remarkably short time the site of the carcinoma is replaced by avascular scar.

It is generally agreed that prolactin is richly contained in the mammalian placenta, where it may be elaborated or, more probably, stored, and the dramatic growth regression of the Foulds tumour at parturition suggests that it is "placental-prolactin" dependent. Strict hormone dependence is also characteristic of the malignant tumours in animals produced experimentally by hormone administration.

Hormone dependence in mammals may therefore be regarded as an induced or spontaneous biological characteristic whose existence should dispel any doubts regarding the reality of hormone-dependent human breast cancer.

Summary

About 50% of all human breast cancers are hormone-dependent. Progressive growth of such tumours is conditioned by an adequate supply of those hormones which govern physiological growth in the hormone-dependent epithelium of the normal mammary gland.

Normal breast growth is controlled by the synergistic action of the pituitary hormone prolactin acting at a relatively high concentration, with ovarian oestrogen acting at a relatively low one.

Combined oophorectomy and adrenalectomy deprive a breast cancer of oestrogenic steroids, and if the tumour is hormone-dependent growth regression follows. This effect seems to be almost always temporary, oestrogen production is slowly re-established, and progressive growth of the tumour recurs probably when oestrogen production from an unknown site reaches the low level required for normal mammogenesis.

Total hypophysectomy in all probability completely deprives the tumour of oestrogen and prolactin.

This operation can have no effect on the growth of a hormone-independent tumour.

The urine of all pre-menopausal women and of approximately 50% of post-menopausal women contains one or more mammotrophic hormones. It seems probable that it contains prolactin.

If the urine of a breast-cancer patient has no mammotrophic activity it seems very probable that her tumour would be hormone-independent and that hypophysectomy would have no effect on its progressive growth. A short series of investigations supports this supposition.

REFERENCES

Coppedge, R. L., and Segaloff, A. (1951). *J. clin. Endocr.*, **11**, 465.
Cowie, A. T., and Folley, J. S. (1955). In *The Hormones*, vol. 3, chap. VIII, edited by G. Pincus and K. V. Thimann. Academic Press Inc., New York.
Foulds, L. (1947). *Brit. J. Cancer*, **1**, 362.
—— (1949). Ibid., **3**, 240, 345.
—— (1951). *Ann. roy. Coll. Surg. Engl.*, **9**, 93.
—— (1954). *Cancer Res.*, **14**, 327.
—— (1956). *Ann. roy. Coll. Surg. Engl.*, **18**, 384.
Hadfield, G., and Young, J. Stretton (1956a). *Brit. J. Cancer*, **10**, 145.
—— —— (1956b). Ibid. In press.
Harris, G. W., and Jacobsohn, D. (1952). *Proc. roy. Soc. B*, **139**, 263.
Lyons, W. R. (1943) In *Essays in Biology*. Univ. of California, Berkeley.
—— Johnson, R. E., Cole, R. D., and Li, C. H. (1955). *Hypophyseal Growth Hormone, Nature and Actions: International Symposium*, p. 461. McGraw-Hill Book Co. Inc.
—— and Page, E. (1934). *Proc. Soc. exp. Biol. (N.Y.)*, **32**, 1049.
Scowen, E. F., and Hadfield, G. (1955). *Cancer*, **8**, 890.
Segaloff, A. (1953). Ciba Foundation Colloquia on Endocrinology, **5**, 106. Churchill, London.
—— Gordon, D., Horwitt, B. N., Schlosser, J. V., and Murison, P. J. (1951). *Cancer*, **4**, 319.

CORTISONE IN TREATMENT OF CHILDREN WITH CHRONIC ASTHMA

BY

M. C. S. KENNEDY, M.R.C.S.
Medical Research Council Staff; Clinical Assistant in Respiratory Physiology, Stoke-on-Trent

AND

D. C. THURSBY-PELHAM, M.R.C.P., D.C.H.
Consultant Paediatrician, North Staffordshire Royal Infirmary, Stoke-on-Trent

The conflicting reports on the value of corticotrophin (A.C.T.H.) and cortisone in "asthma" relate chiefly to adults and are probably due in part to the ephemeral nature of the disease and in part to the different methods of assessment employed.

In the investigation reported here the main object was to assess the value of oral cortisone in improving the ventilatory function of children with chronic "wheezy" chests. A further object was to compare the effect on the ventilatory function of such children of cortisone given by mouth and adrenaline given by inhalation.

Present Investigation

Children Studied.—Twelve children attending an asthma clinic were selected for study, all of whom had asthma associated with a poor ventilatory function. The children selected had all attended regularly at the clinic for respiratory function tests for not less than six months, and seven had done so for from two to four and a half years. Only those who could attend regularly twice weekly and could co-operate well in the tests were selected. Details of each child are summarized in Table I. There were nine boys and three girls, whose ages ranged from 9 to 15 years. All had been found to have impaired ventilatory function between their acute attacks and also when free from symptoms. The duration of their symptoms ranged from two and a half to twelve years, six children having started their attacks in the first three years of life. When possible, the patients were grouped into two main types—allergic spasmodic asthma and infective asthmatic bronchitis—as judged by their histories, and special notes were made on the psychological background, which varied in importance. Seven cases were of allergic type, and in four of these psychological factors were thought to be of special importance. One case was primarily infective and four cases were of mixed type, having characteristics of both the allergic and the infective groups.

Method of Assessment.—After having observed "asthmatic" children attending the clinic for periods of up to five years we are convinced of the necessity of employing an objective measure for the assessment of therapy. In this investigation we have measured the expiratory flow rate over the first 0.75 second of expiration (E.F.R.^{40}) as described by Kennedy (1953). This measure is an index of the maximum ventilatory capacity at a theoretical respiratory rate of 40 breaths a minute (hence E.F.R.^{40}), and we consider it to be valid and practicable in the assessment of children with asthma.

Treatment Regime.—As a routine, all children attended the clinic twice weekly, when they were given an inhalation of adrenaline (1/1,000) for a period of

five minutes. The E.F.R.[40] was measured before and after the adrenaline inhalation. Children selected for treatment with cortisone were allocated at random to treatment with either cortisone or placebo tablets. The placebo tablets, consisting of lactose with a trace of quinine, were dispensed in such a way as to be indistinguishable from the cortisone tablets either to the patient or to the physician. Six of the 12 children were started on a course of 100 25-mg. cortisone tablets and were later given a course of 100 placebo tablets, while the six others were started on placebo tablets and were later changed to cortisone. The children were given three tablets daily for three weeks and two tablets daily for two weeks: thus when on cortisone they had 75 mg. of cortisone acetate daily for three weeks and 50 mg. daily for two weeks. This dosage was modified only if undesirable side-effects occurred or if a child was unable to attend for assessment frequently enough.

Results

(*a*) *Symptomatic.*—Leading questions were avoided so far as possible. Six of the children volunteered that they felt very well when on cortisone. Two of these and three others were noticed by their parents to have increased appetites. While on cortisone the weights of all children increased by 2 to 9 lb. (0.9 to 4 kg.), the average gain being 5 lb. (2.3 kg.) during the course, and all the children appeared to be more lively and energetic than previously. A careful watch was kept for side-effects, and the patients were examined once weekly. No side-effects were encountered except occasional "mooning" of the face if the dose of 75 mg. was continued for more than two weeks. One child had nose bleeding, but his blood pressure was not raised. The tablets were discontinued if the patient developed an infection—this occurred in two cases during treatment. Five children had wheezing attacks during treatment with cortisone, as well as with placebo. Seven children had no wheezing attacks while on cortisone; two of these also had no attacks while on placebo and in three cases no satisfactory symptomatic comparison was possible, owing to respiratory infections.

(*b*) *Changes in the Ventilatory Function During Treatment.*—The E.F.R.[40] values of each child before and after adrenaline inhalations, whilst on placebo tablets and whilst on cortisone tablets, are given in Table II. During treatment with placebo tablets a total of 128 E.F.R.[40] assessments were made on the 12 children (averaging just over 10 assessments a child) before and after an inhalation of adrenaline. The mean E.F.R.[40] of the 12 children before adrenaline was 47 l./min., which was increased to 58 l./min. after adrenaline: In other words, short-acting adrenaline inhalations produced an overall improvement in the E.F.R.[40] of 13%. During treatment with cortisone a total of 141 E.F.R.[40] assessments were made on the 12 children (averaging nearly 12 assessments a child). During this treatment their mean E.F.R.[40] before adrenaline was 53 l./min., and if this value be compared with the mean E.F.R.[40] before adrenaline while on placebo tablets (47 l./min.) it may be said that cortisone treatment was associated with an overall improvement in the E.F.R.[40] of 13%. During cortisone

TABLE I.—*Summary of Children Studied*

Case No.	Sex	Age (Years)	Duration of Asthma Attacks	Frequency of Asthma Attacks	History of Other Allergy	Family History of Allergy	Expiratory Rhonchi	*Mean E.F.R.[40] Values (l./min.)		No. of E.F.R.[40] Assessments	Type of Asthma
								Before Adrenaline	After Adrenaline		
64	M	12 6/12	10 years	Once a month	None	Yes	Occasional	46 (26-59)	51 (33-63)	9	Allergic
28	M	12 11/12	5 ,,	Every two months	,,	None	,,	46 (41-53)	50 (45-56)	17	Infective
37	M	10 5/12	6 ,,	Every two weeks	,,	Yes	,,	45* (42-47)	52* (49-57)	3†	Allergic
41	M	14 3/12	12 ,,	Monthly	Hay-fever	,,	,,	68 (66-73)	73 (64-77)	7	,,
11	M	9 11/12	7 ,,	,,	Infantile eczema	,,	Almost constant	45 (35-53)	51 (64-56)	26	Allergic+psych.
26	F	10 2/12	2½ ,,	Two or 3 times a month	Hay-fever	,,	Occasional	45 (35-53)	53 (48-59)	13	,, ,,
23	M	12 4/12	11 ,,	Every 1 or 2 months	Eczema and hay-fever	No	,,	52 (45-58)	64 (59-77)	21	Mixed (allergy+infection)
44	F	15 5/12	8 ,,	Two or 3 times each month	Eczema	,,	Almost constant	24 (21-26)	30 (28-35)	10	Allergic+psych.
71	F	12	10 ,,	Every two months	,,	Yes	Occasional	41 (26-52)	56 (39-67)	18	Mixed (allergy+infection)
54	M	14 11/12	12 ,,	Weekly	,,	Unknown	Almost constant	22 (17-35)	26 (21-45)	14	Allergic+psych.
31	M	13 4/12	3 ,,	Monthly	None	None	,, ,,	50 (42-53)	56 (46-62)	19	Mixed (allergy+infection)
62	M	13 3/12	5 ,,	,,	,,	Yes	Occasional	42 (36-64)	43 (40-67)	7	,, ,,

* The values in this column give the mean E.F.R.[40] (and range) over the four months preceding treatment with either placebo or cortisone.
† This boy had been away at a country school for six months, before which he had been under regular observation at the clinic. The three values given above are of the same order as the E.F.R.[40] values observed before he was sent to the country.

TABLE II.—*Twelve Children with Ventilatory Insufficiency. E.F.R.[40] Values, Before and After Adrenaline Inhalations, During Treatment with a Placebo and with Cortisone*

Case No.	Oral Placebo			Oral Cortisone			Response to Adrenaline	Response to Cortisone	Response to Cortisone+Adrenaline
	No. of Readings	E.F.R.[40] l./min.		No. of Readings	E.F.R.[40] l./min.				
		Before Adrenaline a	After Adrenaline b		Before Adrenaline c	After Adrenaline d	$\frac{b-a}{a}\times 100$	$\frac{c-a}{a}\times 100$	$\frac{d-a}{a}\times 100$
64	14	58 (40-67)	62 (46-67)	14	58 (48-66)	61 (49-69)	+7%	Nil	+5
28	9	48 (37-57)	51 (44-61)	11	49 (41-56)	53 (50-62)	+6%	+2%	+11%
37	10	45 (34-50)	46 (37-57)	14	47 (34-68)	51 (44-66)	+2%	+4%	+13%
41	14	64 (52-82)	68 (48-81)	10	68 (55-74)	77 (63-84)	+6%	+6%	+20%
11	13	45 (19-63)	53 (28-74)	15	46 (12-72)	54 (23-66)	+18%	+2%	+20%
26	5	46 (40-52)	55 (50-62)	9	53 (50-57)	59 (52-66)	+20%	+15%	+28%
23	16	64 (53-80)	77 (61-103)	12	79 (66-96)	89 (81-96)	+20%	+23%	+39%
44	10	26 (18-37)	31 (22-44)	6	28 (19-35)	35 (30-46)	+19%	+8%	+35%
71	10	61 (40-82)	74 (57-88)	17	66 (40-83)	83 (52-99)	+21%	+8%	+36%
54	9	21 (13-44)	25 (11-46)	7	23 (14-33)	29 (16-41)	+18%	+10%	+38%
31	8	42 (30-59)	53 (33-68)	14	61 (27-82)	68 (48-92)	+29%	+43%	+45%
62	10	44 (32-59)	44 (29-57)	12	57 (37-79)	67 (39-79)	Nil	+30%	+52%
Totals	128	564	639	141	635	726			
Means	10·6	47	53	11·7	53	60·5	+13%	+13%	+28%

treatment the mean E.F.R.[40] after adrenaline was 60.5 l./min.: if this value also be compared with the mean E.F.R.[40] before adrenaline while on placebo tablets (47 l./min.), then the cortisone plus adrenaline values show an improvement of 28%.

With the day-to-day changes that occur in the E.F.R.[40] of these children (the ranges are given in Table I) it is difficult to decide what is a "significant" change. After looking at the bi-weekly E.F.R.[40] values of each child in the clinic over a long period we find that if the mean monthly value is increased by more than 20%, then a change of this magnitude is usually associated with a therapeutic procedure. If one arbitrarily accepts a positive change of 20% as significant in a given case, it will be seen that four children show a response to adrenaline, three a response to cortisone, and nine a response to cortisone combined with adrenaline.

The three children showing an average increase of 20% or more of their E.F.R.[40] during treatment with cortisone are discussed in more detail below.

Case 23

A boy aged 12 started having spasmodic asthma in infancy. The attacks occurred every one or two months. He was affected by feathers, dust, and smoke. He also suffered from hay-fever and occasional eczema, but there was no family history of allergy. He was rather backward at school and emotionally immature.

He first attended the clinic in October, 1953. On clinical examination he was found to be a very thin boy, height 69 in. (175 cm.), weight 63 lb. (28.6 kg.), with a dry and scaly skin, round shoulders, pigeon-shaped chest, and poor respiratory movements. Scattered rhonchi were present on both sides of his chest. His general condition and respiratory function were both found to be so poor (E.F.R.[40] between 22 and 28 l./min.) that he was admitted to hospital for two weeks. He improved with breathing exercises and antispasmodics (his E.F.R.[40] rose to a peak of 70 l./min. after six weeks but later fell steeply with attacks). Between November, 1953, and October, 1954, his E.F.R.[40] values ranged from 32 to 76 l./min., the inhalation of adrenaline producing an increase of 15 to 25%. In Fig. 1 the E.F.R.[40] values of this boy before and after adrenaline have been charted for the period August, 1954, to April, 1955. It is apparent from Fig. 2 that the E.F.R.[40] values without adrenaline reached a peak of 96 l./min. after two and a half weeks on 75 mg. of cortisone daily. When the cortisone was reduced to 50 mg. daily the E.F.R.[40] values gradually dropped to 66 l./min., although the fall in the "after adrenaline" values was not so marked. The average E.F.R.[40] values of this child before and after adrenaline were respectively 23% and 39% higher on cortisone than on placebo tablets. His E.F.R.[40] before the trial averaged 52 l./min. (over four months), on cortisone the average rose to 79 l./min., and on changing to placebo it fell to 64 l./min. The changes suggest some prolonged benefit from cortisone.

Case 62

A boy aged 13, with a history of asthma since infancy, had attacks which lasted one to four days and occurred on an average of about one a month, though at irregular intervals, and were characterized by wheezing, coughing, and occasional sputum. They were most frequent in the winter months, when they were thought to be caused by upper respiratory infections. He was also worse during the months of July and August. A smoky atmosphere or changes of district were reported to provoke attacks. There was a strong family history; his mother had suffered from asthma all her life, and died of this complaint five years ago.

He first attended the clinic in March, 1954. He was a round-shouldered boy of normal height—62 in. (157 cm.)—and weight—94 lb. (42.6 kg.)—for his age. His chest expansion was 2½ in. (6.3 cm.), expiration was prolonged, and occasional rhonchi were present.

In Fig. 2 the E.F.R.[40] values of this boy before and after adrenaline have been charted for the period October, 1954,

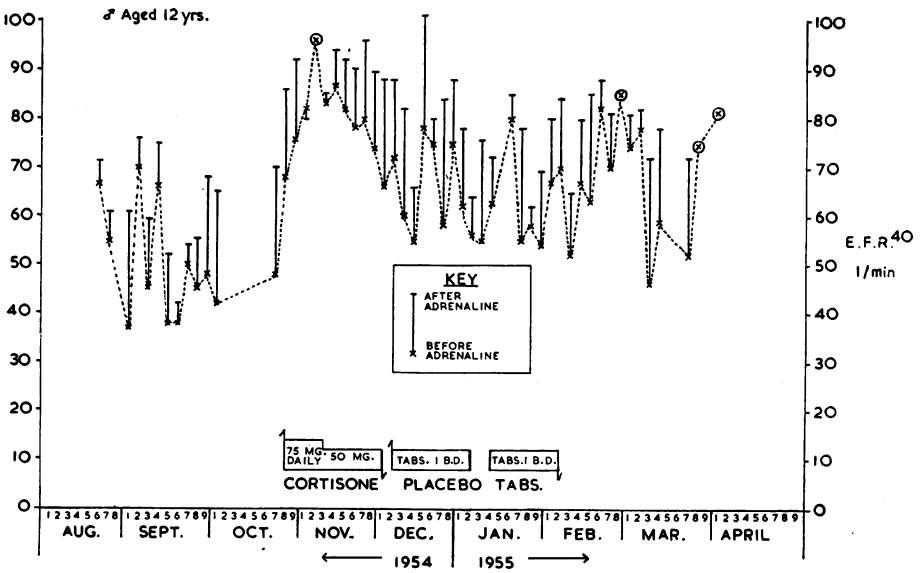

FIG. 1.—Treatment chart of Case 23.

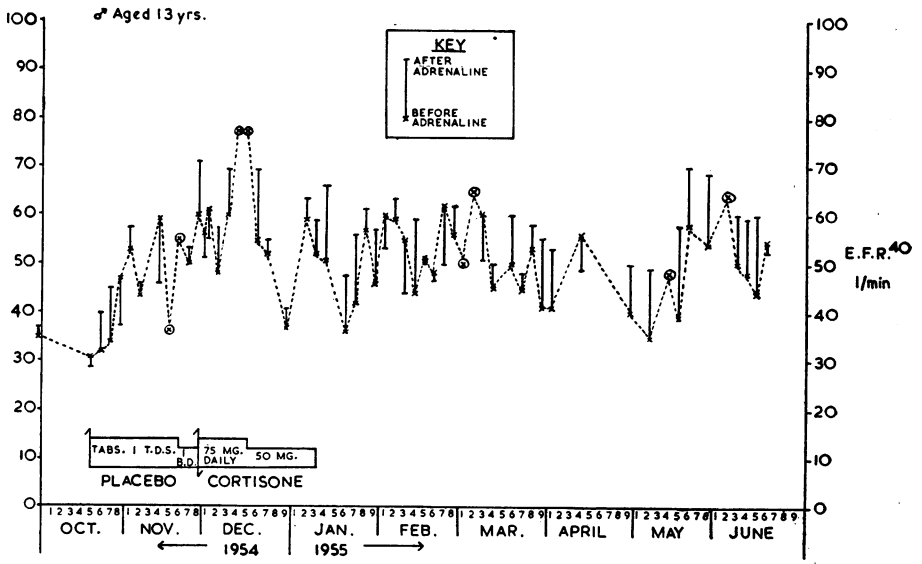

FIG. 2.—Treatment chart of Case 62.

to June, 1955. During treatment with placebo tablets his values before adrenaline ranged between 32 and 59 l./min., and after adrenaline between 29 and 57 l./min. At the end of three weeks on cortisone, 75 mg. daily, he reached a peak level of 79 l./min., which was not maintained when the dose was reduced to 50 mg. daily. However, the average E.F.R.^{40} before and after adrenaline were respectively 30% and 52% higher during treatment with cortisone than during treatment with placebo tablets. The range of the subsequent observations on this patient were almost the same as before treatment, and suggest that the single course of cortisone failed to produce any permanent improvement in the ventilatory function, though his general condition appeared to be better and his attacks happened to be less frequent.

Case 31

A boy aged 13 had had attacks of bronchitis each winter since the age of 18 months. In June, 1952, following whooping-cough, he began having attacks of asthma. The attacks were accompanied by sneezing and coughing, and were occasionally associated with a generalized erythema. They occurred about once a month, and he continued to wheeze for three to six days. Asthma was more frequent in the summer months, and was aggravated by dust and hot weather. Upper respiratory infections also produced wheeziness, and he had frequent coughs with purulent sputum. There was no family history of allergy. He was a sensitive child, and had shown severe nervous symptoms when he failed to get into high school. There was also evidence of parental discord.

He first attended the clinic in August, 1952. He was a thin round-shouldered boy—weight 70 lb. (31.8 kg.), height 59 in. (150 cm.)—with a slightly pigeon-shaped chest and poor respiratory movements. Bronchial spasm was present, and rhonchi were found on both sides. He was treated with breathing exercises and antispasmodics. From August, 1952, until the start of the present trial, his ventilatory function, which was recorded regularly, was poor: the E.F.R.^{40} generally ranged from 20 to 50 l./min. There were peaks up to a maximum of 75 l./min. associated with antispasmodic therapy.

In Fig. 3 the E.F.R.^{40} values of this boy before and after adrenaline have been charted for the period April, 1954, to October, 1955. In December, 1954, he was put on placebo tablets, which were continued through to March, 1955, because he did not attend frequently enough for assessment in January: during this time his E.F.R.^{40} values ranged between 32 and 59 l./min. before adrenaline and between 33 and 68 l./min. after adrenaline. At the beginning of April, 1955, he was given cortisone, 75 mg. daily, for four weeks; at the end of this time his E.F.R.^{40} had risen to 82 l./min., which was increased further to 92 l./min. by adrenaline. He then had two weeks' treatment with cortisone, 50 mg. daily, when his E.F.R.^{40} values progressively dropped. However, the average E.F.R.^{40} values before and after adrenaline were respectively 43% and 45% higher during treatment with cortisone than during treatment with placebo. In June and July a second course of treatment with cortisone was given, and in August and early September a third course, and during both these courses it appeared that his E.F.R.^{40} reached a peak after some two or three weeks on a dose level of 75 mg. daily, but that his values dropped as soon as the dose was reduced to 50 mg. daily. The values listed during a final course of treatment with placebo tablets suggest that the three courses of cortisone failed to produce any permanent improvement in his ventilatory function.

Discussion

We have found it particularly difficult to assess changes in a patient with asthma from the symptomatology, and this difficulty becomes exaggerated when the drug under trial produces a sense of well-being (Hansen-Pruss, 1953).

We agree with Beale *et al.* (1952) that studies of pulmonary function provide a useful objective measure of the response to therapy in asthma, and that long-standing cases of asthma have impaired pulmonary function between their attacks. We also agree with Beale *et al.* that the maximum breathing capacity is reduced to a greater degree than the vital capacity in this condition. For these reasons we have employed the expiratory flow rate (E.F.R.^{40}) test, which correlates very well with the maximum breathing capacity (Kennedy, 1953) and is practicable for the routine assessment of children on an out-patient basis.

We were impressed with the possible danger of adrenal cortical atrophy from long-continued cortisone administration (Salassa *et al.*, 1953; Stoner and Whiteley, 1954; Savidge and Brockbank, 1954), and we therefore limited the course of treatment to 100 25-mg. tablets over a period of five to six weeks. The mean E.F.R.^{40} value of all 12 children during oral cortisone therapy has been compared with that obtained during a comparable period of treatment with placebo tablets. During cortisone the mean value was 13% higher than during placebo therapy. Since in no child was the mean E.F.R.^{40} value on cortisone lower than that on placebo, the advantage of cortisone over placebo is convincing. During treatment with cortisone the average E.F.R.^{40} values were increased by less than 10% in seven children, by 10–19% in two children, and by 20% or more in three children.

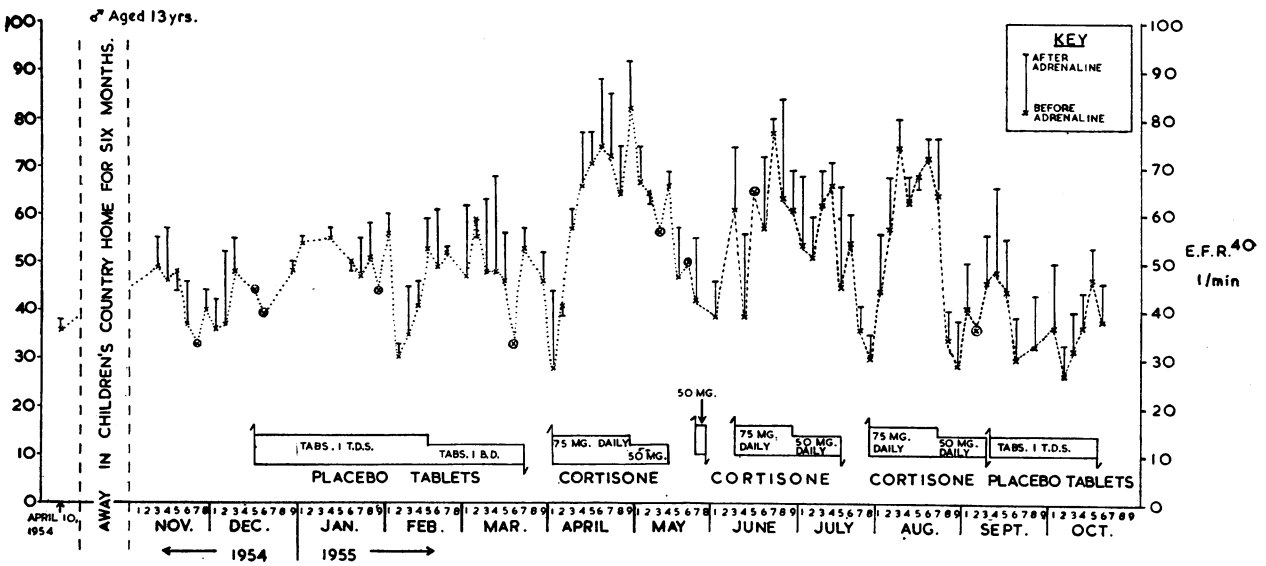

FIG. 3.—Treatment chart of Case 31.

From the detailed study of the three children who had a 20% or more increase in their values it is evident that a dose level of 75 mg. of cortisone daily was effective in producing a gradual response that reached a peak between the second and fourth weeks of treatment (the peak values in these three children were 50%, 70%, and 95% higher than the average E.F.R.^{40} value on placebo), but the response was not maintained when the dose was reduced to 50 mg. daily. Of the three boys who responded well to cortisone, there is suggestive evidence in Fig. 1 but none in Fig. 2 that some improvement is maintained after the withdrawal of cortisone. The study of the third boy, who was given three consecutive courses of cortisone treatment, showed the response pattern to be similar during each course (Fig. 3), but there was no evidence of lasting improvement from the treatment.

It would appear that those children who respond well to aerosol adrenaline have a better chance than others of responding to cortisone, but, apart from this pointer, we find it as yet impossible to predict the type of child asthmatic that might benefit temporarily from cortisone. However, the response to adrenaline is of great help in assessing the degree of reversible broncho-constriction.

One would expect the results with cortisone to vary not only with the daily dose and duration of treatment but also with the type of patient and the method of assessment employed. Davies and Williams (1955) and Baldwin and de Gara (1952) have reported good results with corticotrophin and cortisone in a high percentage of adult patients with intractable chronic asthma, using a similar dose schedule to that used in this report. Savidge (1955), on the other hand, is not enthusiastic about the value of cortisone after nearly three years' experience of 47 asthmatics treated with cortisone and/or a blank substance on a long-term basis. He emphasizes the importance of blind trials in the assessment of asthmatics, who are so open to suggestion, and he personally intends to discourage the use of cortisone except in the most carefully chosen cases. Wayne (1955) has reviewed the dangers and complications of cortisone, which he regards as impressive enough to warrant second thoughts before instituting treatment over long periods in such conditions as rheumatoid arthritis and asthma. In the case of children with chronic asthma we would confine the use of cortisone to the most severe cases which have shown unequivocal evidence of improvement after a short course of treatment. Long-continued therapy would seem advisable only in small doses. However, in the investigation reported here a daily dose of 50 mg. or less failed to maintain improved respiratory function. It seems to us to be very questionable whether it is justifiable to give long-continued therapy in effective doses.

Table I shows that in 11 of the 12 children the combined effect of cortisone and adrenaline is greater than the single effect of either drug alone. The percentage increase in the E.F.R.^{40} of the 12 children during cortisone therapy alone (13%) added to the response from adrenaline therapy alone (13%) approximates very closely to the overall percentage increase during combined cortisone and adrenaline therapy (28%). From these overall values it can be said that the combined effect of the two drugs is additive. In other words, if a child showed a good response after adrenaline inhalations (during treatment with placebo tablets), adrenaline still produced a similar response over and above that obtained from cortisone. Exceptions to this general statement occurred when the E.F.R.^{40} rose to peak levels in the third or fourth week of cortisone therapy and when adrenaline failed to have any effect (Cases 23 and 62, Figs. 1 and 2), owing possibly to the complete relief of bronchospasm by cortisone.

The additive effect of cortisone and adrenaline appears very similar to that of khellin and adrenaline (Kennedy and Stock, 1952), though the time response of the two drugs, cortisone and khellin, is different. It is perhaps of interest to record that one of the children (Case 23) had been treated with oral khellin and adrenaline inhalations before this investigation, when he showed a similar peak response to that produced by cortisone and adrenaline.

Summary and Conclusions

A blind investigation comparing the effects of oral cortisone and placebo tablets on the ventilatory function of 12 children with chronic asthma is reported.

All children had an impaired ventilatory function as judged from the E.F.R.^{40} test, which was carried out as a routine twice weekly, before and after an inhalation of adrenaline.

The short-acting adrenaline given by inhalation produced an overall increase in the E.F.R.^{40} of these 12 children of 13% (varying in individuals from 0% to 29%).

During treatment with cortisone by mouth (2.5 g. over a period of five to six weeks) the mean E.F.R.^{40} of the 12 children was 13% higher than during a similar course of treatment with placebo tablets.

In three children the mean E.F.R.^{40} during treatment with cortisone was more than 20% higher than during treatment with placebo tablets. The cortisone effect, at a dose level of 75 mg. daily, was slow to develop, and reached a peak between the second and fourth weeks of treatment which waned when the dose level was reduced to 50 mg. daily.

Treatment of the 12 children with oral cortisone and adrenaline inhalations was associated with an overall improvement in the E.F.R.^{40} of 28%, suggesting that the combined effect of the two drugs is additive.

No serious side-effects were encountered during cortisone therapy over short periods. However, until more is known of the long-term effect of cortisone on the adrenals, it seems questionable whether it is justifiable to give long-continued therapy in effective doses.

We are indebted to the Medical Research Council for the cortisone tablets and to Roussel Laboratories Ltd. for the placebo tablets; to Mr. J. Booth, S.R.N., and Mr. L. Drury for technical assistance; and to Dr. P. J. Lawther for reading the manuscript.

REFERENCES

Baldwin, H. S., and de Gara, P. F. (1952). *J. Allergy*, **23**, 15.
Beale, H. D., Fowler, W. S., and Comroe, J. H. (1952). Ibid., **23**, 1.
Davies, B. M., and Williams, D. A. (1955). *British Medical Journal*, **2**, 293.
Hansen-Pruss, O. C. (1953). *Sth. med. J.*, **46**, 814.
Kennedy, M. C. S. (1953). *Thorax*, **8**, 73.
—— and Stock, J. P. P. (1952). Ibid., **7**, 43.
Salassa, R. M., Bennett, W. A., Keating, F. R., and Sprague, R. G. (1953). *J. Amer. med. Ass.*, **152**, 1509.
Savidge, R. S. (1955). *British Medical Journal*, **1**, 785.
—— and Brockbank, W. (1954). *Lancet*, **2**, 893.
Stoner, H. B., and Whiteley, H. J. (1954). Ibid., **2**, 992.
Wayne, E. J. (1955). *Practitioner*, **175**, 546.

In September the Trustees of the Lord Mayor Treloar Training College, near Alton, are opening a special school for the grammar-school education of the physically handicapped boy. This will be the first of its kind in the country. It will be housed in new buildings, but form part of the existing college. Boys of "not less than average intelligence" will be admitted from any time after the age of 11. At 16 it will be possible for them to transfer to vocational courses or to a more advanced academic course, which it is hoped to provide if the demand is sufficient. The school will accommodate about 70 boys, and applications for admission will be considered from any area in England or Wales. The vocational training establishment provides for about 60 boys, who are admitted up to the age of 17, though only exceptionally later. The Minister of Education has approved a fee of £300 per annum to be charged to local education authorities in respect of each pupil at the special school or the training establishment. Further details from the Warden, Lord Mayor Treloar Training College, Froyle, near Alton, Hampshire.