lacking. In 1922 the physiological requirements of the pregnant woman were thus summarized by Marshall²: "The dietary conditions which must be observed more particularly are an abundant supply of, first carbohydrates, secondly calcium, and thirdly vitamins." This statement expresses the focal point round which discussion revolves to-day, for dietary systems occupy the most prominent place in prophylaxis. Claims are advanced for fruitarian, flesh-free, and salt-free³ diets, for a high vitamin content and additional supplies of certain mineral salts, such as those of calcium, phosphorus, iodine, and iron, but based more on theories of the cause of the disorders they are intended to avoid than proof of their efficacy by clinical observation. An unintentional trial on large numbers showed a pronounced fall in the eclampsia rate among the half-starved populations of Central Europe during the late stages of the war with a return later to its former level, but the precise reason was not proved. The low protein content is the generally accepted explanation, thus encouraging the adoption of diets of that type, but reliable evidence of their value is lacking. Theobald⁴ has taken up the view that the toxæmias of pregnancy are deficiency diseases, and advocates a complete diet, rich in vitamins, calcium, iodine, and iron. The diet he is trying at present includes two pints of milk daily, a tablespoonful of cod-liver oil, with butter, fruit, and green vegetables. If the oil is not readily tolerated, concentrates of vitamins A and D (and sometimes B and C) with iodized salt are substituted, and iron, if the patient is anaemic. The need for calcium⁵ during pregnancy is clear in view of the increased call on the maternal supply, especially in the last two months, but the problem is rather that of discovering the form in which it is not only assimilated but also made readily available. The interrelationship between calcium absorption and phosphorus and vitamin D indicates the need for consideration of these factors. Milk, butter, and cheese contain calcium in an absorbable form, but the quantity may be insufficient to maintain an adequate and readily available maternal reserve in late pregnancy. Owing to uncertainty and delay in oral administration, intramuscular injection of calcium gluconate is suggested as the best means to this end. To lessen the risk of acidosis, extra carbohydrate, on the same lines as in preparation for a serious operation, is a reasonable precaution in the last few weeks, particularly in cases in which a prolonged labour is anticipated. Little can be added to the dietary requirements quoted from Marshall, beyond stressing the need for fresh food and for the protein element to be supplied by fish, eggs, milk, and cheese rather than meat. Besides diet full attention must be paid to personal hygiene. The importance of regular evacuation of the bowels is well recognized. The mode of life and precautions advised for those liable to, or who have suffered from, chronic nephritis can scarcely be amiss, such as care during sudden changes of temperature, avoiding chills and crowded assemblies where chance infections are readily picked up, together with the search for septic foci and their treatment, if found.

Prevention of Complications.—The lack of a reliable preventive system as a first line of defence necessitates a retirement to the second line, the recognition of the early signs of disordered metabolism followed by remedial

measures directed to the restoration of the normal before more serious trouble arises. It entails, first, the frequent examination of all expectant mothers, next the thorough investigation of all cases exhibiting symptoms or signs that may be regarded as evidence of a toxæmic condition, and, finally, the prompt treatment of those falling within this category by dietetic measures as already indicated, and the administration of magnesium sulphate and alkalis. The woman must be kept in bed to allow of accurate observation and to lower body metabolism, and the duration of observation determined by the history and progress of the case. Distinct improvement under treatment naturally affords sound reason for continuance, while its absence and, still more, increasing gravity indicate termination of the pregnancy before more serious consequences result.

Maternal Prognosis

Up to the last fifteen years or so the risk run by toxæmic pregnant women was reckoned almost wholly in terms of eclampsia, but the supervision of the expectant mother through successive pregnancies brought to notice remoter risks in persistent or recurrent albuminuria, which have attracted increasing attention. Judging from mortality rates it would seem that there is exaggeration in both cases, for no diminution of the death rate from eclampsia is shown from 1921 to 1931, and a scarcely appreciable degree since, in spite of the large number of pre-eclamptics saved from supposititious convulsions by treatment, while the mortality from renal disease of married as compared with single women⁶ does not indicate that added risk anticipated from the gloomy prognostications of obstetricians.

Eclampsia.—The statement that eclampsia is a "preventable disease" is no more than an intelligent anticipation regardless of things as they are at present, when there is no generally accepted means of preventing toxæmic states, and cases under treatment may surprise us by falling into convulsions. Further, there is a material proportion of cases, from 5 to 15 per cent., in which the onset is too rapid to offer even a fleeting opportunity for prevention. The warning of impending convulsions is given, roughly in order of importance, by rising blood pressure, lessened secretion of urine, severe headache, visual disturbance, and epigastric pain. But even these signs may escape notice, particularly during intra- and post-partum onset. As one whose hospital service began before the day of systematic ante-natal care, blood-pressure estimations, and biochemical tests, the impression I obtained of eclampsia was of an acute condition coming on suddenly, and, when recovered from, clearing up rapidly. But enough of the severer types of albuminuria came into the wards, and so seldom attained the expected convulsive stage, for me to regard cases of gradual onset as of chronic renal disease, as doubtless some of them were, or as a chronic type of toxæmia in which renal symptoms were predominant and convulsions unusual. These cases were observed for longer than is the practice to-day, and experience of them left me with grave doubts of their pre-eclamptic nature. The prognosis of eclampsia depends largely on the number and frequency of the fits and their sequelae; deep coma, high fever, rapid pulse rate, being associated with successive and severe convulsions, make the outlook grave. Jaundice also is of bad prognosis. Of good omen after cessation of fits are early return to consciousness, fall of pulse rate, and increased excretion of urine. Occasionally a marked polyuria, up to 200 oz. and more in twenty-four hours, occurs, and within a week urine that boiled solid may show no more than traces of protein.

Toxæmic Albuminuria.—Here prognosis is largely determined by the response to treatment. The daily

amount of urine passed affords a better index than the amount of protein in the urine, and diminution of blood pressure and oedema, and improvement generally, makes the issue favourable. A residual albuminuria is not of moment provided the blood urea and urea-concentration tests are satisfactory. So long as improvement is maintained the pregnancy can be allowed to continue, but the objections to its termination are greatly reduced once the last month is reached.

Recurrence in Subsequent Pregnancies and Permanent Renal Damage.—In this regard prognosis is guided chiefly by the duration of the illness and completeness of recovery. The severity of the attack is of little moment compared with its length, for the chronic type is more likely to be followed by recurrence or chronic nephritis than eclampsia or a shorter and sharper non-convulsive toxæmia. Hence the importance of terminating the pregnancy before permanent damage results. For this reason Arwyn Evans⁷ makes fourteen days of albuminuria the limit, and in so doing seems to me to err in his standard, for he has taken the least reliable one. His finding that young patients run less risk than the older multiparae should encourage longer trial in the former. The same factors govern advice given regarding risk of recurrence in a subsequent pregnancy. It is usual to recommend an interval of two years before the test of another pregnancy, but the time may be shortened for women of an age at which fertility is lessening fast. Husband and wife must fully appreciate the close supervision required throughout such pregnancies; also that failure on a second trial prohibits further chances being taken. If there is no return, the probability is that future pregnancies will also be unaffected.⁸ Persistent high blood pressure is unfavourable. Banister⁹ regards a systolic pressure below 150 mm. Hg as an indication that recurrent albuminuria is unlikely. Sometimes ocular symptoms arise that put the eyesight of the mother in jeopardy; rather than risk this disaster the pregnancy should be ended on this account alone.

Foetal Prognosis

Although there is a definite risk of intrauterine death of the foetus in non-convulsive toxæmia, it is much less than in the convulsive, in which the fits themselves add greatly to this risk. Danger to the foetus from toxæmic states is less than in chronic nephritis.

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A. Schwarz (*Zentralbl. f. Gynäk.*, July 13th, 1935, p. 1648) states that of 258 curettings done from 1929 to 1934 at a Vienna clinic for diagnostic purposes in cases of atypical bleeding during the pre-climacteric or post-menopausal years, no fewer than twenty-six (10.1 per cent.) showed the presence of carcinoma. Subsequent investigations done three to six years after the ensuing radical operations failed to show in any instance that the curetting had favoured extension or metastasis.

OVARIAN AND PITUITARY HORMONES*

BY

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Irregularities of menstruation are very often met with in the routine of general practice, and until recently it has been customary to diagnose excessive or irregular bleeding, exclusive of new growths, as endometritis in one of its many subdivisions—glandular, interstitial, chronic, and so on. It is now an accepted fact that endometritis, due to previous infection, is a comparatively rare disease, and should only be diagnosed when inflammatory cells are present in considerable numbers; in true chronic endometritis, the detection of plasma cells is specially significant. Although sometimes a searching inquiry is entailed, it is generally possible to place these variations from the regular cycle into one of several well-recognized groups: menorrhagia when the cycle is of normal length but the loss is excessive; epimenorrhoea when the cycle is reduced to twenty-one or even fourteen days but the rhythm remains; metrorrhagia when there is intermenstrual bleeding. On the other hand, there may be amenorrhoea for weeks, followed by continuous bleeding, not infrequently diagnosed as an early miscarriage in a woman of child-bearing age; but it is now recognized that these symptoms are often due, not to pregnancy, but to a disease in which ovulation does not take place—namely, metropathia haemorrhagica.

The discoveries of the hormones of the ovary and the anterior lobe of the pituitary gland have revolutionized many of the accepted theories as to the causes of these irregularities, and the aim of this lecture is to give a short review of the, at present, accepted opinions of the source and functions of these hormones.

Changes in Endometrium during the Menstrual Cycle

The normal menstrual cycle is regarded as being one of twenty-eight days, the first day of the bleeding being taken as the first day of the cycle. The endometrium throughout the cycle is in a constant state of change. Immediately after the period repair sets in when the epithelium grows over and covers the denuded areas, the membrane is thin, and the glands simple straight tubules. This is followed by the proliferative stage, which continues to the mid-interval. The glands become lengthened and tortuous, the membrane swollen and uneven. About the sixteenth day the endometrium begins to assume a peculiar structure, which continues to develop until shortly before the onset of menstruation. The membrane increases in thickness, and closely resembles the decidua of early pregnancy. The glands are dilated with secretion, and have a characteristic corkscrew appearance; this is the premenstrual or pre-gestational phase, and it is followed by menstruation, during which the superficial hypertrophied layers of endometrium degenerate and are shed into the cavity, and this, together with the blood which is simultaneously effused, constitutes the menstrual discharge. And then again regeneration and so on to another cycle. Thus the constant change accounts for the rather bewildering old-fashioned classification of endometritis, and when endometrium is required for diagnostic purposes it emphasizes the need for giving the pathologist the exact day of the cycle on which it was removed.

* Post-graduate lecture delivered at Dundee Royal Infirmary, May 9th, 1935.