left were found. An E.C.G. was of low voltage in Lead I, but otherwise the curves revealed no significant abnormality. Breathing exercises brought some benefit, but she relapsed in September, 1943. Rhinorrhoea and sneezing also developed. An E.N.T. report stated that she had the pale type of nasal mucosa often found in asthmatics. Nasal ephedrine drops considerably relieved her.

The patient was first seen by me in October, 1943, when she was 24. Her complaint was of severe asthma, and she had never menstruated. On examination she was pale and looked younger than her age. Her breasts were only slightly developed, being of the type generally seen in girls at the onset of puberty, and her external genitalia were infantile. There was no pubic hair and only slight axillary hair. Pelvic examination revealed an undeveloped cervix and a very small uterus.

The asthma continued unchanged in spite of all the usual palliatives, and in March, 1945, was severe enough to necessitate adrenaline injections. In September, 1945, stilboestrol, 0.5 mg. daily, was started, and by December, 1945, the patient was sufficiently improved to wish to start work. The daily stilboestrol was continued until December, 1947, when the dose was increased to 1 mg. daily. There was slight enlargement of her breasts.

In August, 1948, she was seen by Mr. Leonard Phillips, who advised a course of synapoidin. The size and spacing of the injections given is shown in the accompanying chart. The first 10 injections were followed by uterine haemorrhage lasting for eight days, the first menstrual period of the patient's life, at the age of 29.

By September, 1949, after eight courses of synapoidin and six periods, the cervix was definitely larger and softer and the uterus was a little larger. In April, 1950, the labia were quite normal and the uterus definitely larger. In October, 1950, the labia majora were fully developed and the labia minora were normal. The cervix was that of a normal adult, but the uterus was still small. The breasts were well developed, with prominent nipples and deeply pigmented areolae. A vaginal smear showed an adult type of keratinized epithelium. Treatment with synapoidin is continuing successfully.

The patient attended the London Chest Hospital for review in December, 1950, when she was able to report that she was much better than ever before, her breathing was easier, there was no cough or sputum, and instead of taking four or five $\frac{1}{2}$ -gr. (32-mg.) tablets of ephedrine daily she was now able to continue comfortably with two or three tablets a week.

Summary

A case of primary amenorrhoea with severe asthma is described. The use of endocrine therapy has resulted in the development of secondary sex characters and the establishment of irregular menstruation, and simultaneously there has been considerable improvement of the asthma. Continued treatment may induce a true puberty with regular menstruation. As the patient is now 30 years old this may be very difficult, but the result so far has been most promising. Probably the improvement in the asthma is comparable to that noted in children at the time of puberty.

My thanks are due to Mr. Leonard Phillips for his advice and opinion; to Dr. N. Lloyd Rusby for giving me access to case notes at the London Chest Hospital; and to Dr. Martin Hynes for his encouragement and assistance with the microscopical examination.

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THE ALBUMIN ANTIBODY IN ROUTINE RHESUS GROUPING ADAPTATION OF THE CHOWN CAPILLARY METHOD

BY

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Attention has been drawn in recent months to the difficulty experienced in maintaining adequate supplies to laboratories of Rhesus testing serum, especially anti-D. This difficulty has arisen from the increasing tendency to screen for this factor *all* expectant mothers and patients requiring blood transfusion. For these tests serum containing the complete or saline antibody is generally used, and the examination is carried out by the tube method. It is unfortunate that the blood of mothers of erythroblastotic infants usually shows a comparatively low titre of this antibody; more often the serum contains the incomplete or albumin antibody in high titre. It would appear that if this latter antibody were in general use the supply problem would be solved.

In the laboratory of the North Middlesex Hospital we found that the albumin antibody is suitable for routine screening, using the Chown capillary technique in which a saline suspension of the unknown red cells is allowed to fall through a column of serum containing the Rh antibody in a capillary tube. This tube is inclined at an angle of 45 degrees against an illuminated glass screen, the light source being so disposed as to give a fairly constant temperature of 37° C. across the screen face. The Rh-positive cells agglutinate into clumps which are readily seen with the naked eye, spaced in the length of the fluid with clear intervals between each, whilst the Rh-negative cells fall evenly to the bottom of the capillary type, leaving a clear supernatant fluid. This method combines the advantages of economy of serum and effort with rapidity, the positive results being apparent in 5-15 minutes, and it has been used exclusively in that laboratory since routine Rhesus screening was introduced in December, 1947, and from October, 1949, the albumin antibody has replaced the saline antibody formerly employed.

In the hands of some workers the Chown test seems to be a little difficult, but by rigidly adhering to the details of the technique as originally set out (Chown and Lewis 1946) no difficulty has been encountered by us and, furthermore, technicians become familiar with it after a few demonstrations.

To use the albumin antibody a few minor modifications of the original method have been evolved.

Apparatus.—The apparatus used is the box as described by Chown.

Capillary Tubes.—These are pulled from ordinary glass tubing similar to that used for making Pasteur pipettes. The internal capillary diameter should be about 0.5 mm. and the length about 8 cm.

Serum.—The serum containing the albumin antibody is diluted with an equal volume of 20% bovine albumin. Dilution with weaker albumin solution (15% or 10%) gives satisfactory results, but these take longer to appear, often 30-40 minutes, thus depriving the method of one of its advantages. The speed of the reaction is also affected by the titre, 1:8 being regarded as the lowest satisfactory for general use.

Such dextran solutions as have been available have proved unsatisfactory diluents owing to rouleaux formation.

Red Cells.—The unknown red cells, which may be obtained from either citrated or oxalated blood, or from the blood-stained serum of clotted blood after serum has been taken for Wassermann reaction or antibody investigation, are washed in saline and centrifuged at not more than 1,000 r.p.m. for three to five minutes. The supernatant fluid is withdrawn and the cells are resuspended in saline to approximately 40–50% concentration.

The Test

The test is carried out as described by Chown. The serum-albumin mixture is taken into a capillary tube for a distance of 2 cm. followed by the red-cell suspension for a distance of 0.5 cm. Care must be taken to avoid any intermediate air bubble. The capillary is then inverted and the lower end set in the plasticine bed at the base of the illuminated screen with the red cells uppermost so that they fall through the column of serum: agglutination is apparent in positive cases in 5–10 minutes; negative cases should be left 20 minutes before reporting.

Approximately 300 tests can be performed from 1 ml. of the original serum.

With this antibody the agglutinates tend to be larger than when the saline antibody is used, and they remain suspended in the fluid medium for at least an hour.

Results of Tests

Groups	Cases	Antibody Used	
		Saline (Dec., 1947– Sept., 1949)	Albumin (Oct., 1949– Mar., 1950)
Rh-positive ..	8,570	6,320	2,250
Rh-negative ..	2,024 (19.11%)	1,481 (18.98%)	543 (19.44%)
Total ..	10,594	7,801	2,793

All Rh-negative cases were checked by retesting when the first antibody assay was made or, in the case of blood donors, when the genotype was investigated. In the series of over 10,000 only 15 wrong groupings were found, proportionately divided between the two types of antibody used (saline 11 and albumin 4). No patient reported by us as Rh-positive has subsequently been shown to be Rh-negative.

Our cases were not in any way representative of a cross-section of the population, for the series included many expectant mothers referred to the antenatal clinics with obstetric histories suggestive of Rh incompatibility, most of whom proved to be Rh-negative. In maintaining the hospital blood bank the relatives of Rh-negative recipients also tended to increase the proportion of Rh-negative persons. Thus it is that our percentage of Rh-negative subjects is 19.11, against the figure of 16.8 given by Mollison, Mourant, and Race (1948).

Summary

A modification of the Chown capillary method for Rh grouping using the albumin antibody is described; the suspension of the unknown red cells is increased to 50% and the antiserum is diluted with an equal volume of 20% bovine albumin.

The findings in a series of over 10,000 cases (7,801 tested with the saline antibody and 2,793 with the albumin antibody) are given for a comparison of results obtained by the use of these two antibodies; they are strictly comparable.

As the series included many cases referred to the laboratory for investigation a higher percentage of Rh-negative persons was found in our "population" than in a more representative cross-section.

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Medical Memorandum

Rheumatoid Arthritis : Sustained Improvement on Low Dosage of Cortisone

A case of rheumatoid arthritis is presented which has been successfully treated for eight months with cortisone. After an initial period of treatment with high dosage, maintenance dosage has been reduced—gradually at first—to the lowest level short of provoking relapse.

Case Report

The patient, a boy aged 15, first noticed pain and swelling of the small joints of the fingers in January, 1950, while at his boarding-school. By the end of March, when his parents went to take him home for the holidays, they found him very lame with pain and swelling of recent origin affecting the left knee. He was also complaining of pain and swelling of the wrists and of the small joints of the fingers, so that he had difficulty in using his hands to feed himself.

He was put to bed at home on April 7, and a diagnosis of rheumatoid arthritis was made. The E.S.R. was raised to 90 mm. (Westergren) in one hour. He was given an initial intramuscular injection of 0.01 g. of sodium aurothiomalate and five subsequent weekly injections of 0.02 g. There was only slight improvement in his condition, and on June 24 he was admitted to hospital for treatment with cortisone. He then was afebrile, apart from an occasional temperature of 99° F. (37.2° C.). He was asthenic and of poor physique. His teeth and throat were healthy. His heart was normal. Glands and spleen were not enlarged. There was practically no movement in the right wrist. The left wrist could be flexed to 45 degrees, but there was no dorsiflexion. The wrist-joints were swollen, and attempts to move the wrists were very painful. The proximal interphalangeal joints of the hands were also swollen, and there was well-marked fusiform periarticular swelling of the left knee, with painful and restricted movement and wasting of the quadriceps (Fig. 1). A radiograph of the left knee

FIG. 1.—Photograph taken on June 28.