

ACTH and cortisone therapy of asthma

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ACTH and Cortisone Therapy of Asthma

Bram Rose (Montreal)

Summary

The patients studied in this series comprise a group of 100 asthmatics, some of whom had their first course of ACTH in September of 1949. Since that time, ACTH has been administered intramuscularly, subcutaneously and, more recently, by the intravenous route, and Cortisone either intramuscularly or orally. The effects of long-term therapy, advantages of the various modes of administration, choice of patient, and the complications which may arise will be discussed briefly.

It may be stated that intravenous ACTH is the treatment of choice in acute status, remission usually occurring within 12–24 hours. Either oral Cortisone, or ACTH in gelatin or some other vehicle which delays absorption is suitable for ambulatory patients whose symptoms are not too severe. Resistance to both preparations may occur. Whenever possible, desensitization to inhalants or other modes of standard treatment is preferable and should be tried before resorting to ACTH or Cortisone.

Discussion:

B. N. Halpern (Paris): Nous avons été vivement intéressés par le brillant exposé de notre ami le Dr *Bram Rose*. Notre expérience personnelle avec l'ACTH et la cortisone dans le traitement de l'asthme nous a donné l'impression que si chez les sujets jeunes l'ACTH agit avec régularité et souvent d'une manière spectaculaire, l'effet de l'hormone corticotrope est moins fidèle et moins brillant chez les sujets qui ont dépassé la cinquantaine. Il semble que chez les malades âgés la surrénale réponde moins bien à la stimulation hypophysaire. Or, chez ces malades âgés, la cortisone exerce un effet thérapeutique bien meilleur. Nous administrons généralement à ces malades comme traitement d'attaque pendant 3 jours 200 à 300 mg de cortisone par jour par voie intramusculaire. En général, après ce laps de temps, les symptômes de l'asthme s'estompent; nous diminuons alors les doses et en même temps, nous abandonnons la voie parentérale pour administrer la cortisone par la bouche. Certains de ces malades sont actuellement en traitement depuis 5 mois. Une dose de 50 mg de cortisone tous les deux jours maintient certains de nos malades dans un état d'équilibre. Certains jours, de petites rechutes nécessitent une intensification momentanée du traitement. Pour maintenir une certaine activité surrénalienne que le traitement prolongé par la cortisone tend à amenuiser, nous administrons à nos malades toutes les semaines ou toutes les deux semaines pendant 3 jours 30 mg d'ACTH par voie souscutanée. Le poids, la glycémie, le sang, l'hémodynamique de ces malades sont régulièrement et rigoureusement

surveillés, mais nous leur laissons, sauf en période de traitement intensif, une liberté relative et nous ne leur imposons aucun régime strict. Toutefois ils ont une diète hyposalée et en cas d'augmentation importante de poids, ils sont soumis à une restriction chlorurée sodique et liquidienne plus sévère. Tous les malades reçoivent au cours du traitement de l'acétate de potassium pour parer à la perte de potassium habituelle durant le traitement par cortisone ou ACTH. Nous n'avons observé chez 11 de nos malades soumis à ce traitement prolongé aucun accident imputable à cette thérapeutique.

G. Katsch (Greifswald) stellt die Frage, ob nicht die Insulinschockbehandlung allergischer Krankheiten als eine milde und natürliche ACTH- bzw. Cortisontherapie anzusehen sei. Die zuerst schon vor vielen Jahren von *Wegierko* vorgeschlagene Insulinschockbehandlung allergischer Störungen wird an der Greifswalder-Klinik oft mit gutem Erfolg angewandt, nicht nur bei Asthma. Verwendet werden geringe, nicht krampfauslösende Dosen. Es liegt nahe, anzunehmen, daß durch die Insulinwirkung nicht nur Adrenalin, sondern auch über die Hypophyse Cortison mobilisiert wird, sei es durch direkte Gegenregulation, sei es durch diesen Stoß in das endokrine Regulationssystem.

M. Taubenhaus (Chicago): Are adrenal cortical function tests commonly employed positive in cases of allergy and do allergic manifestations occur more often in Addisonism?

K. Wilken-Jensen (Hellerup): It was the mention of insulin treatment which made me take the word.

Some years ago I gave insulin injections to some patients in Denmark and tried to measure the adrenalin in the blood at the same time, using Kalaja and Savolainen's modification of Huber's method. In patients not too sick I found an increase in the blood adrenalin, while the patient who was worst off did not show any apparent increase, but as the method did not appear to be very accurate I gave it up.

Even if Dr. *Dougherty* said that ACTH could do anything to anything and it thus may be *post festum*, I should like to ask Dr. *Rose* if he has seen the same changes in the blood after insulin as after ACTH.

Dr. *Holten* told us yesterday about the blood sugar which fell below and later rose to above normal after ACTH. I found the same changes after relatively small doses of insulin, probably on account of the rise of blood adrenalin.

Z. Eriksson-Lihr (Helsinki): In his paper Dr. *Bram Rose* mentioned two cases of asthma which reacted in a different way to cortisone. One was a young person suffering from an uncomplicated asthma. Cortisone gave her an excellent and long-lasting improvement. The other person suffered from both bronchial asthma and a chronic sinusitis and her reaction to cortisone treatment was of short duration. I think that these two examples indicate what we have to bear in mind when we start treatment with ACTH and cortisone. These hormones help the patient to overcome a bad attack of asthma or status asthmaticus. After the attack is over, an uncomplicated case remains well until he again comes in contact with his allergen. But a complicated allergic, whose contact with the allergen—for example the infection in the second case—remains, will have remissions in spite of hormonal therapy until the allergen is removed.

As to the question of carbohydrate metabolism in allergics, I did not intend to discuss this problem now, because later this afternoon I am to give a report concerning our studies on this problem. But I will try to give a brief survey of our investigations on this subject, which has interested us since 1948, in connection with our research on the function of the suprarenal hormones in allergy.

We have studied the carbohydrate metabolism in about 250 allergics of different age and suffering from different allergic diseases by the double glucose tolerance test by Staub, the insulin and the adrenalin tolerance tests. These tests showed that the absorption of glucose from the intestines was normal, but the decrease of the blood-sugar after insulin was rapid and it remained low for a long period. A great percentage

of the allergics reacted to the hypoglycemia with a preshock so severe, that the test had to be discontinued by giving glucose. In spite of this some patients developed a major shock with unconsciousness and convulsions. The adrenalin tolerance test showed in about 50% of the allergics an increase of only 25 mg% instead of the normal 45 to 60%.

All these studies showed in about 75–80% of the allergics a disturbance in the carbohydrate metabolism as it is seen in the insufficiency of the 11-oxycorticosteroids of the suprarenals, mainly in Addison's disease.

R. Levine (Chicago): My remarks do not bear directly on the subject under discussion. In view of many remarks made at the Symposium, I should like to point out that we do not as yet possess a «pure» ACTH. The preparations in general use are extremely impure. The work of *Li*, *Morris* and especially that of *Astwood* in the past few years have indicated that ACTH may be a non-protein (?) substance of small mol.wt. Therefore it seems to me that we should postpone our speculations about supposed differences between ACTH and cortisone, and the meaning of the various manifestations which may follow ACTH therapy in man. They may be due to the non-specific materials present in the preparations generally used.

W. Löffler (Zurich): Dr. *Bram Rose* in the second slide showed a case of Purpura Schönlein. May I recall to the audience that in 1833 Schönlein was the first director of the medical clinic of Zurich University. The plan for the old hospital which disappeared just two months ago, was *Schönlein's* work. It was in the same building where our co-worker *F. Koller* found that the injection of ACTH produces a marked raise of *thrombocytes* and is therefore under certain circumstances of considerable help in thrombocytopenic purpura. So our actual work is linked to the research work done at the same place 120 years ago.