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Current Topics

Anæmia in Pregnancy

By DANIEL T. DAVIES, M.D., B.S.C., F.R.C.P.
(From the *Practitioner*, Vol. CXXXIV, March 1935, p. 290)

ALTHOUGH pregnancy is a physiological and natural state it occasionally results in derangements of the maternal metabolism so as to produce or activate pathological conditions. It is not uncommon for a latent disorder to become active during this period. A woman who during normal times is able to maintain a normal blood count may during this period of increased demand become progressively and severely anæmic. The offspring depends solely on its mother for a proper and sufficient supply of blood-building substances, which must be adequate to maintain the growing infant over the milk-feeding period. Bunge showed that the liver of a newly-born animal contains weight for weight six times as much iron as the liver of an adult animal and that this iron content of the liver progressively decreases during the milk-feeding period, until the animal is able to ingest iron-containing foods, when it again increases. This increased iron content of the newly-born animal can only be derived from maternal sources and this transfer must on occasion so deplete the maternal reserves as to produce a failure of hæmoglobin manufacture. However anæmic the mother it is usual for the child to be born with a full complement of hæmoglobin, although recent work by Strauss shows that infants of women suffering from anæmia often

develop a severe anæmia during the first year of their lives. It is probable that the supply to the foetus has been deficient *in utero*.

The anæmias occurring during pregnancy can be roughly divided into two groups—the hypochromic which is relatively common and the macrocytic which, in this country, is rare. This latter form, however, is commoner in tropical countries, especially in certain parts of India, where the extremely restricted diet is probably responsible in large measure.

Hypochromic anæmia in pregnancy

A mild degree of this hypochromic anæmia is common in women drawn from industrial areas. Whereas idiopathic hypochromic anæmia is almost a curiosity in the male, any outpatient department furnishes a large collection of this type of anæmia in women. An interesting study bearing on this problem was made recently by Davidson and his colleagues at Aberdeen; they found that the daily intake of iron in the poorer classes was much below what has been regarded as necessary. Many of these families existed on an average intake of not more than 6 mg. of iron per day. This impoverished iron intake, however, was not accompanied by any anæmia unless there were some extra demands. In children up to 14 years of age and in males, in spite of a poor intake of iron, anæmia was conspicuously absent; on the other hand adult females on a similar diet showed a high proportion of anæmia. Anæmia was present in nearly 50 per cent of over

400 adult females. As Davidson points out, the iron requirement for a woman is obviously tidal and it corresponds with the normal functions of womanhood; at this period the iron intake should be optimal and not minimal. It is certainly uncommon to meet this anæmia in women who lead lives of luxury.

Provided the stores are well stocked the healthy woman passes through pregnancy without any fall in her blood count. Some attention has been drawn to the increased blood volume which is present during pregnancy and the slight reduction in red cell and hæmoglobin values which might be seen in consequence of this hydræmia during the first six months of pregnancy. Shelly and I recently followed through 45 women during their pregnancies; the average fall in hæmoglobin was only 8 per cent and the average fall in red cells 280,000 per c.mm. Any count which is below 75 per cent hæmoglobin should be regarded as pathological.

The anæmia may show itself during the first pregnancy but it is more common in multiparæ after several pregnancies. It may not be obvious until after confinement and a severe blood loss during labour may be the precipitating factor. Some patients admit that they were pale before the pregnancy but that there has been an intensification of the pallor since they have become pregnant. Usually the symptoms are more prominent during the last three months when the iron is transferred from the maternal stores to the fœtus. Many of the symptoms are often and too readily attributed to the pregnancy. The languor, anorexia, giddiness, headache and dyspnœa are often regarded by the laity as usual and 'natural' symptoms which must be tolerated. Occasionally these symptoms are misinterpreted and regarded as the early symptoms of 'toxæmia'. A rigorous restriction in diet is often advised and this results in deprivation of iron-containing foods at a time when the need is greatest.

In a woman who becomes anæmic for the first time during pregnancy there is little obviously abnormal except the pallor. If, however, she has suffered from anæmia for many years, and perhaps from exacerbations in former pregnancies, the signs of chronic anæmia are usually seen; there is a greenish tint in the sclerotics, the angles of the mouth are fissured and often painful, the tongue is red and devoid of papillæ, the hair is dry and thin, the nails brittle and spoon-shaped and spleen palpable. Some or all of these signs may be present and they indicate an anæmia of long standing and naturally intensified by pregnancy.

Examination of the blood shows a reduction in the hæmoglobin. The hæmoglobin is frequently around 40 to 50 per cent, while the red cells are 4 millions. The colour index is therefore low. The red cells are poorly stained and may show changes in shape and size, *i.e.*, poikilocytosis and microcytosis. The outstanding feature, however, is the low hæmoglobin content, and usually advice is sought before the hæmoglobin falls below 40 per cent.

One of the most important points in examining a woman thought to be a case of this anæmia during pregnancy is a careful inquiry into her diet; the foods which contain iron, such as red meat, spinach and other green vegetables, are often absent from the diet and this is especially true of housewives of working class families who live mainly on bread and other starchy foods. This restriction of iron-containing foods is a logical explanation for the break-down during pregnancy, and it is well to explain to the pregnant female the need of iron-containing foods, as a prophylactic measure. Of 46 patients who did not become anæmic while under observation throughout their pregnancies none gave a history of a poor diet intake; on the other hand of 26 who developed hypochromic anæmia during or after pregnancy 18 took grossly inadequate diets. Castle and Strauss have also emphasized this association of inadequate diets with anæmia during pregnancy.

Another important examination which sheds light on this anæmia is the analysis of the gastric secretion. The normal acidity of the gastric juice facilitates the absorption of iron from the intestine and it is believed that in achlorhydric states much of the iron in the food is lost. Deficient absorption may be therefore superimposed on a state of deficient intake of iron, if there is a coexistent achlorhydria. A woman is most prone to develop anæmia due to iron deficiency when there is achlorhydria and especially is this true when the extra strain of pregnancy calls forth an increased demand from the iron stores. In the 20 females who were anæmic following their last pregnancy two only showed a normal gastric secretion, the other 18 presented achlorhydria or a marked hypochlorhydria. Castle and Strauss found that not only is achlorhydria of extreme importance in the development of this anæmia, but that even in the normal female there is a decided reduction in gastric acidity during pregnancy; this is corrected in the puerperium. Two patients with a good gastric secretion in the puerperium were completely achlorhydric during pregnancy.

That gastric defect may be the only explanation for the anæmia is shown by the following case: a woman, aged 28, developed an anæmia of 60 per cent hæmoglobin in the sixth month of her second pregnancy; she had not had any excessive blood loss in the past, and took a good varied diet, yet she showed an anæmia which responded to iron and which could only be explained by the presence of a permanent achlorhydria.

An exact proof of the importance of achlorhydria in this connection is forthcoming from the experimental work of Ivy and his colleagues. They have shown that the dog on which a gastrectomy has been performed can be maintained without the development of any anæmia for an indefinite period, provided the diet is adequate in iron-containing substances. When, however, the animal is allowed to become pregnant an anæmia of this type invariably occurs. In one dog this occurred in five successive pregnancies.

There is a good deal of evidence that this hypochromic anæmia is not uncommon during pregnancy, and this is in all probability the resultant of a deficient intake of iron-containing foods in women who show achlorhydria or hypochlorhydria. It is also not irrational to believe that much disability and chronic ill-health associated with pregnancy and the puerperium could be avoided by the early recognition of this disorder.

Treatment is highly successful in this form of anæmia; iron in large doses results in a rise in hæmoglobin, the disappearance of the symptoms of languor and lassitude and a feeling of well-being equal to that of any specific therapy. The only tardy response that we encountered was in a woman who gave birth to twins. It is unwise to force the liberal use of iron-containing foods if there is an existing anorexia or any abdominal upset, especially since iron in the shape of its salts will accomplish the necessary improvement in a much shorter time. A daily dose of 90 grains of citrate of iron and ammonia is usually well borne. It is an advantage to prescribe the iron some two hours after food to be followed by a sweet orange drink, although the iron is usually well tolerated. The dose of 90 grains a day should be administered until the hæmoglobin reaches a level of at least 80 per cent, and it is a good plan to continue with one daily dose (gr. 30) until the pregnancy is over. If in the puerperium the gastric analysis be repeated and a normal amount of hydrochloric acid be found, iron medication can be dispensed with; if, however, achlorhydria persists the need for iron will be permanent and it should be given at least periodically until after the menopause.

Macrocytic anæmia in pregnancy

This form of anæmia is certainly far less common than hypochromic anæmia as an event in pregnancy. Its importance, however, is that it may appear very

suddenly and seriously endanger life. It is interesting to recall that one of the first references to an anæmia of pernicious type was that by Channing, an American obstetrician in 1842. This anæmia shows the blood characteristics of Addisonian anæmia and its response to liver therapy is equally certain. There is, however, one important distinguishing feature which was well realized in pre-liver days and, namely, that the patient showing this 'pernicious anæmia' during pregnancy frequently recovered spontaneously, in sharp contrast to the then fatal issue of ordinary pernicious anæmia.

Since Addisonian or pernicious anæmia is now easily corrected with substitution treatment, it is of course possible to meet a patient known to have had pernicious anæmia and now pregnant. The strain of pregnancy might be responsible for a relapse which would call for energetic treatment; case records have established this sequence of events. Pregnancy may also precipitate pernicious anæmia in a female predisposed to its development by reason of a gastric defect. These events are of necessity rare for pernicious anæmia usually occurs in women past the child-bearing period. The macrocytic anæmia induced by pregnancy cannot be regarded as identical with Addisonian or pernicious anæmia. It is true that there is macrocytosis, and that there is great reduction in the red count and a high colour index. The spontaneous remissions, however, place it in a category of its own; another important feature is the inconstancy of any gastric abnormality, for many patients have shown a normal acidity.

The anæmia may be gradual in its onset or it may develop with great rapidity during the last trimester of pregnancy. Associated with the pallor there is often a slightly yellowish tint to the skin and this may be accompanied by subcutaneous œdema if the anæmia is severe. There is also frequently a fever and a tendency to premature labour, as the existence of œdema may suggest a renal lesion and the real cause remain untreated. If, as sometimes happens, the anæmia appears in the puerperium, the accompanying fever may suggest puerperal sepsis and treatment directed to this condition result in neglect of the anæmia. Several writers have described the obstetric shock which accompanies delivery and emphasize the importance of adequate treatment before this takes place. Recurrences in future pregnancies have often been observed and Whitby believes that in some cases a degree of hypoplasia of the marrow is produced, a condition in which the response to treatment becomes particularly resistant.

The exact cause of this anæmia is unknown, the gastric juice is often normal and there is certainly no obvious dietetic factor. Castle and Strauss, who showed that there is such reduction in gastric acidity during pregnancy, suggest that it is due to a temporary arrest of secretion of the intrinsic factor. It may be that many causes operate and that the condition is a non-specific failure of blood formation. In the macrocytic anæmia as seen in India, Wills has shown that in all probability the cause is a lack of the extrinsic factor in the diet.

The treatment of the condition is the same as that of pernicious anæmia, and the earlier the treatment is instituted, the less risk the mother runs. If the anæmia is severe the active principle should be given intramuscularly. In those whose condition is desperate or in whom labour is imminent a blood transfusion is life-saving. Cæsarean section preceded by a blood transfusion is the method of choice when the patient is seen at term to be severely anæmic. Since auto-agglutination is a potential danger much care is necessary in testing the blood prior to transfusion. Provided the gastric secretion is normal treatment can be discontinued after delivery when the blood has returned to normal. If, however, there is achlorhydria it is safe to regard the patient as an example of pernicious anæmia in need of constant supervision and treatment.

Favourite Prescriptions

By CECIL WALL, D.M., F.R.C.P.

(Abstracted from the *Practitioner*, Vol. CXXXIV, February 1935, p. 226)

Aperients.—Probably aperients are the most extensively used medicines in hospital practice. The official Black Draught, which seems to have obtained an impregnable position in the British Pharmacopœia, is too expensive for hospital use; it is represented now by the *Haustus aperient*:—

℞ Magnesium sulphate	.. grains 150
Emulsion of chloroform	.. minims 7½
Infusion of senna	.. 1 oz.

Chloroform is introduced partly as a flavouring agent and partly as a preservative. The emulsion of chloroform is made with tincture of quillaia and is less expensive than the solution in spirit.

The cascara mixture is another favourite aperient; its evolution is of some interest. In 1882 it contained 20 minims of the liquid extract with a drachm of the liquid extract of liquorice and chloroform water to the ounce. In 1901 the cascara was increased to 30 minims, the liquorice reduced to 30 minims, and 30 minims of syrup of ginger was added to prevent griping, and the chloroform water was reduced to half an ounce. In 1914 the cascara went up to a drachm, and instead of the ginger, 40 minims of sal volatile were added. Even this was not sufficiently potent and a compound cascara mixture was introduced and remains the popular aperient mixture:—

℞ Liquid extract of cascara	.. minims 60
Liquid extract of senna	.. minims 30
Liquid extract of liquorice	.. minims 60
Tincture of hyoscyamus	.. minims 30
Tincture of nux vomica	.. minims 10
Emulsion of chloroform	.. minims 10
Compound decoction of aloes	to 1 oz.

As a prescription it savours of polypharmacy and can scarcely be called 'elegant', but it is reputed to be efficient with the torpid bowels of habitual constipation. Personally I doubt whether it is any more efficient than the pil. coloc. c̄ hyosc. of the B. P. which, if uncoated, maintains perennial popularity with the same class of patient and goes by the name of 'Uncle Henry'.

Astringents.—The hospital pharmacopœia no longer includes an astringent mixture which formerly was so necessary and popular that a large keg was kept on tap in the receiving-room. Motors have ousted horses, flies, contaminated food and summer diarrhœa. The old formula, however, is worth recording:—

℞ Aromatic sulphuric acid	.. minims 15
Spirit of chloroform	.. minims 20
Compound tincture of camphor	minims 20
Decoction of logwood	to the fluid ounce.

Aromatic sulphuric acid was the famous Mynsicht's elixir of vitriol of the seventeenth and eighteenth centuries, and sentimental regret for its disappearance from the B. P. is mingled with the feeling of satisfaction that it is no longer an important preparation.

Anti-dyspeptic formulæ.—In the sixteenth and seventeenth centuries, and probably long before, the value of insoluble carbonates and phosphates in the treatment of dyspepsia was well known; chemistry could not then explain either the nature or the action of the drug, but the reputation of powdered unicorn's horn (narwhal's tooth), of calcined snail shells, of crabs' 'eyes' and crabs' 'claws' of the early pharmacopœias was evidently based on the relief of pain after food on their administration. Aqua Tofana, the favourite poison of the Borgias, seems to have been an acid solution of arsenic: if it was put into a cup made of 'unicorn's horn' effervescence occurred and the arsenic was thrown out of solution—small wonder that the

value of the rare narwhal's tooth was great in those days! Modern chemistry has brought to us other and more easily obtained insoluble carbonates, and we still use them to relieve gastric pain, which was then so often attributed to poison in the food. Until 1901 it was customary to prescribe the insoluble carbonates of bismuth and magnesium in combination with an emulsifying agent such as compound tragacanth powder; when this addition was found to be unnecessary the most popular prescription became the pulv. bismuthi co., of which the patient is told to take a teaspoonful stirred up in water. The composition is as follows:—

℞ Oxycarbonate of bismuth .. 10 parts
Heavy magnesium carbonate 25 parts
Sodium bicarbonate .. 25 parts

In the pulvis calcii carbonatis co., prepared chalk is substituted for the bicarbonate of soda. The acid and alkaline gentian mixtures are used extensively, but are so well known that comment is needless. The hospital formula for the gentian and rhubarb mixture is designed for economy:—

℞ Gentian grains 5
Rhubarb grains 5
Ginger grain 1
Sodium bicarbonate .. grains 10
Peppermint water to fl. oz. $\frac{1}{2}$
Macerate for 24 hours and strain

Such a prescription is satisfactory in a hospital where the medicine is compounded in large quantities, but is not suitable for private practice. A better though more expensive formula would be:—

℞ Tincture rhei compound .. minims 30
Tincture zingiberis fortis .. minims 5
Liquor ammonium dilutum .. minims 10
Tincture gentian compound minims 30
Aqua menthœ piperitœ ad fl. oz. $\frac{1}{2}$

A favourite prescription for the dyspepsia of chronic alcoholic is mist. capsici sedativa:—

℞ Potassium bromide .. grains 10
Sodium bicarbonate .. grains 10
Tincture of capsicum .. minims 5
Strong tincture of ginger .. minims 5
Infusion of quassia to fl. oz. $\frac{1}{2}$

Fever mixture.—Simple diaphoretic mixtures are often of considerable value when the temperature is high. Mixture ammonium acetate compound is an example:—

℞ Spirit of nitrous ether .. minims 30
Strong solution of ammonium acetate minims 30
Aromatic spirit of ammonia minims 20
Chloroform water to fl. oz. $\frac{1}{2}$

Cough mixtures.—In the dry stage of bronchial catarrh nauseating expectorants act by reflexly exciting the secretion; to secure this end the drug must be given in doses just short of producing the sensation of nausea. The ammonia and ipecac. mixture of the London Hospital contains 20 minims of the tincture of ipecac. with 3 grains of ammonium carbonate in some camphor water, and the dose of ipecac. is not found to be at all excessive. Acting in a somewhat similar manner is the standard cough mixture which is taken mixed with hot water:—

℞ Sodium chloride .. grains 3
Sodium bicarbonate .. grains 10
Emulsion of chloroform .. minims 5
Oil of anise minim $\frac{1}{25}$
Water to fl. oz. $\frac{1}{2}$

Seeing that aniseed water is no longer included in the B. P., 5 minims of the aqua anethi concentrata may be substituted for the oil of anise in private practice; moreover, it is often desirable to colour the medicine by adding some compound tincture of cardamoms.

In the more chronic forms of bronchitis the alkaline iodide mixture is of great value. Clinical experience supports the pharmacologist's view that large doses of potassium iodide are of less value than the small ones; the formula is:—

℞ Potassium iodide .. grains 3
Ammonium carbonate .. grains 3
Potassium bicarbonate .. grains 10
Camphor water to fl. oz. $\frac{1}{2}$

When the coughing reflex is weak it is often useful to add tincture nucis vomica to the mixture. When there is evidence of bronchial spasm, inhibition of the vagus is desirable; in such circumstances stramonium is often combined with potassium iodide. The mixture potassium iodide et stramonium contains the following:—

℞ Potassium iodide .. grains 3
Tincture of stramonium .. minims 10
Liquid extract of liquorice .. minims 20
Chloroform water to fl. oz. $\frac{1}{2}$

The dose of stramonium is small because some patients are readily affected by it; generally it is necessary to increase the dose until it causes some dryness of the mouth and then to make a slight reduction.

Sedative cough mixture.—The most commonly employed is Gee's linctus, of which the formula was borrowed from St. Bartholomew's Hospital—equal parts of paregoric, syrup of squill, and syrup of tolu—but a similar preparation is found in the old mixture scillæ compound:—

℞ Vinegar of squill .. minims 15
Camphorated tincture of opium minims 20
Emulsion of chloroform .. minims 10
Infusion of gentian to fl. oz. $\frac{1}{2}$

Blunderbuss prescriptions.—The old pathology which obtained for so many centuries held that disease was due to excess or defect of one or more of the four humours: blood, phlegm, black bile or yellow bile, and treatment was based on the hypothesis that the disturbance could be corrected by the administration of appropriate drugs—*contraria contrariis curantur*. Uncertainty as to the action of the drugs led to polypharmacy in the hope that if enough were given some would procure the desired result. The modern reversion to humoral pathology under the more attractive and 'scientific' title of endocrine imbalance seems to be associated with a like expectation. This is apparent not only in the proprietary mixtures of the wholesale druggists, but even in the hospital pharmacopœias.

The last edition of the London Hospital Pharmacopœia contains several examples of formulæ which can be justified only by the results of practical experience; at first sight it would seem to be undesirable to combine pharmacological and chemical incompatibles in the same prescription, for instance, in mixture ammonium carbonate compound:—

℞ Ammonium carbonate .. grains 4
Tincture of squill (B. P. 1914) minims 10
Camphorated tincture of opium minims 10
Syrup of tolu drachm 1
Camphor water to fl. oz. $\frac{1}{2}$

There is a stimulant and a sedative of the respiratory centre and an alkaline carbonate to interact with the benzoic acid of the paregoric. In the mixture oxymel scillæ the pharmacologist might ask why the potassium iodide is introduced to increase the bronchial secretion and the opium to check expectoration; the formula is:—

℞ Oxymel of squill .. minims 15
Camphorated tincture of opium minims 20
Potassium iodide .. grains 2
Dextrose grains 30
Chloroform water to fl. oz. $\frac{1}{2}$

Practical experience may show that the pharmacologist's inquiry is indiscreet. Another ultra-modern prescription, seemingly designed as a panacea, but unlikely to captivate pharmacists, pharmacologists or the

older generation of physicians is the mixture ferri alkalina, of which the formula is:—

R Citrate of iron and ammonium	grains	20
Sodium bicarbonate	.. grains	15
Solution of arsenic	.. minims	3
Aromatic spirits of ammonia	minims	30
Tincture of nux vomica	.. minims	10
Infusion of calumba to fl. oz.		$\frac{1}{2}$

Possibly because of its eponymous title, Broadbent's mixture retains a measure of popularity. The therapeutic intention is not easy to understand, but it demonstrates that a skilled pharmacist may circumvent chemical incompatibility for about 48 hours. It contains:—

R Ammoniated solution of quinine	fl. drachm	1
Strong solution of ammonium acetate.	minims	15
Camphorated tincture of opium	fl. drachm	$\frac{1}{2}$
Ammonium carbonate	.. grains	2
Tragacanth	.. grain	$\frac{1}{2}$
Peppermint water to fl. oz.		$\frac{1}{2}$

In the present overcrowded state of the medical curriculum it is scarcely possible for the student to study intensively the subjects of pharmacy and materia medica. The British Pharmacopœia has become a book of standards. The newly-qualified practitioner needs help in the art of prescribing, and his own hospital pharmacopœia should provide that help; it should enable him to employ those medicines of which he has seen the effect when clerking in the wards. The conditions which govern dispensing in a hospital are, however, different from those which obtain in private practice, and consequently while approving the large majority of the formulæ given in our pharmacopœia, I have pointed out some which might lead to disappointment if prescribed outside the walls of the institution. Perhaps when the promised reform of the medical curriculum is effected, greater stress will be laid upon the training in materia medica and pharmacy, and they will be studied at a period more appropriate than at present. Surely the craftsman should know his tools and how to use them with economy and skill.

Anterior Pituitary and Anterior Pituitary-like Substances: Therapeutic Applications

By EMIL NOVAK, M.D.

(From the *Journal of the American Medical Association*, Vol. CIV, 23rd March, 1935, p. 998)

Up to a few years ago, efforts at anterior pituitary therapy were limited to the use of oral or hypodermic preparations, either of the anterior lobe alone or of the whole gland, in conditions of supposed deficiency, such as adipogenital dystrophy, pituitary obesity or amenorrhœa, dwarfism or infantilism. In this respect the common practice was almost analogous to the early methods of ovarian therapy in conditions of supposed ovarian hypofunction. Just as the clear differentiation of the ovarian hormones has completely changed the complexion of ovarian therapy, so have the recent advances in anterior pituitary hormonology changed the points of view and methods in pituitary organotherapy. The tendency now is to aim at hormone therapy rather than at mere gland treatment.

The important physiologic advances to which reference has been made have been fully reviewed in previous articles of this series. The present paper, like the one on oestrogenic therapy, makes no pretense of being an exhaustive review, being offered rather as a brief summary and appraisal of the present status of the subject, and including only a minimum of references to the extensive and somewhat bewildering literature.

As a basis for the discussion of the therapy of the anterior lobe, the following hormones have been enumerated as having their source in this structure:

1. The growth hormone, commonly accepted as being the product of the eosinophilic cells.

2. The gonadotropic hormone or hormones, generally believed to be formed by the basophilic cells.

3. The lactogenic hormone, shown by Riddle to be the cause of lactation, but only when the mammary gland is previously subjected to the action of the oestrogenic hormones.

4. The thyrotropic hormones on which the activity of the thyroid is dependent.

5. The fat metabolism hormone.

6. The blood sugar raising hormone.

7. The adrenotropic hormone.

Of all these, only the first two would seem, in the present state of knowledge, to merit any discussion from the standpoint of organotherapy. The lactogenic hormone (prolactin) may perhaps prove of clinical value as a galactagogue, but only one brief report, based on a very small series of cases, has so far been made on this subject. Encouraging results are said to have been obtained.

CLINICAL CONDITIONS INVOLVING GROWTH HORMONE

Growth abnormalities.—The best known of these, gigantism and acromegaly, are due to excessive production of the growth hormone, most often by adenomas of the acidophilic cells. Here the problem is not one of organotherapy but of correcting the endocrine excess by means of surgery or irradiation.

As types of deficiency of the growth hormone may be mentioned the growth deficiencies characterizing the various types of pituitary dwarfism and infantilism, especially the so-called Lorain-Levi and Brissaud types. While these are believed most often to be due to adenomas of the chromophobe cells, the obvious growth deficiency would seem to justify the use of preparations containing the growth hormone. Simmonds' disease (cachexia hypophyseopriva), a rare disorder due to destructive disease of the entire anterior lobe, and characterized by emaciation, a prematurely senile appearance, amenorrhœa and other symptoms, has in a few cases been treated by anterior pituitary preparations, either orally or hypodermically, but the results have not been striking.

Preparations available.—No commercial preparation of the growth hormone has as yet been recognized by the Council on Pharmacy and Chemistry of the American Medical Association, which is not surprising in view of the present inability of manufacturers to prepare it in pure forms, and the meagreness and unconvincingness of clinical reports. In this country only three commercial preparations, so far as I know, are available; *viz*, the 'Antuitrin G' of Parke, Davis & Co., the 'Phyone' of the Wilson Laboratories and Anterior Pituitary Extract Squibb. These extracts all contain other active principles of the anterior pituitary in addition to the growth-promoting factor. The more purified form of the growth hormone with which Evans has achieved such striking results in animals is not yet available commercially, although the manufacturers to whom it has been entrusted have been able to furnish small amounts for a few clinical and experimental studies. Engelbach in 1930 reported satisfactory growth results in a pituitary dwarf of 9 years in whom treatment with the Evans' purified growth hormone was carried out, with daily injections of the substance, for nine and a half years, 2.7 inches (7 cm.) in height being gained during this period. Engelbach and Schaefer have recently reported encouraging results in seven cases of dwarfism. In these the growth hormone preparation (antuitrin G) was combined with thyroid, which Smith has shown to increase the effect on skeletal growth. Both Evans and Reichert emphasize the importance of having such growth hormone extracts free of gonadotropic principles, which might result in excitation of sex maturity, with epiphyseal closure and the cessation of growth.

There are a few clinical reports by Cushing and others of the use of preparations of the growth hormone in cases of pituitary growth deficiency, but, on the whole, the results have not been impressive. The chief hope for the future seems to lie in the preparation

of the growth hormone in a purified form. If this is accomplished, there would be reason to expect far better results than those obtainable with the admittedly uncertain preparations now available. The recommended dosage of antuitrin G is 1 to 3 c.c. two or three times a week.

CLINICAL CONDITIONS INVOLVING GONADOTROPIC HORMONES

An enormous impetus to anterior pituitary organotherapy was given by the discovery in 1926, by Smith and Engle in this country and Zondek and Aschheim in Germany, of the remarkable effects produced on the gonads of experimental animals by anterior pituitary implantations. Because of the impracticability of implants for clinical use, and also because of the difficulty of preparing satisfactory extracts for clinical purposes, this discovery in itself would not have had much therapeutic significance had it not been for the further discovery by Zondek that the urine of pregnant women, even in the earliest phases of gestation, contains large quantities of 'prolan', a substance believed by Zondek to be identical with the gonad-stimulating hormones produced by the anterior lobe. It is on the presence of this factor in early stages of pregnancy that the now universally employed pregnancy tests (Aschheim-Zondek, Friedman, Schneider, Brouha, and the like) are based, the principle producing in the sex glands of the injected animal changes that in most respects are similar to those produced by the pituitary hormones from the gland itself. As to the actual identity of the latter and the urinary factors, there has arisen much discussion, although this has no bearing on the reliability of the pregnancy test.

Likewise there has been much discussion as to the unity or the duality of the pituitary gonad-stimulating principle. Zondek early differentiated two principles, one ('prolan A') having a follicle ripening effect and having to do with the production of oestrogenic substance, while the other ('prolan B') is responsible for luteinization and the production of the corpus luteum factor, 'progesterin'. There are many excellent investigators, however, who look on these two different effects as merely different phases in the activity of a single principle. This question, as well as that of the identity or lack of identity of the urinary and the pituitary gonad-stimulating hormones, has been discussed in a previous article and need not be elaborated on here.

The practical point is that anterior pituitary-like extracts made from the urine of pregnant women have been made available commercially and have achieved wide clinical vogue in disorders in which there is a supposed deficiency of the anterior pituitary gonadotropic hormones.

Preparations available.—The chief American preparations of this type are the following: 'Antuitrin S' (Parke, Davis & Co.) prepared from the urine of pregnant women by a modification of the Zondek-Aschheim technic. It is put up in 10 c.c. rubber diaphragm-capped vials, each cubic centimetre containing 100 rat units. The rat unit is described as the minimum quantity of hormone that will cause the formation of one or more corpora lutea within 96 to 100 hours when injected subcutaneously in six doses, twice daily for three days, into female white rats 30 days of age and taken from a colony the members of which become sexually mature normally in from fifty to sixty days. 'Follutein' (Squibb) is described as a 'sterile glycerine solution of the anterior pituitary-like gonadotropic hormone found in pregnancy urine'. It is prepared from the latter by a technic essentially that described by Zondek and Aschheim. 'It is then dissolved in glycerine physiologically assayed, berkefelded and filled into 1 c.c. syringe containers. Each cubic centimetre contains 1,250 rat units. Before administration the content of the syringe is added to 9 c.c. of sterilized water, thus making 10 c.c., each cubic centimetre having a potency of 125 rat units'. The rat unit is described as 'the minimum amount which, given in six injections on three consecutive days, produces

mature follicles, hæmorrhagic follicles and corpora lutea in the ovary within 100 hours after the first injection in 30-day-old female rats'.

It is quite possible that if the actual pituitary hormones, as obtained from the anterior lobe itself, are made available, they may prove to be much more effectual than the anterior pituitary-like principles of pregnancy urine now supplied commercially, for there seems to be much difference of opinion among investigators as to the exact source and nature of these principles, while their effect on the human ovary is certainly not what would be expected from the pituitary hormones themselves. One or two firms are now, I understand, engaged in efforts to produce the gonadotropic hormones from the gland itself, but there has as yet been no opportunity for worth while clinical investigation with them.

Functional menorrhagia.—In this very frequent and very troublesome disorder, encountered at any age during the reproductive epoch, not infrequently during puberty or adolescence, and most often at or near the menopausal phase, clinical evidence indicates the definite value of therapy with anterior pituitary-like principle from the urine of pregnant women. This plan, suggested by Novak and Hurd in 1931, was based on the fact that corpora lutea and progesterin are lacking in this disorder and that there is presumably a lack of the luteinizing principle of the anterior lobe.

It was thought that the injection of a luteinizing principle obtainable from the urine of pregnant women would supply this deficiency. Since such a substance produces marked luteinization of the ovaries of mice and rats, it was even at first thought that the human follicle could be luteinized and progesterin thus be produced, with a completion of the cycle and cessation of the bleeding. Opportunities to study the ovaries of patients who had received this substance have shown that the response is not at all similar to that of experimental animals and that luteinization is not produced. And yet the abnormal bleeding, in a large proportion of cases, is controlled. What the mechanism is one can only speculate, though it is obviously in some way dependent on the reciprocal functions of the anterior lobe and the ovaries.

The chief indication for such therapy is found in the cases of functional bleeding in younger women, in whom any form of radiotherapy is undesirable. In women approaching the menopause, once the diagnosis is established, radiotherapy is the method of choice, yielding success in practically 100 per cent of cases. In younger women and children, on the other hand, the frequent and often alarming recurrences of functional bleeding must be treated either by curettage, often repeatedly, or by organotherapy. Transfusion is not infrequently necessary.

No method of organotherapy yields as large a proportion of successes as follows the employment of the hypophyseal-like preparations, though there are many failures. Why the treatment is so strikingly successful in some cases and so unsatisfactory in others one cannot say, but certainly a proportion of the failures must be due to the uncertainties of the preparations used, for they are notoriously prone to deterioration, even with refrigeration. For this reason some clinics prefer to prepare their own material freshly from the urine of pregnant women, while some have utilized the serum of such women. Even the rectal infusion of the urine of pregnant women has been resorted to with apparent success.

When the commercial preparations are employed, as is commonly the case, a good plan is to withhold them until the onset of the bleeding, or, if it is not too free, until it can be determined whether it is actually to be abnormally long or profuse. Daily intramuscular injections are then begun, in doses of from 100 to 200 units, depending on the severity of the bleeding. In a few cases the hæmostatic effect is remarkably prompt, bleeding being checked within a matter of hours. In others the injections may have to be given for four or five days, and the bleeding may be only markedly lessened

instead of being checked entirely. In still others, as already stated, there may be little or no effect on the bleeding, so that other measures may be necessary. There is no objection to the plan of beginning the injections several days before the expected bleeding, although irregularity is so common in these cases that the patient cannot usually be sure of the date of onset.

Endocrinopathic amenorrhœa.—The anterior pituitary-like preparations (antuitrin S or follutein) are apparently of little or no value in the treatment of endocrinopathic amenorrhœa, although, when combined with oestrogenic substances (given either together or in sequence, the gonadotropic factor being administered last), they sometimes produce uterine bleeding. This method of ovarian therapy is usually combined with the administration of thyroid extract.

Adiposogenital dystrophy (Frölich's syndrome).—This extremely common clinical picture with its adiposity of characteristic distribution (heavy girdle about the abdomen, hips and buttocks, large busts, shoulder pads) together with amenorrhœa or scanty menstruation, undoubtedly has its chief source in a functional disturbance of the anterior lobe. Whether this may be a purely functional disorder or whether there is always present a chromophobic adenoma is a question that cannot be answered at the present time. Certainly there are many adenomas which, because of their small size and their position, cannot be demonstrated by any clinical or laboratory procedure at present. It seems certain, too, not only that in most cases of adiposogenital dystrophy, the gonadotropic hormones and the fat metabolism hormones of the anterior lobe are concerned but that the metabolic disturbance involves also, and perhaps chiefly, the immediately adjoining hypothalamic regions of the brain. This is indicated by the investigations of Smith and others.

The organotherapy of this condition is very unsatisfactory. The common plan utilizes various combinations of pituitary preparations, thyroid extracts, and ovarian preparations. The oral administration of pituitary preparations is looked on by most clinicians, and practically all laboratory investigators, as having no value. Other clinicians, however, employ these preparations quite extensively. Some, again, believe that while of no value in the usually advised dosage of 5 or 10 grains (0.32 or 0.65 gm.) a day, they are effective in extremely large doses [from 60 to 100 grains (4 to 6.5 gm.) daily]. As the preparations are expensive, and as their use must be kept up for periods of many months and even years, this method would be prohibitive to most patients.

Thyroid therapy is probably of much greater value and may be used even when the basal metabolism is normal or only slightly subnormal, as is the usual rule. Comparatively small doses, for example $1\frac{1}{2}$ or 2 grains (0.09 or 0.13 gm.) of desiccated thyroid daily, will usually suffice. When there is any noteworthy loss of weight from combined pituitary and thyroid therapy, it seems likely that it is the latter which is chiefly responsible.

As for the use of the anterior pituitary-like and the ovarian hormones in an effort to correct the amenorrhœa and the genital hypoplasia, the indications and the results are not different from those pertaining to the treatment of endocrinopathic amenorrhœa in general.

Undescended testicle.—An interesting clinical application of laboratory investigations is seen in the recent employment of the gonad-stimulating preparations from the urine of pregnant women in the treatment of undescended testes. A scientific basis for this has been furnished by the observation by Engle, in 1932, that the injection of these substances in immature monkeys brought about a descent of the testes, although this form of therapy had been employed before this (Shapiro, 1930). Goldman and Stern have reported two cases of undescended testis, in which the use of injections of antuitrin S (100 units three times a week) was followed in a short time by descent of the gonads.

In a series of six boys suffering with the same condition, Sexton obtained successful results in four. A very recent paper by Cohn reports that similar treatment (with antuitrin S) was successful in five of six cases. In some of these, the descent of the testis seems to have occurred with amazing rapidity. For example, in a boy of 11 the undescended right gonad, previously palpable at about the middle of the inguinal canal, 'descended six hours after the injection of anterior pituitary-like substance and remained well down after four months'. Finally, reference may be made to the very recent study by Aberle and Jenkins of the effects of this form of organotherapy in both human beings and monkeys. In two of four boys receiving the treatment the testes descended, but in only one was the descent complete. In immature monkeys complete descent occurred in one animal and only partial descent in four, although Engle had obtained complete descent in eight of ten monkeys.

In view of the frequent failure of surgery to correct this condition, the endocrine treatment, as outlined, would seem to be indicated in cases of undescended testis before operation is resorted to, although a far larger experience with the method is necessary before one can draw conclusions as to its degree of dependability. The recent report by Geschickter, Lewis and Hartman that the anterior pituitary-like gonadotropic factor produced hypertrophy of the prostate in a monkey to a degree that urethral obstruction resulted, indicates the necessity for caution in the clinical use of this principle.

Other indications.—Habitual abortion, which often presents a baffling problem, has not infrequently been treated with the anterior pituitary-like factor, in the form of ether antuitrin S or follutein. The cause of this condition cannot in many cases be determined, and it is believed that some at least are due to a deficiency of the corpus luteum secretion so important for implantation and for the maintenance of fixation of the ovum in the early stages of pregnancy. Since no active preparation of the corpus luteum hormone (progesterin) is available, it is not surprising that the pregnancy urine preparations have been employed as the next most rational means of treating this condition. Failures are common, though they are not usually reported. On the other hand, some successes have been reported, and the treatment seems a justifiable one to employ, but more needs to be known of the underlying cause or causes of this condition.

Primary dysmenorrhœa, another *bête noire* of gynecologists, is a disorder of protein ætiology. Many causes have been advanced and the methods of treatment suggested have been legion. The psychogenic factor is unquestionably the important one in many cases, the constitutional one in others, while in still others it seems probable that an endocrine imbalance may be concerned. No gynecologic disorder, therefore, makes greater demands on the knowledge, thoroughness and common sense of the gynecologist. A summary of the plan of treatment is given elsewhere.

The physiologic investigations of Reynolds and many others indicate that, just as oestrogenic substance is the natural stimulant of the normal rhythmic uterine contractility, so progesterin and the anterior pituitary-like principle contained in pregnancy urine are inhibitors of this contractility. This fact, together with the fact that the immediate factor in the pain of primary dysmenorrhœa seems to be a spasmodic contraction of the uterine musculature, has led to the suggestion that a part of the treatment in some cases—but only a part—should consist of the administration of antuitrin S or follutein beginning several days before the onset of the painful periods.

The dose suggested is from 100 to 200 units each day until the first or second day of the flow, after which most patients ordinarily suffer little pain with or without treatment. Because of the ever-present psychic factor which must be considered in the evaluation of results in such a subjective disorder, it is difficult to appraise the effect of this addition to the therapeutic

armamentarium. At times the results seem brilliant, in other cases only improvement without disappearance of the pain is reported by the patient, and in still others the results are disappointing. However, in the treatment of a disorder in which there is so much therapeutic floundering as in that of primary dysmenorrhœa, the plan suggested is worthy of trial, especially as it is far more rational than most others which have been suggested. It should again be emphasized, however, that in all cases of this group there should be a comprehensive survey of the constitutional, pelvic, psychic and even sociologic status of the patient.

In 1933 Brosius and Schaefer reported a case of complete aspermia in which the intramuscular injection of antuitrin S (2 c.c. twice a week) was followed by spermatogenesis, so that at the end of nine weeks numerous motile spermatozoa were found in the semen, while the testes showed a definite increase in size. Needless to say, this observation, interesting as it is, needs confirmation through trial in a large number of cases. In two recent cases of sterility in my practice in which the responsible factor was the husband's aspermia, the method suggested here failed to produce spermatogenesis.

In 1931 Bengtson reported striking results in sixteen cases of alopecia treated by anterior pituitary substance. He recommended the hypodermic use of a pituitary gland preparation as preferable to the oral route, although the combination of the two methods gave the most rapid response. While he considered that all these cases belong to the category of glandular alopecias, he suggested that possibly other common types of baldness might also respond to the treatment. In spite of the author's own conservatism in this regard, the paper was taken up rather sensationally by the daily press. There has been no confirmation of his observations, and Lord and others have reported unsuccessful results from the method. There seems to be no reason to expect benefit from it except perhaps in cases of genuine hypopituitarism in which the alopecia is a part of the general picture. Even here the usual limitations and uncertainties of pituitary therapy would prevail.

SUMMARY

The employment of the growth hormone preparations is indicated in the various types of pituitary growth deficiency. The results are usually not striking and will probably not be improved until biochemists isolate the hormone and produce more potent preparations.

The anterior pituitary-like preparations are probably of no value when used alone in the treatment of amenorrhœa, and even when combined with œstrogenic substance the results are very little improved.

The anterior pituitary-like preparations made from pregnancy urine have appeared to give excellent results in many, though not by any means all, cases of functional uterine bleeding, so that, when this disorder is encountered in young women, in whom radiotherapy is undesirable, the method should certainly be tried.

The comparatively small group of cases thus far reported in which undescended testis has been successfully treated by the anterior pituitary-like preparations make this method seem promising and worthy of more extended trial, especially as the surgical treatment of this condition is not as satisfactory as might be wished.

There is no objection to a trial of the anterior pituitary-like preparations in the occasional mysterious and baffling cases of habitual abortion, although the results are not much more clearly defined than is the ætiology of the condition.

These preparations appear rational as adjuvants in the treatment of primary dysmenorrhœa, although correction of constitutional and psychic factors is often much more important, and should never be overlooked.

As to other conditions, such as aspermia and baldness, the clinical data thus far available are much too meagre to draw conclusions as to the results of treatment with the anterior pituitary-like preparations, and

there are physiologic reasons to make one question the value of this plan.

It is possible that the results of organotherapy in various forms of anterior hypopituitarism may be improved with preparations of the gonad-stimulating hormones obtained from the anterior lobe itself.

The Treatment of Whooping-Cough

By W. T. BENSON, M.D., F.R.C.P. (Ed.), D.P.H.

(From the *British Medical Journal*, Vol. I, 30th March, 1935, p. 657)

WHEN an infant or young child who has not previously suffered from whooping-cough develops a persistent, troublesome cough with scanty clinical signs of bronchitis, and if within two or three days the cough, which is worse at night, tends to occur in paroxysms giving rise to suffusion or blueness of the face and occasionally terminates by a vomit, suspect infection with *H. pertussis*. If in such a case there is a history of recent intimate contact with whooping-cough then the clinical diagnosis can be made with some confidence during the catarrhal stage. Failing a history of exposure to infection the diagnosis may be aided by examination of the blood picture or confirmed by the isolation of the Bordet-Gengou bacillus.

The presence of a leucocytosis (commonly 15,000 to 25,000 white cells per c.mm.) with a well-marked relative lymphocytosis (from 50 to 70 per cent of lymphocytes) is highly suggestive of whooping-cough. For bacteriological diagnosis two Petri dishes containing a special culture medium for *H. pertussis* will have to be obtained from a laboratory. Instruct the parent or nurse to expose the surface of this medium five inches in front of the patient's mouth for fifteen seconds during a natural paroxysm of coughing. Expose the second dish in a similar manner. Should the patient's cough be mainly short, sharp, and occasional, then expose each dish on four occasions. Return the dishes to the laboratory as soon as possible. Should examination of the cough plate after seventy-two hours' incubation show colonies of *H. pertussis* then a diagnosis of whooping-cough may be confidently made. The causal organism can apparently be isolated from approximately 75 per cent of cases during the catarrhal stage of the disease. It is to be noted that a negative report does not exclude the possibility of whooping-cough.

It must be remembered that in infants and in adults the typical whoop may not appear throughout the whole course of the illness; bacteriological aid would simplify the diagnosis of such cases.

GENERAL TREATMENT

Most clinicians with an extensive experience of whooping-cough are of the opinion that when the primary essentials of medical care have been arranged for the patient we have practically exhausted our effective therapeutic armament. Vaccines, drugs, and ray therapy may be regarded as adjuvants to be given a trial when special indications arise.

When whooping-cough is suspected the patient should be confined to bed and strictly isolated from other members of the family who have not already suffered from the disease. Isolation should be enforced for a period of five weeks dating from the onset of symptoms. The bedroom, with a sunny exposure for choice, should be kept freely ventilated, but at an equable temperature around 60° to 65°F. If the weather is warm and sunny the bed may be placed at the widely open window during the day; otherwise the patient should be screened from draughts. The bedclothes should be light yet warm, and the child clothed in a flannel nightgown. A flannel binder firmly applied round the abdomen is of supportive value during the strain of coughing. Some trustworthy individual should be constantly in attendance to support and to comfort the child during the paroxysms of coughing and to have a receptacle ready for the vomit.

Providing the attack is afebrile, uncomplicated, and not unduly severe, the child may be allowed out of bed about the third day of the whoop. When the paroxysms exceed thirty in the twenty-four hours, or when there is a previous history of chest trouble, confinement to bed until convalescence is well established is advisable. If the weather is equable and sunny the patient should spend most of his time in the open air—precautions being taken to avoid contact with susceptible children. The clothing should be warm but not excessive, and mild exercise should be encouraged. The bowels should be regulated by occasional doses of syrup of figs or liquorice powder.

IMPORTANCE OF DIET

The dietetic management of a case of whooping-cough is of the utmost importance. In severe attacks, particularly if improperly handled, the persistent vomiting results in a serious degree of malnutrition. The secret of feeding is to give small amounts at frequent intervals. Large meals should be avoided, and food administered preferably about ten minutes after a paroxysm. For babies 'feeding by the clock' may have to be adjusted to the necessities of the case. If vomiting and loss of weight continue then the interval between feeds should be decreased and the bulk of each feed lessened. Various modifications of the diet may be necessary. The milk may be diluted, boiled and citrated, or peptonized; whey and albumen water may have to be temporarily resorted to. In the worst cases mouth feeding may require to be supplemented by rectal or intravenous saline to which 5 to 10 per cent of glucose has been added. Lavage of the stomach twice daily with 0.6 per cent solution of sodium bicarbonate is a useful measure when vomiting is frequent and persistent.

With older children large meals must be avoided, but no material alteration in diet is necessary. Milk, eggs, butter, fish, chicken, meat, and vegetable soups are better than an excess of potato, bread, milk puddings, jams, and similar starchy or saccharine foods. Biscuits, rusks, oatcakes, or other dry crumbly foods should be avoided. Fresh orange juice drinks sweetened with 5 to 10 per cent of glucose may be freely administered. A prolonged convalescence, with if possible a change of air, is advisable.

VACCINE AND SERUM THERAPY

Very conflicting reports have been published regarding the value of vaccine treatment. It is generally agreed that no improvement can be expected to follow vaccine therapy unless the initial injections have been given during the catarrhal stage of the disease. A vaccine containing *H. pertussis* alone, or preferably a mixed vaccine containing in addition *H. influenza* and the pneumococcus, may be employed. Six subcutaneous injections rising from 100 million to 1,000 million Bordet-Gengou bacilli should be administered on alternate days. This method of treatment has been given a prolonged trial in the wards of the Edinburgh City Hospital, but the results have proved disappointing.

Human convalescent whooping-cough serum or whole blood injected intramuscularly on one or more successive days in doses of 10 to 20 c.cm. has been reported favourably by various French physicians. If circumstances permit this specific method of treatment might be tried in severe attacks in infants.

DRUGS

In spite of the numerous drugs that have been recommended for the treatment of whooping-cough the writer, after an extensive experience of many preparations—including belladonna, antipyrine, bromoform, benzyl benzoate, ether, adrenaline, and ephedrine—is of the opinion that none can be looked upon as a specific.

In a mild attack there is no need for medication. If desired a simple expectorant mixture may be administered thrice daily:

- R. Tinct. camph. co. ℥ij.
- Vin. ipecac. ℥iij.
- Syrup. scilla ℥x.
- Aq. q.s.

When the paroxysms are frequent and severe, resulting in considerable exhaustion and loss of sleep, a sedative or antispasmodic drug should be prescribed. One or other of the following sedatives may be prescribed four-hourly: syrup of codeine phosphate, 10 minims; Dover's powder, 1/2 grain; or chloral hydrate 2 grains, with potassium bromide 2 grains. If necessary the dose may be cautiously increased until either improvement ensues or the child becomes drowsy. Phenobarbital (luminal) in doses of 1/6 grain to 1/4 grain three times daily occasionally results in a rapid amelioration of symptoms; because of its toxicity this drug should be employed with discretion. Belladonna is probably the most popular drug in the treatment of whooping-cough: in the dosage commonly prescribed it is quite ineffective. In an endeavour to control the paroxysms belladonna must be pushed to the physiological limit. Commence with three drops of the tincture three times daily; then, providing no idiosyncrasy is present, promptly change to four-hourly administration, followed by a daily increase of one drop per dose until dilatation of the pupils, flushing of the cheeks, and dryness of the mouth indicate that the limit of safety has been reached. During convalescence the patient should take cod-liver oil and malt with some preparation of iron; the syrup of the iodide of iron is excellent.

ULTRA-VIOLET RAY AND X-RAY TREATMENT

Whilst of value as a general tonic during convalescence, particularly in the winter months, ultra-violet light therapy has no specific effect on the paroxysmal stage of the disease. In the absence of pulmonary complications a daily general exposure of one minute to both back and front at a distance of thirty-six inches may be tried. The exposure may be increased by half a minute daily, care being taken to avoid pigmentation. Although some American physicians have obtained beneficial results from x-ray treatment in 75 to 80 per cent of cases, due apparently to a reduction in size of the bronchial lymph glands, other investigators have not been so successful.

COMPLICATIONS

The most important complications of whooping-cough are bronchopneumonia, convulsions, and gastro-enteritis. These complications are most apt to occur in young children, in whom they are a frequent cause of death. Bronchopneumonia usually develops at the height of the paroxysmal stage, and seems to predispose to convulsions. Gastro-enteritis is manifested by frequent vomiting and profuse diarrhoea in the intervals between the paroxysms. Subconjunctival hæmorrhage, epistaxis, and bleeding from the mouth occasionally are seen but are not of serious import. Otitis media is not uncommon. Meningo-encephalitis and various forms of paralysis are interesting but very rare complications.

PROPHYLACTIC MEASURES

Whooping-cough is most highly infectious during the catarrhal or pre-paroxysmal stage. To control the spread of infection the patient must be isolated early in the catarrhal stage of the illness, and herein lies the importance of early diagnosis. Every precaution should be taken to prevent young children, in particular, from being needlessly exposed to infection with *H. pertussis*. Practically all the deaths from whooping-cough occur during the first three years of life.

Prophylactic vaccination is of value not so much in preventing the development of the disease as in modifying the severity of the subsequent attack. Five subcutaneous injections of 1,000, 2,000, 4,000, 8,000, and 8,000 million Bordet-Gengou bacilli should be given on

alternate days to contacts who have not previously suffered from whooping-cough. The injection of serum or of whole blood of a whooping-cough convalescent or of those who have had whooping-cough at some time in their life has been reported as resulting in complete or partial protection in a large proportion of cases.

For children under 3 years of age 5 c.cm. of serum or 20 c.cm. of whole blood should be injected intramuscularly.

In spite of the multiplicity of remedies recommended in the treatment of whooping-cough an effective therapeutic agent has yet to be found.

Reviews

GYNÆCOLOGY.—By Brooke M. Anspach, M.D. Fifth Edition. 1934. J. B. Lippincott Company, Philadelphia and London. Pp. xii plus 832, with 679 illustrations of which 10 are in colour. Obtainable from Messrs. Butterworth and Company (India), Limited, Calcutta. Price, Rs. 31-8

THE fifth edition of Anspach's *Gynæcology* is a worthy successor of the previous issues. The first edition appeared only twelve years ago; this is a testimony of the popularity of the work. The chapters on physiology, disturbance of function and treatment by radiation are largely new. The views therein are reliable and up to date. The chapters on diseases of the external genitalia, endometriosis, ovarian tumours, amenorrhœa, uterine bleeding, sterility and dysmenorrhœa have been re-written and modernized.

We think that a great improvement would be effected in future editions if operative gynæcology were dealt with in a separate part of the volume and in a more detailed manner. The performance of a total hysterectomy by the abdominal route—Wertheim's hysterectomy is not being criticized—is described only in a few lines in the present edition. The operation of implantation of the ureters into the rectum is not described at all in the text but appears in two illustrations. We are compelled to point out that it is not in accordance with modern pathology to carry out the removal of any ovarian tumour by 'evacuation of the contents of the largest cyst by means of a trocar, delivery of the collapsed cyst through the incision and ligation of the pedicle'. We do not concur in the recommendation of Watkin's interposition operation and are in complete agreement with the views of another eminent American gynæcologist—Graves—on its numerous disadvantages.

Apart from operative gynæcology, the work is concise, modern and one of well-balanced views. There are one or two statements, however, which we consider unusual; e.g., that non-operative treatment of retroversion is to be preferred during the child-bearing age; that the introduction of a pessary after pregnancy has started in a retroverted uterus is likely to cause abortion. These, however, are minor details and do not detract from the general excellence of the non-operative part of the volume which we can recommend to all interested in the subject. The printing is very good and the illustrations clear and copious.

S. A. McS.

SYNOPSIS OF OBSTETRICS AND GYNÆCOLOGY.—By A. W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.). Sixth Edition, fully revised. 1935. John Wright and Sons Limited, Bristol. Pp. vii plus 444. Illustrated with numerous diagrams. Price, 15s.

THE recently published synopsis presents the facts concerning obstetrics and gynæcology in the concentrated space of 450 pages. The first half deals with obstetrics, the second with gynæcology.

Both sections have been completely revised and new additions are the sections on obstetric shock and sex hormones.

The author has based his work on well-known textbooks and has enunciated current views with a clarity that is remarkable in a book of this size. A large number of small-sized diagrams are a valuable addition

to a work that has definite value firstly to students preparing for examinations and secondly to practitioners as a means for ready reference.

The author has always wisely insisted that his book must not be regarded as a textbook and students would do well to follow his instructions.

The type though clear is small, and one looks forward to the time when synopses in general are printed in type that will reduce ocular stress to a minimum.

S. N. H.

HYGIENE FOR NURSES.—By J. Guy, M.D., D.P.H. (Camb.), F.R.F.P. & S. (Glas.), F.R.C.P. (Edin.), and G. J. I. Linklater, O.B.E., M.D., D.P.H., D.T.M. & H., M.R.C.P. (Edin.). Third Edition. 1935. E. and S. Livingstone, Edinburgh. Pp. xi plus 212. Illustrated. Obtainable from Messrs. Butterworth and Company (India), Limited, Calcutta. Price, Rs. 3-12

IT is a testimony alike to the usefulness of the book and to the increasing contacts between curative and preventive nursing that a third edition of *Hygiene for Nurses* by Guy and Linklater has been called for less than two years after the publication of the second edition.

The arrangement of the book into personal, communal and social hygiene on the one hand and environmental hygiene on the other is unchanged and the emphasis remains on the former. One or two useful additions on the hygiene of menstruation and the menopause have been made and the chapter on heating has been largely re-written.

The book offers the nurse an excellent introduction to the wider aspects of her duties. Her immediate responsibility is the restoration of her patient to health but if the restored health is to be maintained a new way of life and improved physical surroundings may be necessary, and in teaching this the nurse's responsibilities are heavy and her opportunities many. She will find much help in *Hygiene for Nurses*. A little more space devoted to mental hygiene would perhaps add to the value of an already useful book. The recommendation given to the second edition may be safely repeated for the third.

J. M. O.

MEDICAL CASE-TAKING AND DIAGNOSIS.—By A. J. Kohiyar, B.A. (Bom.), M.D. (Lond.), M.R.C.P. (Lond.). 1935. The Medical Bulletin, Empire Automobile Building, Queen's Road, Bombay. Pp. 133. Price, Rs. 3

THE contents of this book appeared as a series of articles in *The Medical Bulletin*. They are now published in book form, primarily for teaching students on their first joining the hospital. It includes in small compass the kind of information which may be helpful, as a supplement to larger books. A beginner will find it useful in helping him to follow his tutor in clinical medicine. The book consists of fourteen small chapters of which six are devoted to the nervous system (pages 79 to 114). The arrangement is not very satisfactory. On page 3 the author suddenly describes Kernig's sign and Brudzinski's signs while interrogating a patient under 'history and general inspection'. The 'lymphatic system' and 'joints' have been included in the chapter (XIII) on 'urinary system'. Chapter VI