preparations are available, when a true substitutive therapy can be carried out, the most hopeful preparation seems to be the serum gonadotropic hormone alone or combined with the urinary gonadotropic hormone.

No differentiation has been made between primary and secondary amenorrhoea, as it has been found that when congenital defects are excluded the findings are comparable in both types, and therefore the treatment is similar. The prognosis is just as favourable in primary as in secondary amenorrhoea.

Summary

1. The investigation required in a case of amenorrhoea is detailed, and some consideration is given to the value of each procedure.

2. The primary and secondary factors responsible for the inhibition of menstruation are discussed.

3. The results of treatment based on the investigation findings are presented.

My thanks are, first of all, due to the members of the honorary gynaecological staff of the Royal Infirmary, Edinburgh, for permission to investigate and treat cases under their care. I also most cordially thank Dr. A. N. Macbeth of Organon Laboratories, Dr. H. Neumann of Schering Ltd., Dr. T. A. Lloyd Davies of Boots Pure Drug Co., and Messrs. Paines and Byrne Ltd. for the generous way in which they have placed their preparations at my disposal. I also express my appreciation and thanks to Glaxo Laboratories for making available to me large amounts of anterior pituitary preparations.

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D. Whyte and R. O'Regan (*N. Zealand med. J.*, December, 1937, p. 381) refer to a previous paper published in February, 1937, in which they stated that the treatment of complete prolapse of the rectum by Gabriel's injection technique was "safe, painless, and effective." They now wish to qualify this statement, as a case has been seen in which the patient's life was in serious danger for some weeks from sloughing of the rectal wall and secondary haemorrhage, although the final result was satisfactory. The patient, a man of 55, was suffering from intractable prolapse of the rectum with continued mucous discharge. Seven submucous injections were given, each of 2 c.cm. of 5 per cent. carbolic acid in almond oil, and three perirectal injections of saline solution. Vomiting and headache persisted for a week, and on the eleventh day after operation a sudden copious haemorrhage from the rectum occurred. Examination under anaesthesia was carried out, and a large sloughing area was found on the posterior wall of the rectum extending into the pararectal tissues, the sacrum being palpable through a mass of blood clot. An acriflavine gauze pack was inserted, and was replaced two days later by a small flavine-vaseline pack. Nineteen days after the original operation a left inguinal colostomy was done. Six blood transfusions had been given during this period, and repacking had been carried out several times on account of bleeding. At the end of two and a half months proctoscopy showed the rectum to be healed and firmly fixed in the sacral hollow, and at the end of a further month the colostomy was closed and the patient made a good recovery.

RATE OF SEDIMENTATION OF RED BLOOD CELLS AS A CLINICAL TEST IN GENERAL PRACTICE

BY

E. SCOTT, B.A., D.M., B.Ch.

This investigation was undertaken two years ago to determine the value of the blood sedimentation rate (B.S.R.) as a test for the general practitioner. From my material I have chosen the experiments which are most likely to be of use. For the test to be practical it must conform to certain conditions. It must be quick, easy of application, and independent of elaborate apparatus. These conditions are satisfied. The blood can be collected and the tube filled in the time it would take to spread a blood film, and the reading, which takes place an hour later, can be jotted down by any educated person. The work has been done in three places—Ashford Hospital, my surgery, and the patient's home. As regards the last-mentioned, to avoid the dangers of transport with a filled tube it is a good plan to leave the tube to be read by the patient at the required time or marked with a strip of stamp paper. Attention to minute differences in end-results is undesirable and may be misleading. The B.S.R. is altered in a variety of pathological conditions that affect the body as a whole. It is thus, within limits, an indication of the existence of organic disease, particularly of an inflammatory nature, and a guide in the assessment of recovery. In theory it runs parallel to the temperature chart, but it covers a wider field, is slower to rise and decline, and can indicate infection in the absence of pyrexia. It affords a closer comparison with the Arneth count. It is the extent and scope of the test which constitute its strength and weakness and render its investigation difficult. The test has become a routine one in hospital practice in many parts of the Continent, particularly Germany, Scandinavia, and Switzerland. It is rapidly becoming popular in England, where it is used as a standard control in the treatment of tuberculosis and chronic rheumatism. Individual readings are not very instructive. I have, in consequence, endeavoured to gain information by choosing cases of known disease and compiling charts with B.S.R. readings as far as possible from inception to cure. In most cases these are correlated with temperature readings.

Technique

There is a somewhat wide choice of tubes, but I have found that Linzemeier's answers all requirements. This tube is marked at the level reached by 1 c.cm. of fluid, and is graduated in millimetres downwards to 24. The reading is particularly easy, and it is noteworthy that if these graduations are extended they divide the c.cm. into 48, so that figure 1 on Linzemeier's tube represents roughly a B.S.R. of 2 per cent. This affords a useful method of comparison with other apparatus. With a hypodermic syringe and needle a solution of 3.8 per cent. sodium citrate is drawn to the 0.2 c.cm. mark and blood is collected from a vein until the 1 c.cm. point is reached. The piston is then withdrawn slightly and the syringe contents are thoroughly mixed by repeated inversion. The citrated blood is injected into the sedimentation tube up to the top mark (1 c.cm.). The tube is placed vertically in a stand and the height of the supernatant clear fluid read off in an hour's time. These tubes are made by Hawksley and Sons, and I have obtained them from

Allen and Hanburys, who also supply the sodium citrate solution in convenient rubber-capped bottles. It is well to run sterile water (not alcohol) through the syringe and needle and to cleanse the tube with sterile water immediately before use. There is usually slight maladjustment to the 1 c.cm. mark owing to the presence of bubbles in the citrated blood, but the margin of error is seldom greater than 1, and is too small to be of clinical importance. The arbitrary limit where the B.S.R. becomes pathological has been suggested by Dr. T. C. Hunt to be at the 10 mark, and I have adopted this as a working criterion of the normal. It must be understood that B.S.R. = 10, like 98.4° F. on the temperature chart, represents a maximum and not an average or ideal.

to be more stable in the male. (Note the rise to 9 on March 18, which is analysed more fully in Chart B.) No. 2 is very unstable at the beginning: a period of malaise followed by the rise to 15 on June 25 culminated in a violent bilious attack—an unexpected occurrence with no apparent explanation. The rises to 9 on October 9 and to 10 on December 18 were the accompaniments of a severe head cold. No. 3 presents many difficulties. The B.S.R. was very high in the early stages. At this time the individual was greatly below weight (7 st. 7 lb.), but this began to go up in the autumn, reaching 8 st. 4 lb. in October and thereafter remaining steady. This was an index of a general improvement in health, which is probably reflected in the lower level and increased stability of

CHART A (1, 2, and 3)

The temperature to which the tube is exposed has been stated to exercise a disturbing factor on the end-result. A few simple experiments have convinced me that this factor can be disregarded in practice. The tubes should be stood in an ordinary room. So long as the direct rays of the sun or the immediate vicinity of a fire are avoided I do not anticipate any difficulty from variations in temperature. Anaemia can of course profoundly affect the result. It is sufficient to say here that small degrees involving a haemoglobin content of not less than 80 per cent. are not of material importance.

The B.S.R. in Normal Health and its Relation to Minor Disturbances

With this particular technique 10 has been generally adopted as the maximum B.S.R. reading in normal health. Making a series of tests in persons apparently in normal health, I found the average reading to be 4 in men and 6 in women. Most observers agree that the B.S.R. tends to be at a higher level in women than in men. Another interesting find is that if the B.S.R. of the same individual is taken at different times a variation of two, three, or even four in the reading is frequently encountered for no obvious cause and corresponding to no obvious deviation from health. In order to investigate this more thoroughly charts were instituted of three individuals—myself (Chart A, No. 1) and two nursing sisters (Chart A, Nos. 2 and 3). Readings were taken at weekly intervals throughout the year and omissions reduced to a minimum. Minor maladies not sufficient to incapacitate, such as colds, are indicated as far as possible.

If we attempt to analyse these three charts separately we note the comparative stability of No. 1: it is probable that, as in most clinical tests of this sort, the B.S.R. tends

to be more stable in the male. (Note the rise to 9 on March 18, which is analysed more fully in Chart B.) (Note the disturbance caused by a cold on December 18.)

The consideration of Charts A 1, 2, and 3 leads to the conclusion that each individual has an optimum B.S.R. and that moderate deviations indicate minor maladies. In the case of No. 1 the optimum is 3, that of No. 2 is 6,

CHART B

and that of No. 3 is 9. Consequently a B.S.R. of 9 in the case of No. 1 would indicate minor illness, whereas the same reading in the case of No. 3 would be compatible with complete well-being. The 10 mark is not in every instance a true maximum of the normal, but it affords a fairly accurate working criterion. Chart B is an analysis of my own B.S.R. during a severe influenza cold in March. Note the fairly rapid rise and the slow decline, the latter lagging after the clinical symptoms had cleared up.

The B.S.R. in Pregnancy

Fahraeus was the first to point out that the B.S.R. is constantly raised during pregnancy, the only physiological condition in which this phenomenon has been observed.

The change, however, does not take place until the later months, and the test is valueless in the diagnosis of pregnancy during the early stages. Chart C was that of a primipara, and began at the tenth week of gestation. For Chart D I am indebted to Dr. J. A. Moore Hall. The B.S.R. readings during pregnancy have been charted, and the matter is pursued to its conclusion where the B.S.R. returns to normal in the fourth week of the puerperium.

B.S.R. in Infections

In the role of the B.S.R. in acute and chronic infection lies its main claim to merit as a clinical guide. It can be discussed under three headings: (1) localized; (2) pulmonary; (3) general. The last two have been, and are still being, the subject of extensive investigations by many

discomfort the patient made a normal recovery. The B.S.R. was only 6 on the day following the onset of the illness, and on the fourth day reached 18, where it remained for a few days before starting to decline.

Case 2 (Chart F).—A healthy man, aged 49, was admitted to hospital for inguinal hernia. Operation was performed and progress was satisfactory until the seventh day, when severe pain was felt in the right side with rise of temperature, apparently from pulmonary congestion or a small infarct. Pain lasted for a few days after the temperature had fallen. Note the slow but steady fall of the sedimentation rate and the (presumably) steep rise. The B.S.R. apparently started at normal. It reached 18 on the third day after the onset of symptoms and its peak (28) on the fourth day, which was two days after the pyrexia had declined and the patient's symptoms had nearly cleared up. Subsequently its fall was uneventful.

CHART C.—Readings during pregnancy

CHART D.—Readings during pregnancy

CHART E (Case 1)

CHART F (Case 2)

CHART G (Case 3)

workers throughout the world, particularly as regards pulmonary tuberculosis in the one case and rheumatoid arthritis in the other. I accordingly devote myself to the phenomena observed in localized infection.

The characteristic of the B.S.R. curve in the case of an acute infection which ends in recovery is a comparatively steep rise and a slow gradual descent. Though the rise is steep it is slow compared with temperature or pulse-rate variations, which, in the case of fulminating disease, can show extreme disturbance within a few hours. The B.S.R. is unlikely to present much change in the first forty-eight hours, and is hardly likely to reach its peak before the fourth day—often an appreciable time after the maximum pyrexia. This is demonstrated in Charts E, F, and G.

Case 1 (Chart E).—In this case, that of a man aged 37, operation was performed for acute appendicitis on November 4, 1934, the second day of the illness, which had supervened on a subacute condition lasting three weeks. The appendix was full of pus. Drainage was not done. After a few days'

Case 3 (Chart G).—The patient, a man of 50, was pale, thin, and anxious. Appendicectomy for chronic abdominal pain was performed on October 25, 1934. Recovery was uneventful until October 29, when he complained of acute pain in the left side. The temperature rose steeply, and he developed the physical signs of pleurisy in the left base. Recovery took place and the temperature subsided by November 7, a few days after which he was allowed to get up. Radiographs taken on November 12 revealed a patch, indefinite in outline, at the left base, and a small quantity of pleural fluid. The next day the fluid had disappeared, but the patch was still distinctly visible in the film. The patient was discharged well on November 17. His B.S.R. was 12 on the first day of the pleurisy, when his pyrexia was at its peak at 102° F. The B.S.R. reached 24 three days later and remained there for four days, starting a steady decline four days after the main febrile disturbance had subsided.

This methodical use of the B.S.R. limits its value in the diagnosis of acute disease, and reserves its main field of usefulness for chronic infection. For instance, it is valueless as a guide in acute appendicitis, where operation

should be undertaken in the first twenty-four hours. Fortunately, in these and similar cases enough evidence should be provided by clinical examination.

I will now deal with the decline of the B.S.R. This is always comparatively slow and lags behind the symptoms. It appears to indicate not only the elimination of infection, but actually the completion of the process of repair. In this way it offers a highly reliable criterion of recovery. We may conveniently divide these descents under the headings "satisfactory," "interrupted," and "unsatisfactory." A satisfactory decline in the B.S.R. is simply one that is continuous. It may be either quick or slow, and it is likely that the time it takes is an assessment of the extent rather than the acuteness of the infection, and the amount of cleaning up that the damage to the tissues requires. Complicated and important systems of the body such as the biliary passages need an elaborate process of

mastoid drainage on April 20 and the final return of the B.S.R. to normal.

Case 4 (Chart H).—This patient, a man aged 37, had been in poor health for some weeks and had had his teeth extracted. A week before admission to hospital he sustained a scratch on the knuckle, and the hand and forearm began to swell and become red. When admitted on October 29 the swelling was extensive, with much tenderness and redness. The scratch on the knuckle had become septic, and there was severe lymphangitis. Treatment by fomentations brought about immediate improvement, and on November 4 the swelling had become localized proximally to the knuckle. On November 6 pus was squeezed from this through an exit in the scar. On November 7 there was no pain, swelling, or tenderness.

Case 5 (Chart J).—A man aged 59 was admitted with pain in the ear and pronounced mastoid tenderness for about four days. He looked ill; there was no pyrexia, but a slight dis-

CHART H (Case 4)

CHART J (Case 5)

CHART K (Case 6)

repair. Charts E, H, and J represent satisfactory descents with various rates of decline.

An interrupted decline in a B.S.R. chart affords evidence of the occurrence of a complication. Charts F and G are illustrative; Chart G deserves comment. The patient's appearance, the x-ray findings, and the symptoms suggested an activated tuberculous patch in the lung. The failure to find tubercle bacilli and, above all, the satisfactory decline of the B.S.R. negated this assumption. It is well known that the return of the B.S.R. to normal in active pulmonary tuberculosis is slow.

Charts which show an unsatisfactory decline are those in which the return of the B.S.R. to normal does not take place although the clinical symptoms disappear up to a point. They generally indicate the continuance of the original infection and call for active treatment. Chart K is one of these. Note the unsatisfactory fall of the B.S.R. after myringotomy on March 15, and compare with Chart J. Note also the steady decline following the

charge from the ear occurred one night. Myringotomy was performed. Clear fluid was seen for two or three days only, and the symptoms cleared up. At the time of operation the temperature was 97° F. and the sedimentation rate 21.

Case 6 (Chart K).—This patient, a woman aged 70, developed influenza with bronchitis one month before admission to hospital. Improvement was followed by relapse, with ear symptoms consisting of pain, deafness in the right ear, some mastoid tenderness, and slight pyrexia. The ear "grumbled" for two weeks. The patient was admitted to hospital on March 15, 1935, and myringotomy was performed. Drainage was established, but it was not very efficient. The symptoms slowly subsided and she then left hospital. On April 3 she was still very deaf, and there was some mastoid tenderness and slight discharge. In a few days the symptoms began to return, gradually getting worse. Neuralgic pains radiating from the right ear were felt, and there was mastoid tenderness and deafness, with discharge from the tympanum. Eventually it was decided to operate on the mastoid. The patient was readmitted on April 20, and a Schwartze operation was performed. The mastoid was

thoroughly cleared, pus being found. Convalescence was uneventful, and she was discharged on May 15 with the wound and the tympanum healed and hearing nearly restored to normal. Complete recovery ensued, and the patient had no complaints to make when last seen on September 25.

Summary

1. A simple method is described in which Linzemeier's tube is employed.

2. The figure 10 is selected as the usual maximum reading attained in health.

3. A chart method is employed. By taking weekly readings throughout the year it is shown (a) that the B.S.R. varies in health within moderately wide limits; (b) that each individual has an optimum reading; (c) that moderate deviations from this can usually be attributed to minor ailments.

4. During pregnancy the B.S.R. is undisturbed until about the fourth month, when a steady rise takes place till term.

5. General principles are deduced from the behaviour of the B.S.R. in local infection. The rise of the B.S.R. to an appreciable degree takes about three days. Its decline is comparatively slow, and is (a) continuous and satisfactory; (b) interrupted, due to complications; or (c) incomplete and unsatisfactory. Cases should be followed up until the B.S.R. returns to normal.

I owe my thanks to Dr. T. C. Hunt, who first aroused my interest in the subject, and to Professor J. R. Fraser for suggestions and criticism.

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ASCORBIC ACID IN BRONCHIAL ASTHMA

REPORT OF A THERAPEUTIC TRIAL ON TWENTY-FIVE CASES

BY

H. B. HUNT, M.D.

There is a certain amount of evidence that ascorbic acid may play a part in allergic conditions in general and asthma in particular which, although suggestive, is difficult to correlate exactly, and is perhaps best classified in three groups as follows:

Theoretical Considerations

1. Hypersensitivity to foreign proteins results after adrenalectomy in dogs (Simpson, 1937). In asthma a condition of protein hypersensitivity also exists, and hypoplasia of the adrenal glands has been noted in asthmatics coming to necropsy (Adam, 1931; Waldbott, 1933-4). An eosinophilia is not uncommon in either asthma or Addison's disease. At least one case has been recorded of the association of these two conditions (Wilkinson, 1937).

2. Adrenaline, the most potent anti-allergic remedy yet known, is a secretion of the adrenal medulla. The fact that cortical extracts have been employed in asthma without any marked success (Cohen and Rudolph, 1934-5; Wilmer and Miller, 1936) tends to show that if the suprarenal glands are affected in this condition, then the medulla rather than the cortex is involved.

3. Ascorbic acid is normally present in the adrenals. Indeed, it was from this source that Szent-Györgyi originally isolated vitamin C.

From these disjointed observations it appears probable that (1) asthma or allergy may be associated with adrenal hypofunction; (2) the medulla is chiefly at fault; (3) some especial relation exists between ascorbic acid and the adrenals. Dr. L. J. Harris has suggested (in a personal communication) that as, in the light of recent observations, one of the functions of ascorbic acid appears to be to prevent the oxidation of adrenaline, it may be possible, by giving suitable doses, to conserve sufficient adrenaline to prevent the occurrence of asthmatic symptoms.

Vitamin C in Anaphylaxis and Allergy

Claims have been made that ascorbic acid will protect guinea-pigs against anaphylaxis (Hochwald, 1935; Salomonica, 1936), and in human beings will diminish the cutaneous reactions to tuberculin, in positive reactors when given intravenously (Heise *et al.*, 1937). Hochwald (1936) has employed ascorbic acid in cases of bronchial asthma, and found it of some value in preventing symptoms when given regularly, or aborting symptoms when injected intravenously in massive doses (500 to 1,500 mg.). Epstein (1936), while unable to confirm the work of Hochwald when he used ascorbic acid in either asthma or hay fever, did find that it was distinctly valuable in the treatment of asthma if employed in conjunction with injections of gold salts.

Investigations

In view of what has been said above there is reason to expect that ascorbic acid may prove useful in the treatment of bronchial asthma. It is not suggested that asthma is a deficiency disease or even that the majority of asthmatics suffer from a subclinical C avitaminosis. Ascorbic acid was given to exert any anti-allergic properties which it may possess rather than to correct a specific deficiency. As all of the cases were out-patients it was not practicable to employ the usual laboratory procedure of estimating any possible avitaminosis. However, among the whole of the patients attending the asthma clinic of the Birmingham General Hospital during the last year I detected only one who showed any clinical signs of vitamin C deficiency. In this case the symptoms—bleeding of the gums and lassitude—were very mild, and cleared up after suitable treatment with ascorbic acid.

Clinical Material.—Twenty-five patients were investigated—sixteen females and nine males; five of them were children. Other allergic symptoms were present in seventeen cases, and chronic bronchitis in nine. Thus, although small, the series was fairly representative.

Dosage and Method of Administration

The ascorbic acid was dispensed in tablets of 50 mg. (the synthetic preparation of Roche Products Ltd., redoxon, was employed throughout), two of these being given for each day, one to be taken in the morning and one at night. Each patient received one or two weeks' supply of tablets when attending the clinic. The course was designed to last for eight consecutive weeks, but as attendances were not as regular as could be desired all the patients did not complete eight weeks' treatment, and, of those who did, not every one covered the course in eight consecutive weeks. During this treatment no medicine or injections such as vaccines were given, apart from antispasmodics—for example, ephedrine or "felsol" powders—or medicine for a troublesome cough. Five patients (quite apart from the group of twenty-five mentioned above) seen when symptoms were present were