Intravenous ACTH Therapy in the Treatment of Bronchial Asthma*

MAURICE S. SEGAL, M.D. F.C.C.P.† and J. AARON HERSCHFUS, M.D.††
Boston, Massachusetts

ACTH intramuscularly is being used in the treatment of many diseases. The drug has to be administered every six hours because of the short duration of the effects of a single injection, regardless of the size of the dose. Resistance suggesting tachyphylaxis, eosinophil escape, allergic and anaphylactic reactions have been observed with ACTH administered intramuscularly.

Sayers et al.1 administered to two subjects a large dose of ACTH (Armour equivalent of 100 mg. and 50 mg. respectively) intravenously over a one-hour period. In both the metabolic changes effected by ACTH occurred promptly, were maximal by the third hour and had returned to pretreatment levels by the sixth hour. One subject had a shaking chill and fever, the other subject experienced no untoward effects.

Gordon et al.2 subsequently reported their observations on the effects of continuous intravenous infusion of ACTH. A small dose of ACTH administered in this fashion to humans was able to maintain increased adrenocortical activity over a prolonged period of time. Fifty milligrams of ACTH were given in two or three liters of fluid over eight to 24 hours. Measurable responses were prompt, maximal and sustained.

Recently Renold et al.3 reported their clinical and laboratory

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†Clinical Professor of Medicine, Tufts College Medical School; Director, Department of Inhalational Therapy, Boston City Hospital.

††Research Fellow in Medicine, Tufts College Medical School.

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### TABLE I

<table>
<thead>
<tr>
<th>PATIENT</th>
<th>ACTH TREATMENT</th>
<th>EOSINOPHILS</th>
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<tr>
<td></td>
<td>Total Dose (mg.)</td>
<td>Duration (days)</td>
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<tr>
<td>1. C.T.</td>
<td>92.5</td>
<td>4</td>
</tr>
<tr>
<td>2. H.O'R.</td>
<td>110</td>
<td>9</td>
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<td>3. J.G.</td>
<td>145</td>
<td>3</td>
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<tr>
<td>4. E.W.</td>
<td>120</td>
<td>6</td>
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<tr>
<td>5. J.O.</td>
<td>10</td>
<td>1</td>
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*Results: Excellent remission for 6 weeks. Severe asthma 2 weeks later requiring hospitalization and second course of i.v. ACTH.

Comments: Four previous courses of i.m. ACTH, total 8640 mg. i.v. ACTH was preceded by 440 mg. ACTH i.m. with little effect. Resistance to i.m. therapy and eosinophil escape promptly overcome with i.v. therapy.

| C.T. (2nd admission) | 160 | 9 | 14 | 0 |

*Results: Excellent remission for 1 week.

Comments: Improvement less prompt than observed with first course.

| 2. H.O'R. | 110 | 9 | 250 | 0 |

*Results: Complete remission for 2 weeks followed by gradual exacerbation.

Comments: Two previous courses of ACTH i.m. required 720 mg. with good results and 600 mg. with poor results. Effective results were obtained with much smaller i.v. dose.

| 3. J.G.  | 145 | 3 | 94 | 6 |

*Results: Good remission from status asthma. Low grade fever and persistent severe bronchitis required intensive antibiotic therapy to control.

Comments: Two previous courses of ACTH i.m. required 800 and 620 mg. Good clinical results with i.v. ACTH but developed anxiety state.

| 4. E.W.  | 120 | 6 | — | — |

*Results: Good partial remission (5 weeks).

Comments: Intensive therapy (no ACTH) for 48 hours had little benefit. Good improvement with small doses of i.v. ACTH.

| 5. J.O.  | 10  | 1 | 636 | 243 |

*Results: Good partial remission (5 weeks).

Comments: Became symptom-free with minute dose of i.v. ACTH.
**Table I (Continued)**

<table>
<thead>
<tr>
<th>PATIENT</th>
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<td>-----------------------</td>
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<tr>
<td>6. W.L.</td>
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*Results*: Excellent remission from bronchial asthma for 5 weeks. Persistent bronchitis required intensive antibiotics and iodides for control.

*Comments*: Had 5 day febrile episode beginning 2nd day after course of i.v. ACTH. Etiology not determined.

| 7. J.K. | 210 | 7 | — | — |

*Results*: Completely symptom-free for 6 weeks. Required no therapy in remissive state.

*Comments*: Seriously ill, non-responsive to all treatment prior to i.v. ACTH.

| 8. N.K. | 130 | 4½ | 738 | 0 |

*Results*: Symptom-free for 6 weeks. Low grade bronchitis persisted, ultimately responded to therapy.

*Comments*: Striking improvement from bronchial asthma after 12 hours of i.v. ACTH.

| 9. L.F. | 100 | 5 | 819 | 7 |

*Results*: Excellent remission (1 week).

*Comments*: Two previous courses of ACTH i.m. required 845 mg. with 1 week remission and 520 mg. with 5 months excellent and 3 months partial remission.

| 10. C.L. | 55 | 4 | 969 | 6 |

*Results*: Excellent remission.

*Comments*: Prolonged hospitalizations during June and July in past 3 years. Complete remission with i.v. ACTH in 5-day hospitalization.

*Follow-up to date, July 1, 1951.*
observations with intravenous ACTH infusions in a large series of patients. They pointed out that the longer the period of the infusion, the longer the effects of adrenocortical stimulation last, that only a small daily dose (20 mg.) is required for maximal effect and that a daily eight-hour infusion continued for more than three days may result in a constant, maximal level of stimulation from the third day on.

Mandel et al.4 administered ACTH intravenously to 25 patients; four of these were treated for bronchial asthma. The total dose for these four patients ranged from 10 mg. to 88 mg. given over a period of two to eight days. Two patients received the ACTH infusions for 20 out of each 24 hours. One patient received an eight to 12 hour infusion daily and the fourth patient was given intravenous injections every six hours. All four patients had excellent immediate results and no untoward effects from the infusions. The authors concluded that, in comparison with the intermittent intramuscular route, the intravenous route results in a more prompt and complete clinical response, as well as an earlier and more marked change in eosinophil count and in sedimentation rate.

We have described our laboratory and clinical results in the management of severe bronchial asthma with ACTH administered intramuscularly.5-7 The total dose of a single course of therapy ranged between 240 mg. and 1070 mg. and the duration of treatment from 2½ to 19 days. Since April 1951, we have given 11 courses of intravenous ACTH to 10 patients suffering from severe acute or intractable bronchial asthma. In Table I are listed the particulars about each patient and the treatment. Brief case reports are given at the end of this paper.

**Technique**

The patient was started on a continuous infusion of 5 per cent glucose in distilled water (three liters per 24 hours, 30 drops per minute flow), usually with 0.5 gm. of aminophyllin per liter of fluid. ACTH was added, 10 mg. per liter, and a total dose of 30 mg. per 24 hours was given for one or more days. As improvement occurred, the dose was usually decreased to 15 or 10 mg. per 24 hours until satisfactory recovery was observed.*

The total dose of a course of therapy ranged from 10 mg. to 210 mg. of ACTH and the duration of treatment from one day to nine days.

*Recently we have modified our routine as follows: After the second day of continuous ACTH i.v. therapy, the ACTH is administered only in the first liter of fluid daily. The infusion of glucose, with or without aminophyllin, is continuous.
Results

In Table I are the results of treatment. Seven patients became symptom-free for variable lengths of time, followed by partial remissions. The others had only partial remissions. There were no complete therapeutic failures. To date (follow-up from one week to 10 weeks) there have occurred two severe recurrences, Case 1 (C.T.) about eight weeks after i.v. ACTH treatment, and Case 2 (H.O'R.) about three weeks after treatment. All other patients have remained in good partial remission up to the present, the longest period being eight weeks.

Discussion

Several advantages are obvious at once when ACTH is administered by continuous intravenous infusion rather than by intermittent intramuscular injections. A more rapid therapeutic effect may be observed and this apparently is maintained throughout the 24-hour period. The total dose is about one-fifth to one-eighth of that required intramuscularly. Some effects are obtained at an accelerated rate.

Cases 1, 2, 3 and 9 demonstrate the great saving in material and expense when ACTH is given by the intravenous rather than the intramuscular route. Case 2 (H.O'R.) previously had received 720 and 600 mg. of ACTH i.m. which had given her a remission of one month and one week respectively. The intravenous course of ACTH totalled 110 mg. and was followed by two weeks of complete and one week of partial remission. Case 3 (J.G.) had received previously 800 mg. and 620 mg. of ACTH i.m. which was followed by five months and four months respectively of satisfactory partial remissions. The intravenous course of ACTH was 145 mg. and was followed by a good remission to date. Case 1 (C.T.) had received a total of 8200 mg. of ACTH i.m. over five months (three intensive courses and maintenance therapy in between these courses) during which time he suffered three severe bouts of status asthmaticus. During the third course he received a total of 740 mg. of ACTH and this was followed by nine weeks of partial remission. At the outset of his fourth hospital admission, he was given a fourth course totalling 440 mg. of ACTH i.m. without clinical improvement and without effect on the eosinophils. When i.v. ACTH was started, prompt clinical effect and striking eosinopenia were observed. A total dose of only 92.5 mg. was followed by six weeks of complete and two more weeks of partial remission. This case, moreover, demonstrates that resistance to i.m. ACTH and eosinophil escape was overcome by i.v. administration.

Case 9 (L.F.) was given i.m. ACTH in August 1950, a total dose...
of 845 mg. over 12½ days. She had an excellent remission which lasted eight days only. A second course was given, 520 mg. over five days, which was followed by five months of excellent remission and three months of partial remission. The present course of i.v. ACTH totalled 100 mg. given over five days and resulted in excellent remission to date (six days).

Physiologic effects, particularly "moonning" of the face, weight gain and a sense of well-being, with psychic manifestations varying from elation to anxiety, eosinopenia and subjective clinical improvement were noted quite promptly with i.v. therapy. However we are not prepared to conclude from our small series of cases that the duration of hospitalization will be shortened by using the intravenous route.

Case 3 (J.G.) had a temperature elevation of 100 degrees F. one day after cessation of i.v. ACTH therapy. Several days later he complained of a profuse rhinorrhea and coughing paroxysms which were productive of several ounces of white mucoid sputum in a 24-hour period. The temperature subsequently rose to 102.2 degrees F. The white blood count ranged from 13,000 to 15,000 and the eosinophil count had risen again at this point. The aureomycin, which he had received since admission, was omitted and penicillin was substituted. The febrile episode subsided and his clinical findings improved. It is interesting to speculate that the acute sinobronchitic flare-up was possibly related to the withdrawal of ACTH with subsequent lymphoid hyperplasia.

Case 6 (W.L.) had chills and fever lasting five days after having received ACTH i.v. for two days. He was the only patient who did not receive antibiotics during ACTH therapy. Forty milligrams of ACTH, even though given intravenously, is a small dose; its relation to this febrile episode is not certain.

All of our patients receiving ACTH are placed concurrently on penicillin or aureomycin to protect against the possibility of greater susceptibility to infection which may follow in the wake of ACTH therapy. A persistent type of bronchitis, generally responding to intensive antibiotic therapy, iodides and antihistaminics, has been observed in most of our patients who have received ACTH by both the i.m. and i.v. routes.

Although some clinical and laboratory studies would suggest beneficial effect from ACTH initially in combating infection, on the other hand there are conclusive studies indicating that cortisone and perhaps ACTH may actually depress resistance to infection. Recently this subject has been reviewed most thoroughly by Kass and Finland.8 These authors also presented evidence suggesting that adrenocortical hormones themselves may be of pathogenic importance in some diseases.
Case Histories

Case 1 (C.T.), a 50 year old white male executive, was well until 18 months ago, when he developed severely progressing bronchial asthma and emphysema. During this period he was hospitalized three times because of severe status asthma and was given three intensive courses of ACTH i.m. Interim daily maintenance ACTH therapy was continued at home for several months. A total of 8.2 grams of ACTH was administered. He appeared to have made an excellent recovery. In January 1951, pulmonary function studies revealed: vital capacity, 5.1 liters; maximum breathing capacity, 92 per cent of predicted normal; an enlarged residual air and total lung volume and a high residual air to total lung volume ratio of 44 per cent (normal, 30 per cent).

His subsequent admission was for severe progressive cough and wheezing which followed a severe upper respiratory infection one month ago. He was admitted on April 2, 1951 in marked respiratory stridor and status asthma. He was treated with bronchodilator sprays, a continuous intravenous infusion of 5 per cent glucose in distilled water plus 0.5 gm. of aminophyllin per liter of fluid, saturated potassium iodide, Demerol and penicillin. Despite these procedures, he grew worse and a fourth course of ACTH i.m., totalling 440 mg. was administered. He appeared to be somewhat improved. The initial eosinophil count was 377/cu. mm. and decreased to 118/cu. mm. in 24 hours; but then rose daily to a high of 2600/cu. mm. on the fifth day of i.m. ACTH therapy. ACTH was discontinued and all other medication was continued, but in 48 hours he was again acutely ill with severe respiratory stridor. The eosinophil count at this time was 2481/cu. mm. In the hope of effecting a better clinical response, as well as a more adequate eosinopenia, he was started on intravenous ACTH. Ten milligrams of the Armour ACTH preparation were added to each liter of the intravenous infusion which had been maintained since admission. He received 30 mg. per 24 hours for the first two days, and 15 mg. per 24 hours thereafter; total dose was 92.5 mg. over four days. Striking subjective and objective improvement occurred within several hours after the i.v. ACTH was started, and he was free from cough and wheezing on the second day. There was striking reduction in eosinophils from 2481 to 611/cu. mm. on the second day, 27/cu. mm. on the third day and 88/cu. mm. on the fourth day of i.v. ACTH treatment. "Mooning" occurred within 24 hours but no other abnormalities were noted. He was discharged symptom-free on April 22, 1951; the eosinophils were 1493/cu. mm. He was placed on maintenance aminophyllin solution per rectum, potassium iodide and antihistaminic drugs by mouth.

In his sixth week of remission, he again required bronchodilator sprays in addition to other maintenance therapy. Two weeks later he developed a severe recurrence of coughing and wheezing and he had to be readmitted in status asthmaticus on June 7, 1951. He was started on a continuous intravenous infusion of 5 per cent glucose in distilled water, three liters per 24 hours, containing 0.5 gm. of aminophyllin and 10 mg. of ACTH per liter. He also was given ether in oil, oxygen, Vaponefrin aerosols and penicillin. He did not become free of severe asthmatic crises until the third day of ACTH therapy. Remarkable improvement was noted on the fifth day. He received a total dose of 160 mg. of ACTH over nine days. The eosinophil count was 14/cu. mm. on admission and became zero the next day; two days after the ACTH, the eosinophil count was 1706/cu. mm. He was discharged well on June 23, 1951.
Case 2 (H.O'R.), a 40 year old housewife, had suffered from continuous progressive bronchial asthma for nearly one year. In December 1950, she was hospitalized because of intractable coughing productive of purulent sputum, and wheezing. For four weeks, she was treated with bronchodilator aerosols, oxygen, penicillin, aureomycin and various other drugs. Nevertheless she progressively grew worse, became stuporous and finally comatose. Bronchoscopic aspiration was performed without benefit. A course of ACTH i.m. was started. During the first 24 hours, she appeared terminal. However, during the second 24 hours she was "alive" and improvement progressed rapidly. She required a total of 720 mg. of ACTH over a 10 day period. She continued to improve for one week after discharge and remained well for a total period of one month.

Then the coughing, wheezing, expectoration and dyspnea recurred and progressed, requiring readmission on February 1951, about eight weeks after discharge. She was treated with the usual therapy for two weeks, during which time her condition deteriorated. A second course of i.m. ACTH was started. She received 600 mg. over an eight days' period. Striking improvement did not appear until the fourth day. She was discharged feeling partly relieved but within four weeks she had to be readmitted for the third time.

Once again she was treated intensively with penicillin, terramycin, bronchodilator aerosols, aminophyllin, infusions, oxygen, etc., over a five weeks period. Despite these procedures she grew worse and again filled up with purulent secretions and became stuporous. On May 4, 1951 she was started on her third course of ACTH, this time intravenously. For the first three days she received a continuous i.v. infusion, totalling 50 mg. of ACTH, then 10 mg. daily for the following six days. She received a total of 110 mg. of ACTH over nine days. By the end of the first 24 hours (20 mg. ACTH), she was slightly improved. After the next 24 hours (about 40 mg. ACTH), she was considerably improved. She was discharged 10 days after i.v. ACTH was started in good remission. A two weeks follow-up revealed complete remission; she felt much better than she ever had before. At four weeks after discharge she again was suffering from troublesome productive cough and dyspnea. These symptoms grew progressively worse. She was readmitted on June 19, 1951, dyspneic and slightly cyanotic. The intern administered adrenalin and Demerol without benefit and she died suddenly three hours after admission. The gross pathologic sections revealed diffuse bronchiolar obstruction, severe emphysema, and a mitral stenosis of rheumatic etiology.

Case 3 (J.G.), a 55 year old grocer, suffering from bronchial asthma for 10 years, had frequent hospitalizations in status asthmaticus. In 1949 he had a sympathetic denervation. In July 1950 he received 800 mg. ACTH i.m. followed by about five months of good remission. A second course of ACTH i.m. was given in December 1950, totalling 620 mg. followed by about four months of partial remission. Four days before present admission, he developed intractable coughing with continuous asthma which could not be relieved by i.v. aminophyllin and Demerol.

On admission May 24, 1951, he was started on a course of continuous infusions of 5 per cent glucose in distilled water, three liters per 24 hours, containing 0.5 gm. of aminophyllin and 10 mg. of ACTH per liter of fluid. In addition he was given aureomycin, potassium iodide and Demerol. Objective improvement was noted in 10 hours. However, on the second day he appeared anxious and nervous and alternatingly depressed. The
ACTH was increased to 25 mg. per liter and he was also given nasal oxygen. This was continued until the fourth day when ACTH was omitted (total dose 145 mg.), because of rather severe anxiety and apprehension. All other medications were continued. The following day his temperature was 100 degrees F. and he ran a low grade fever for several days. After a few days of normal temperature, he developed a fever of 102.2 degrees F. He had a profuse rhinorrhea and recurrence of bouts of coughing productive of mucoid sputum. Sputum culture revealed a gamma streptococcus, and nasal culture revealed staphylococcus aureus and alpha streptococcus. The aureomycin was discontinued and replaced by penicillin. Ten days later he showed good improvement. The vital capacity, which could not be obtained at the time of admission because of severe coughing paroxysms, rose progressively to four liters. He was finally discharged symptom-free on June 22, 1951.

Case 4 (E.W.), a 22 year old female with non-seasonal bronchial asthma since childhood, required daily medication to maintain comfort. She developed an acute asthmatic attack which progressed over a two weeks period despite a host of medicaments, including several i.v. injections of aminophyllin. On admission April 11, 1951, she was in status asthma. During the first 48 hours she was treated with continuous aminophyllin i.v., adrenalin i.m., potassium iodide and chloral hydrate p.o., nasal oxygen and penicillin with bronchodilator aerosols. There was no appreciable improvement. All medication was stopped and she was started on a constant infusion of 5 per cent glucose in water containing 10 mg. ACTH per liter of fluid. She received 30 mg. per 24 hours for two days and 15 mg. per 24 hours thereafter, totalling 120 mg. over six days. She required only one i.v. aminophyllin injection about eight hours after i.v. ACTH had been started. She became comfortable within 24 hours and she was discharged on April 21, 1951, in partial, but good remission. Her partial remission has continued and she feels greatly improved.

Case 5 (J.O.), a 10 year old schoolboy, had bronchial asthma since the age of two years, with exacerbations during spring and fall. The present attack of intractable asthma started three weeks before admission, and was not relieved by bronchodilator aerosols and other medications. He was hospitalized on May 4, 1951, in a condition of chronic depletion, cyanosis and severe asthma. He was treated with Demerol, potassium iodide, aureomycin and a continuous i.v. infusion of 5 per cent glucose in water to which was added 0.25 gm. of aminophyllin and 5 mg. of ACTH per 1500 cc. of infusion. He received a total of 10 mg. of ACTH over 24 hours with striking clinical improvement. The eosinophils decreased from 636 cells to 243/cu. mm. He was discharged on May 11, 1951, symptom-free and was placed on rectal aminophyllin, potassium iodide and bronchodilator sprays, maintaining a partial remission.

Case 6 (W.L.), a 49 year old white male machine-inspector, had been suffering from low grade chronic morning cough for about 25 years. Two years ago he developed non-seasonal bronchial asthma, frequently associated with upper respiratory infections. The past history was negative except for an attack of pleurisy two years ago.

The present acute illness started the day before hospitalization with intense coughing and wheezing which did not respond to aminophyllin, adrenalin and antihistaminic preparations. On admission May 7, 1951, he was started on i.v. ACTH, 10 mg. per liter of 5 per cent glucose in
water with 0.5 gm. aminophyllin. Three liters were administered in each 24-hour period. He received a total of 40 mg. ACTH over 48 hours. The circulating eosinophils decreased from 175/cu. mm. to 19/cu. mm. Potassium iodiode, expectorant cough mixture, chloral hydrate and bromides were given as adjuvants. Clinical improvement was striking by the second day; the i.v. ACTH was stopped and rectal aminophyllin solution was substituted. Two days later (fifth hospital day) he developed a fever of 100 degrees F, and he ran a febrile course for five days with temperatures up to 103.6 degrees F, with a concomitant rise in pulse and in respiration. He had profuse perspiration and several shaking chills at the height of the fever. Physical examination was negative, as was also an x-ray film of his lungs. The white blood count ranged between 10,000 and 12,000 with a normal differential count. Blood cultures, cold agglutination tests and other serologic studies were negative. He was given aureomycin for three days without effect on the fever; this was followed by penicillin i.m. every three hours for five days. He made a complete uneventful recovery. At the time of discharge on May 20, 1951, he was symptom-free and this state was maintained at the time of a follow-up five weeks after the noted improvement from i.v. ACTH.

In contrast to all the other patients on i.v. ACTH, he had not received antibiotic therapy during treatment with ACTH. The cause for the febrile episode could not be determined.

Case 7 (J.K.), a 61 year old housewife, had been aware of nasal polypi and chronic bronchial asthma for approximately 13 years. The present illness was characterized by progressive wheezing and coughing over a two week period, and on May 4, 1951 she required hospitalization because of status asthmaticus.

She was first treated with i.v. aminophyllin, adrenalin in oil and barbiturates but failed to respond. She was then started on a continuous i.v. infusion of three liters of 5 per cent glucose in distilled water per 24 hours, containing 1.5 gm. of aminophyllin and 30 mg. of ACTH, and was also given Demerol and oxygen. After 48 hours, she was free of asthmatic attacks and from that time on, she showed rapid improvement. Treatment was continued for seven days; the total dose of ACTH was 210 mg.

She was discharged symptom-free on May 15, 1951. Her vital capacity, which could not be measured at first, was 2.2 liters. Complete remission has been maintained.

Case 8 (N.K.), a 46 year old secretary, has had chronic bronchial asthma since the age of 27, with seasonal variations, due largely to pollens and infections. She suddenly developed an attack of severe bronchial asthma during an acute atypical pneumonia in January 1951. She responded to therapy and remained comparatively well on maintenance treatment until May 1, 1951 when she again developed severe bronchial asthma, relieved only slightly and temporarily by i.v. aminophyllin injections and Demerol. Hospitalization was necessary two days later.

Upon admission she was given a continuous i.v. infusion of 5 per cent glucose in water with 0.5 gm. of aminophyllin per liter, and Demerol, 50 mg. a.c. every eight hours. When there was no evidence of improvement after 12 hours, ACTH was added to the infusion (10 mg. per liter). She received 30 mg. per 24 hours of ACTH over a period of 4½ days; a
total dose of 130 mg. ACTH. Aureomycin, 500 mg. p.o. every six hours was also given. Improvement was observed within 12 hours. Puffiness of the face was noted after 48 hours of continuous i.v. administration of ACTH. On the fifth day, the lungs were clear and she was discharged symptom-free on May 10, 1951. The eosinophils decreased from 738/cu. mm. to 3/cu. mm. 24 hours later and to zero the next day. On the day of discharge, the eosinophil count was 163/cu. mm. Complete remission has been maintained.

Case 9 (L.F.), a 52 year old housewife, had suffered from bronchial asthma for about eight years. In August 1950 she developed a progressive severe attack of bronchial asthma and she became refractory to epinephrine, aminophyllin and antihistaminics. She was given 845 mg. of ACTH i.m. with complete remission which lasted only eight days. She was given a second course of ACTH i.m. totalling 520 mg. Clinical remission was complete and lasted five months, followed by three months of partial remission. During the spring of this year, she again became refractory to epinephrine and aminophyllin and was given two courses of oral prednisone, about 500 mg. each, with temporary improvement.

The present admission (June 15, 1951) was necessitated by severe intractable bronchial asthma of six days duration, not relieved by i.v. aminophyllin and Demerol. She was started on a course of continuous infusions of 5 per cent glucose in distilled water, three liters per 24 hours, containing 10 mg. of ACTH per liter. She also received potassium iodide, Demerol, sedatives, penicillin and i.v. aminophyllin for severe attacks of asthma. She became free of asthmatic attacks in about 24 hours, but coughing and wheezing did not disappear until the fifth day of i.v. ACTH therapy. The total dose of i.v. ACTH was 100 mg. The eosinophils decreased from 819/cu. mm. (control level) to 19/cu. mm. in 24 hours, 7/cu. mm. on the fourth day, and rose to 200/cu. mm. two days after ACTH was discontinued.

While this patient had previously reacted to iodides with rashes and edematous eyelids, she was able to tolerate large doses of potassium iodide this time while receiving i.v. ACTH. She was discharged symptom-free on June 22, 1951 and has remained well one week to date.

Case 10 (C.L.), a 67 year old painter, has had bronchial asthma since the age of 30 years, with severe exacerbations during June and July. During the past few years hospitalization for several weeks at a time has been necessary during these months because of the severity of the bronchial asthma. Attempts at hyposensitization with June grasses have been unsuccessful.

He was hospitalized on June 26, 1951 because of severe bronchial asthma which had failed to respond to adrenalin and aminophyllin i.v. He was started on a continuous i.v. infusion of 5 per cent glucose in distilled water to which was added 10 mg. of ACTH per liter. In the first 24 hours, he received a total of 25 mg. of ACTH, and 10 mg. in one liter of fluid daily for the next three days, totalling 55 mg. of ACTH.

Striking improvement was noted 16 hours after the infusion was started. The eosinophil count on admission was 969/cu. mm. and decreased to 6/cu. mm. the next day. The vital capacity, which could not be obtained on admission because of dyspnea, improved progressively to 2.8 liters at the time of discharge. He was discharged symptom-free on the fifth hospital day, and remission has been maintained to date.
SUMMARY

1) Eleven courses of intravenous ACTH by continuous infusion were given to 10 patients with severe bronchial asthma.
   2) The total dose ranged between 10 mg. and 210 mg. given over a period of one to nine days.
   3) Seven patients obtained excellent remissions lasting up to six weeks. The others obtained partial remissions only. There was no complete therapeutic failure.
   4) One patient who demonstrated clinical resistance and eosinophil escape with i.m. ACTH responded promptly to i.v. ACTH.
   5) Antibiotics should be administered concomitantly, particularly to those patients with bronchitic manifestations, to combat possible depressed resistance to infection produced by ACTH.

CONCLUSIONS

The use of i.v. ACTH offers an effective means in the treatment of severe bronchial asthma. The total dose, and thus the cost to the patient, is cut to one-fifth to one-eighth of that required when ACTH is given intramuscularly. It appears to be an effective way of sending an infant on a man's errand. This route of administration is particularly effective when the patient demonstrates resistance to i.m. ACTH or eosinophil escape. No allergic reactions were observed in this small but intensively treated series. Two patients had febrile episodes following shortly after ACTH therapy, the pathogenesis of which could not be determined.

Occasionally, one observes following the cessation of ACTH therapy a rapid recurrence of respiratory difficulties. We have attempted to prevent such recurrences as well as to prolong the remissive state by the administration of large doses of oral* or rectal aminophyllin and antibiotics when indicated.

*Large doses of oral aminophyllin were given without gastric distress in the form of a proprietary tablet (Dainite®) kindly supplied by Irwin, Nelsler Co., Decatur, Illinois.

RESUMEN

El uso del ACTH intravenoso ofrece un medio efectivo en el tratamiento del asma bronquial severo. La dosis total, y por consiguiente el costo para el paciente, se reduce a de una quinta a una octava parte de la requerida para administración intramuscular. Parece ser una forma efectiva de que un niño haga la tarea de un adulto. Esta ruta de administración es especialmente efectiva cuando el paciente muestra resistencia al ACTH intramuscular, o persistente eosinofilia. En esta serie pequeña pero que recibió tratamiento intenso, no se observó ninguna reacción alér-
gica. Dos pacientes tuvieron episodios febriles poco después de la terapia con ACTH, cuya patogénesis no pudo ser determinada.

Ocasionalmente se observa, al suprimir la terapia con ACTH, un rápida reaparición de los trastornos respiratorios. Hemos procurado evitar tales reapariciones y prolongar el estado remisivo por medio de la administración de dosis grandes, orales o rectales, de aminofilina y antibióticos, cuando son indicados.

RESUME

L'utilisation de l'A.C.T.H. par voie intraveineuse est un moyen efficace pour lutter contre les formes graves de l'asthme. La dose totale est abaissée au cinquième ou au huitième de celle qui est nécessaire quand l'A.C.T.H. est employé par voie intramusculaire. Cette diminution des doses entraîne une diminution parallèle du prix de revient du traitement. Ce mode d'administration est particulièrement efficace quand le malade se montre résistant à la voie intramusculaire ou ne devient pas éosinophylque. Les auteurs n'ont pas constaté de réactions allergiques. Deux malades eurent des épisodes fébriles suivant de peu le traitement par l'A.C.T.H., la pathogénie n'en a pu être éclaircie.

Dans certains cas, on a pu observer la rapide réapparition des troubles respiratoires après cessation du traitement par l'A.C.T.H. Les auteurs ont essayé de prévenir de telles rechutes et de prolonger la période de rémission. Ils ont utilisé dans ce but de fortes doses d'aminophylline par voie buccale ou rectale et des antibiotiques quand ils étaient indiqués.

REFERENCES


