exists a bewildering variety in the production and mode of action of these substances. In so far as their activity during pregnancy is concerned, it appears, however, possible that the diversity of action in this respect might be partly explained by the hypothesis that the uterine contents have, to various extents for different species, taken control of, or even superseded, functions otherwise performed by endocrine structures in the host organism.

Summary

1. The properties of the hypophyseal and gonadic hormones produced during pregnancy and responsible for changes which then occur are briefly described.

2. The concentration of hormones in the urine, the blood, the placenta, and the pituitary during pregnancy is reviewed in (a) the human being, (b) certain higher primates, (c) the mare, and (d) some other animals.

3. The relation of the sex hormones to the alterations occurring during gestation in various species is discussed; an attempt is made to evaluate their significance in the processes responsible for the maintenance of pregnancy and initiation of parturition.

BIBLIOGRAPHY

- *Allen, W. M.: *Sex and Internal Secretions*, Williams and Wilkins, Baltimore, 1932.
- Allen, E., Diddle, A. W., and Elder, J. H.: *Amer. Journ. Physiol.*, 1935, cx, 593.
- Anderson, J.: *Veterinary Journal*, 1934, xc, 295.
- Barrie, M. M. O., Patterson, J. B. E., and Underhill, S. W. F.: *Quart. Journ. Pharmacy and Pharmacol.*, 1935, viii, 424.
- Bourne, A.: *Proc. Roy. Soc. Med.*, 1934, xxvii, 56.
- Brindeau, H., Hinglais, H., and Hinglais, M.: *C. R. Soc. de Biol.*, 1934, cxv, 1509.
- Butenandt, A.: *Zentralbl. f. Gynäk.*, 1935, lix, 71.
- Butenandt, A., Westphal, U., and Hohlweg, W.: *Zeit. Phys. Chem.*, 1934, ccxxvii, 84.
- Butenandt, A., and Kudzus, H.: *Hoppe-Seyl Zeit.*, 1925, ccxxxviii, 75.
- Catchpole, H. R., Cole, H. H., and Pearson, P. B.: *Amer. Journ. Physiol.*, 1935, cxii, 21.
- Catchpole, H. R., and Lyons, W. R.: *Amer. Journ. Anat.*, 1934, lv, 167.
- Cohen, S. L., and Marrian, G. F.: *Biochem. Journ.*, 1934, xxviii, 1603.
- Cohen, S. L., Marrian, G. F., and Watson, M.: *Lancet*, 1935, i, 674.
- Courrier, R.: *C. R. Soc. de Biol.*, 1934, cxvii, 1117.
- Courrier, R., and Gros, G.: *Ibid.*, 1935, cxx, 5.
- Deansley, R., and Parkes, H. S.: *British Medical Journal*, 1936, i, 257.
- Engle, E. T.: *Amer. Journ. Physiol.*, 1934, cviii, 528.
- Haeussler, E. P.: *Helvet. Chim. Acta*, 1934, xvii, 531.
- Hamburger, C.: *Endokrinologie*, 1934, xiii, 305.
- Hart, G. H., and Cole, H. H.: *Amer. Journ. Physiol.*, 1934, cix, 320.
- Hellbaum, A. A.: *Anat. Record*, 1935, lxiii, 147.
- Hill, R. T.: *Journ. Physiol.*, 1934, lxxxiii, 129.
- Lipschutz, Z. A., Alba, A. F., and Vivaldi, T.: *C. R. Soc. de Biol.*, 1935, cxx, 323.
- Marrian, G. F., and Newton, W. H.: *Journ. Physiol.*, 1935, lxxxiv, 133.
- Newton, W. H.: *Ibid.*, 1935, lxxxiv, 196.
- Robinson, A. L., Datnow, M. M., and Jeffcoate, T. N. A.: *British Medical Journal*, April 13th, 1935.
- *Robson, J. M.: *Recent Advances in Sex and Reproductive Physiology*, Churchill, London, 1934.
- Idem: *Journ. Physiol.*, 1935, lxxxiv, 121.
- Idem: *Ibid.*, 1935, lxxxiv, 148.
- Idem: *Ibid.*, 1936, lxxxvi, 171.
- Idem: *Ibid.*, 1936, lxxxvi, 415.
- Robson, J. M., MacGregor, T. N., Illingworth, R. E., and Steere, N.: *British Medical Journal*, 1934, i, 888.
- Ruzicka, L., and Wettstein, A.: *Helvet. Chim. Acta*, 1935, xviii, 986.
- Selye, H., Collip, J. B., and Thomson, D. L.: *Endocrinology*, 1935, xix, 151.
- Siebke, H.: *Arch. Gynäk.*, 1934, clvi, 317.
- Slotta, K. H., Ruschig, H., and Fels, E.: *Berl. deut. chem. Ges.*, 1934, lxvii, 1624.
- Snyder, F. F.: Quoted by Zuckerman, *Amer. Journ. Physiol.*, 1935, cx, 597.
- Struck, M.: *Deut. Tierarztl. Woch.*, 1935, xliii, 260.
- Wintersteiner, O., and Allen, W. M.: *Journ. Biol. Chem.*, 1934, cvii, 321.
- Wolfe, E., and Ginglinger, A.: *C. R. Soc. Biol.*, 1936, cxxi, 1476.
- Zondek, B.: *Skand. Arch. Physiol.*, 1934, v, 133.
- Zuckerman, S.: *Amer. Journ. Physiol.*, 1935, cx, 597.

Only the most recent references have been given. Reviews of the subject in which previous work is discussed are marked with an asterisk.

A CENTRE, OR CENTRES, IN THE HYPOTHALAMUS CONTROLLING MENSTRUATION, OVULATION, PREGNANCY, AND PARTURITION

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It is only within the last few years that our conception of the menstrual cycle in man has been freed from false analogies to the oestrous cycle in other mammals. It is now generally believed that the cycle is dependent on the varying amounts of folliculin and corpus luteum hormone circulating in the blood, this ovarian activity being stimulated and controlled by a substance or substances elaborated in the anterior pituitary gland.

The purpose of this communication is to advance evidence of a clinical nature in favour of the thesis that there are one or more centres in the brain, probably in the hypothalamus, which control menstruation, ovulation, pregnancy, and parturition. It is suggested that this centre receives afferent stimuli from (a) the ovaries (hormonal in nature); (b) the external generative organ (by nervous paths); and (c) the special senses and psyche (that is, psychological). The efferent impulses operate through (a) the anterior pituitary gland, and (b) nervous impulses to the generative organs.

Hypothalamic Centres

Evolution from the unicellular forms of life to that of the mammal, and the consequent "division of labour," has necessitated the vesting of the ultimate control of every function in the central nervous system. The centres in the cerebral cortex—such as those for vision, speech, and hearing—are not, like the vasomotor and respiratory centres situated in the medulla, essential to life. It is not always realized that centres exist which either initiate or control coughing, salivation, expectoration, body temperature, and vomiting. That at least some of these activities cannot occur apart from their centres is evidenced by the fact that herbivora cannot vomit. In general, the activity of the centre is dependent on afferent stimuli which may be either nervous or chemical, specific or catholic. Likewise the efferent stimuli may be either nervous or chemical, or both nervous and chemical.

The vegetative centres, of which the carbohydrate centre may be taken as an example, are situated in the hypothalamus. Removal of the pancreas results in death from diabetic coma. If, however, the anterior pituitary gland is extirpated subsequent excision of the pancreas is compatible with life. It would seem that the anterior pituitary substance tends to raise, and the secretion of the islets of Langerhans to lower, the level of the blood sugar, and that the carbohydrate centre co-ordinates the activities of these two opposing hormones. Situated in this region of the brain are two cell masses, named the paraventricularis and the supra-opticus. Greiving has shown that nerve fibres from these cell masses pass into the pituitary stalk. Not only do they receive a very rich systemic blood supply, but they are also freely bathed with blood returning from the pituitary sinusoids. Further, it is now accepted (Clark and Boggon) that the prefrontal cortex and the cortex of the gyrus cinguli are connected with the thalamus, and the mid-line nuclei of the thalamus with the hypothalamic nuclei. It may therefore be postulated that these cell masses are rendered sensitive to the difference in the hormonal content between the systemic blood and that returning from the pituitary

sinusoids, and that they may receive nervous impulses from the generative organs and the cerebral cortex. It would, moreover, be reasonable to assume that efferent impulses pass from them down the pituitary stalk. For these reasons it is suggested that the menstrual, and possibly the water, centre is situated in one or other of these cell masses.

The fact that menstruation does not occur until puberty merely implies that the centre is not until then adequately stimulated by the ovarian secretions. Seeing that pseudo-menstruation may take place in early infancy it is evident that the uterus is always capable of menstruation and the centre—if it exists—of functioning. That there is no centre as yet described peculiar to one sex is clearly no objection to the thesis, but it is probable that the sexual orgasm is controlled by a centre and that the sex centre in woman controls not only the orgasm but the functions under consideration.

The clinical evidence in favour of this hypothesis will now be considered.

Regularity of the Menses

There is no rhythmical function of the body, apart from menstruation, which is not accepted as being controlled by a centre in the brain. It is true that the isolated perfused heart beats rhythmically, but in the active intact animal its rhythm is dependent on a normally functioning vasomotor centre and could not be maintained apart from central nervous control. The remarkable regularity of the menses in the vast majority of healthy women is a phenomenon that suggests a central rather than a haphazard hormonal control. This is particularly true of that small group of women who are so regular that they can almost set their clocks by the time that the flow begins. The question immediately suggests itself as to whether the regularity would be influenced by the total absence of clocks. I know of one woman who, if she does not menstruate at a given time on a certain date, does not have a period for a further four weeks. This regularity of the menses is all the more suggestive when it is remembered that most girls are very irregular for some months when the periods first appear.

Amenorrhoea

Swimmers who plunge into cold water experience a temporary amenorrhoea, which may last from ten minutes to one hour. In some women the mere introduction of the feet into a bath—whether hot or cold—at the time the period is expected, or at its beginning, causes menstruation to cease and not to recur until four weeks later. A certain nurse, brought up not to bath during her periods, changed her habits, and, in spite of the fact that she was convinced that she had been wrongly advised on this matter as a child, it took more than six months before her periods became regular under her more enlightened hygienic practice.

It is well known that a change of climate or a change of occupation may cause amenorrhoea. This phenomenon is particularly evident in nurses, more especially when they first go on night duty. The amenorrhoea may persist for several months and in some instances be associated with obesity and no little disturbance of the general health. It is most easy to explain amenorrhoea of this nature on the assumption that it follows a mental disturbance, and this assumption receives support from the fact that the condition is frequently "cured" by the threat of a gynaecological examination. Shocks and excitements of all kinds may result in the same symptom, while in some individuals over-worry and excessive fatigue cause the periods to be heavier than usual and to appear more frequently.

A CASE HISTORY

The effect of fear on menstruation may best be illustrated by a short history of a lady doctor, aged 30 years. Her periods began when she was 13½ years old, and after a few months' irregularity settled down to a normal rhythm of 4-5/28-30 days. She married when she was 17 years old, and thereafter the periods became very irregular, the intervals being as long as three months. Four years later she became pregnant, and in the fifth month after a normal delivery menstruation recommenced and remained very irregular. When the child was 3 years old the husband went away for eight months, during the whole of which time the menses were regular in every respect. So soon as he returned they again became irregular, the cycle lasting from two to three months. Three years later the patient herself went away for six months' post-graduate study, and during this time menstruation was regular. Immediately she returned they became grossly irregular, with long periods of amenorrhoea. A year later the patient again went on a course for six months, and again the periods became regular.

The patient herself is a normal, healthy, active person who had had a successful career. She is very fond of her husband and child, but has no confidence in the method of birth control which she uses. When living with her husband she lives in fear of becoming pregnant, and the period rarely comes on until, after the lapse of from two to three months, she is satisfied that she is not pregnant.

Effect of Hypnosis

This evidence may be considered in the light of the effects on the menstrual cycle produced by hypnosis. Heyer (1927) states that he has always found it possible to delay menstruation in the cases of artistes who have important engagements to fulfil. The period is either delayed until after the event or missed for a month. He further states that it is possible to alter a twenty-eight-day cycle and cause the woman to menstruate on a fixed day of each month—that is, the first Monday in each month. Paneth was able to change a regular three-weeks into a regular four-weeks cycle by a single hypnotic suggestion.

It is well known that "menstruation" may continue with regularity for many years after double ovariectomy. The explanation which has always been offered for this phenomenon is that remnants of ovarian tissue are left behind. It is here suggested that the centre has become so accustomed to a rhythm that it initiates menstrual bleeding in the absence of ovarian stimulation. It is, moreover, of interest that uterine haemorrhage beginning long after the menopause occasionally shows a monthly rhythm, and the patient herself is constrained to believe that her monthlies have recommenced. Further, it is difficult on the accepted hypothesis to explain the following undoubted facts: a woman may "menstruate" during the first three months of pregnancy; a woman possessing a bicornuate uterus may "menstruate" from one horn during the whole course of pregnancy in the other; superfecundation and superfoetation.

Effect of Morphine

Further evidence is that of the action of morphine on menstruation. Most women who become addicted to opium or one of its derivatives cease to menstruate and lose their libido sexualis. Cessation of menstruation, however, does not interfere with either ovulation or conception (Krauss, 1918). If the drug is withheld during pregnancy miscarriage or premature labour is likely to occur. This is generally attributed to the fact that the foetus becomes lively and that its movements result in the termination of pregnancy.

An alternative explanation of this phenomenon might be held to lend support to the theory that there is a pregnancy centre in the brain. A hollow muscular organ

like the uterus should attempt to expel any contents, and the termination of pregnancy is much more likely to be due to the cessation of the inhibiting influence of some hormone than to an increase of any oxytocic substance in the blood. In the normal individual the centre acted on by the hormone would, elaborated in the corpus luteum, inhibit any movements calculated to expel the foetus. In the morphine addict the centre would be dull, and less inhibitory hormonal activity would be required. When the drug is suddenly withheld the labour centre becomes relatively stimulated and the uterus expels its contents. Some support for this view is afforded by the observation that young female rats chemically poisoned with morphine in amounts up to 70 mg. per kilo of body weight daily for from three and a half to five months continued to show cyclic changes in the vaginal epithelium, mated readily, and bore litters of apparently healthy young in average numbers (Meyers, 1931).

The final evidence to be offered is the fact that among the sequelae of encephalitis lethargica sexual precocity, amenorrhoea associated with obesity, and forms of diabetes insipidus have been recorded (Borthwick, 1927; Livet, 1921; Lachaux, 1924; Serin, 1924). Indeed, it may well be that a thorough histological examination of the hypothalamic lesions in the brains of women dying from this disease subsequent to manifesting these disturbances might offer direct evidence as to the existence or non-existence of such a centre as has been postulated. It is at least certain that the hypothalamus is the region of the brain which suffers most as a result of this infection.

It will probably be conceded that, if a centre controls menstruation, then ovulation, pregnancy, and parturition are similarly controlled, and for this reason the evidence in favour of the latter three functions being so regulated will be but briefly discussed.

Ovulation

If it may be assumed that ovulation in a healthy woman with a normal menstrual cycle occurs between the twelfth and the seventeenth day of the cycle, and that the spermatozoa cannot live in the female genital tract for more than forty-eight hours, it follows that most of the cycle is a "safe period" for the woman. Clinical experience proves this contention false, for conception may take place on any day of the cycle—even during menstruation. I have the clear record of a woman's becoming pregnant on the twenty-seventh day of the menstrual cycle—the night before her period was due. On the other hand, it would appear to be true that the optimum period of fertility in the great majority of women lies between the middle of the second and the middle of the third week of the menstrual cycle.

It is well known that ovulation in the rabbit does not normally occur except following coitus or after an orgasm (Heape, 1905; Hammond and Marshall, 1914). Marshall and Verney (1935) have recently succeeded in bringing about ovulation in this animal by either cephalic or lumbar electrical stimulation with an alternating current. They presume that this stimulation acts through the intermediation of the anterior pituitary gland, but point out that so far as the rabbit is concerned there is no anterior pituitary rhythm controlling the follicular and luteal phases. It is possible that in man ovulation normally follows a certain rhythm, but that unusual excitement of the centre associated with the sexual libido might bring about ovulation at any time during the cycle. This view might explain the relative infertility of women who practise birth control during the first years of married life and the remarkable infertility of prostitutes, which cannot be entirely attributed to gonococcal and other infections of the genital tract.

Pregnancy and Parturition

It has already been stated that the uterus, being a hollow muscular organ, should expel or attempt to expel any contents, and that the onset of labour probably results from the cessation of this inhibition rather than from the increase of any oxytocic principle or principles in the blood stream. The effects of the withdrawal of morphine in women addicts who are pregnant has been mentioned. It is well known that labour pains often cease when the doctor enters the room, and that relatively rapid dilatation of the cervix may follow the injection of morphine or some other narcotic which cuts off the inhibitory control of the higher centres. These effects of the mind in labour have been stressed by G. D. Read (1933). The belief is widely held that intense fear may cause both abortion and miscarriage, and that they are more likely to take place at those dates when the woman would have menstruated had she not been pregnant. During the bombardment of Strasbourg in 1870 there were a great number of abortions and miscarriages as the result of fright (Kohts), and Baudelocque reported that ninety-two cases of abortion came to him for treatment almost simultaneously following a terrific explosion.

Commentary

It is not disputed that changes associated with the menstrual cycle are normally dependent on the varying amounts in the blood of the hormones secreted by the anterior pituitary gland and the ovaries. The question at issue is as to whether these hormones, and in particular those secreted by the anterior pituitary gland, are under the control of a centre in the brain which may in certain circumstances, particularly after the menopause, operate apart from ovarian hormonal stimulation.

If double ovariectomy is performed in a young girl her secondary sex characteristics fail to develop and she neither menstruates nor ovulates. The secondary sex characteristics are undoubtedly dependent on substances elaborated in the anterior pituitary gland. Pathological changes in this gland, its experimental extirpation in animals, and biochemical investigations in man, make it certain that the normal rhythm both of menstruation and of ovulation is also dependent on its activity. The conclusion would therefore appear inevitable that the sex hormones elaborated in the anterior pituitary gland are stimulated by, and stimulate, the ovarian hormones. Evidence adduced in this paper makes it equally certain that mental disturbances can, and frequently do, upset the menstrual cycle. It would follow that the liberation of the anterior pituitary sex hormones can be affected both by nervous impulses from the cerebral cortex and by hormonal stimuli from the ovaries.

Not only must there be some "threshold" of resistance to the liberation or retention of these hormones, but it is clear that the nervous impulses, whatever the emotion from which they arise, must ultimately travel through the same nervous paths to the anterior pituitary gland.

It is therefore suggested that the known facts are most easily explained on the assumption that there is a menstruation centre situated in the hypothalamus and possibly in the cell masses which have been described. It is postulated that the centre is stimulated both by the ovarian hormones and by nerve impulses from the generative organs and from the higher centres in the brain. It operates through the anterior pituitary gland and nervous impulses to the sex organs. All the phenomena recorded can be explained on this hypothesis. Conversely, it is impossible to explain the effects of hypnosis on the menstrual cycle by a vague admission that its rhythm may be affected by mental disturbances. The

temporary cessation of the menses following a plunge into cold water could be satisfactorily explained on the assumption that the blood supply to the uterus was temporarily altered, but it would not be possible to explain why the menses stop altogether if a girl takes a warm bath or even puts her feet into warm water. Temporary vasomotor disturbances in the uterine blood vessels could not explain this fact. Moreover, seeing that large numbers of women do bathe during their menses it is clear that the flow is not stopped by the water but by the assault against the mind which has been taught that bathing during the period is harmful.

Of all the drugs in the *Pharmacopoeia* morphine would appear to be the most peculiar in the way in which it acts on different centres in different ways. It depresses the central nervous system generally and the pain centre in particular. It depresses the cough and respiratory centres, but stimulates the nucleus of the third nerve, the vagus centrally (slowing the pulse), and the salivation and vomiting centres. The fact that morphine addicts cease to menstruate, although they ovulate and may conceive, may be considered as strong evidence in favour of a menstruation centre. The fact that if morphine is withheld from such a patient during pregnancy the onset of premature labour is likely to occur is evidence in favour of the existence of a parturition centre.

PRACTICAL IMPLICATIONS OF HYPOTHESIS

It may be objected that such a conception is of academic rather than practical significance. It is, however, of fundamental importance not only in the understanding of the factors involved but in the treatment of disturbed function in man. Attempts have been made to estimate the amounts of such substances as oestrin and the anterior pituitary hormones circulating in the blood and to treat disorders of menstruation by the injection of these and other substances into the patient. If, however, the ovaries and anterior pituitary gland be normal, and the disturbance of function be due to inadequate and inharmonious control of the hormones they secrete, then, if the hypothesis be true, it would be more logical to treat the centre directly by suggestion or indirectly by promoting the well-being of the body by dietetic and hygienic measures. If, on the other hand, either the ovaries or the pituitary gland are imperfectly developed or diseased it is unlikely that substitution therapy will often be of the value it is in the case of thyroid insufficiency, except at and for some time after the menopause.

The thesis advanced would therefore support the view, held by many clinicians, that fresh air, an adequate diet, sound hygiene, attention to the bowels, and the taking of iron are as likely in the majority of cases to produce as good results in the treatment of menstrual disorders as hormonal therapy, which is not as yet placed on a scientific basis. Not only is hormonal therapy not placed on a scientific basis, but so-called anterior pituitary hormones are in fact but waste products excreted in the urines of pregnant women. It might also be inferred not only that dysmenorrhoea, some forms of irregular uterine bleeding, and irregular dilatation of the cervix during labour are due to defective central control, but that the development of the uterus may be to a large measure dependent on the adequate operation of this centre.

It may be mentioned in parenthesis that the vasomotor centre is very unstable in some individuals, so there are adequate grounds for the assumption that a centre may, for various reasons, fail to act properly.

There is some justification for the belief that imperfect sexual development may be due to mental strain or excessive athletic activity at the time of and during the years immediately following the onset of the menses. The acceptance of a menstruation centre in the brain

would therefore of necessity demand a radical change not only in our conception of the menstrual cycle but also in the treatment of menstrual disturbances. Further, it would follow that ovulation, pregnancy, and parturition are in all probability controlled by a centre or centres closely related to that which controls menstruation.

Summary

1. The ultimate control of every function in the body is vested in the central nervous system.

2. Every rhythmic function of the body is controlled directly by a centre, or centres, in the brain.

3. The regularity of the menses, the facts that amenorrhoea may be caused by mental strain, fear, or merely immersing the feet in water at the time when the period is due, offer evidence in favour of a menstruation centre.

4. The facts that the menstrual cycle can be changed by hypnosis and that the periods cease in women addicted to morphine, to return when they are cured of the drug habit, although ovulation and conception are unaffected, are in favour of this hypothesis.

5. Evidence is brought forward to suggest that ovulation, pregnancy, and parturition are similarly controlled by a centre or centres which, it is suggested, are situated in the hypothalamus.

6. It is postulated that the afferent stimuli to the menstruation centre are provided by the ovarian hormones and by nervous stimuli from the generative organs and the cerebral cortex, and that the efferent stimuli from the centre operate through the anterior pituitary gland and to a certain extent through nervous impulses to the generative organs.

7. If this hypothesis is true it follows that the correct method of treating menstrual disorders in the majority of cases, providing the ovaries and anterior pituitary gland are normal, is to treat the centre directly by suggestion or indirectly by promoting the general well-being of the body by dietetic and hygienic measures.

8. The wider implications of the hypothesis are indicated.

BIBLIOGRAPHY

- Baudelocque: Quoted in *Emotions and Bodily Changes*, H. F. Dunbar, New York, 1935.
 Borthwick, G. L.: *Rep. Met. Asylums Board*, 1926-7, p. 161.
 Clark, W. E. L., and Boggon, R. H.: *Brain*, 1933, lvi, 83.
 Heape, W.: *Proc. Roy. Soc. Biol.*, 1905, lxxvi, 260.
 Hammond, J., and Marshall, F. H. A.: *Ibid.*, 1914, lxxxvii, 422.
 Heyer, G. R.: *Die psychischen Heilmethoden von Karl Birnbaum*, Leipzig, p. 73.
 Kohts: Quoted in *Emotion and Bodily Changes*, H. F. Dunbar, New York, 1935.
 Kraus, W. M.: *Journ. Nerv. and Ment. Dis.*, 1918, xlviii, 36.
 Livet, L.: *Bull. et Mém. Soc. Méd. des Hôp. de Paris*, 1921, xlv, 656.
 Marshall, F. H. A., and Verney, E. B.: *Journ. of Physiol. (Proc.)*, 1935, lxxxv.
 Meyers, H. B.: *Journ. Pharmacol.*, 1931, xli, 317.
 Paneth: Quoted in *Emotions and Bodily Changes*, H. F. Dunbar, New York, 1935.
 Read, G. D.: *Natural Childbirth*, London, 1933.
 Serin: *Ann. Méd.-psychol. Paris*, 1924, lxxxii, Part I, 319.

The Home Secretary has made the following further Rules under Section 23 of the Pharmacy and Poisons Act, 1933: (1) the Poisons (Colouring) Rules, 1936 (S.R. and O., 1936, No. 363); (2) the Poisons (Amendment) Rules, 1936 (Provisional). The former require the addition of a dye to certain arsenical substances sold for use in agriculture and horticulture, such as sheep dips, fruit sprays, vermin and weed killers, and replaces the colouring provisions of the Arsenic Act, 1851, which lapsed on May 1st, 1936. The Poisons (Amendment) Rules add to the articles in the Third Schedule to the Poisons Rules, 1935, which are exempted from the provisions of the Act. The poisons affected are ammonia dinitrophenol and potassium hydroxide (caustic potash). Copies of the new Rules (price 1d., post free 1½d.) and the Home Office Memorandum (3d., post free 4d.) may be purchased from H.M. Stationery Office at the following addresses: Adastral House, Kingsway, London, W.C.2; 120, George Street, Edinburgh; York Street, Manchester, 1; St. Andrew's Crescent, Cardiff; or through any bookseller.