The Effect of Adrenocortical and Androgenic Steroid Supplements in Tuberculous Patients Receiving Chemotherapy*

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INTRODUCTION

This study was undertaken to determine whether combined adrenocortical-androgenic steroid therapy would potentiate the patient response to chemotherapy for pulmonary tuberculosis. Although spread or reactivation of a tuberculous process has been attributed to the administration of corticosteroids alone, there is evidence that when properly administered in the presence of adequate antibiotic coverage, steroid hormones do not enhance dissemination. One of the present authors' has commented on the advantages of combined steroid-chemotherapy in tuberculous patients exhibiting severe, untoward drug reactions to one or more of the available anti-tuberculosis agents. The corticoids used in these cases had no harmful effect on the underlying tuberculous process, as evidenced in serial roentgenologic examination of the chest, and also in sputum cultures over a period of 21 to 28 months following steroid treatment.

The beneficial effect of doses of testosterone propionate (androgen) too small to cause edema, gynecomastia or increased excretion of 17-ketosteroids has been reported by one of us. Because of the possibility that the catabolic action of the adrenocortical steroids might be offset by the anabolic effect of an androgenic steroid, both were used in the present study. A careful evaluation of response was made in 20 tuberculous patients, equally divided into two groups (new and re-treatment cases) as noted below. The results of treatment were recorded three to 20 months (average 11.5 months) after discontinuance of adrenocortical endogenic steroid therapy.

SELECTION OF CASES

Group A: Ten patients with active pulmonary tuberculosis (seven far advanced and three with moderately advanced disease) who had not been hospitalized or treated with chemotherapy previously. Their ages ranged from 17 to 51 years. All had cavitation, and nine had positive sputum prior to the institution of antimicrobial therapy supplemented by adrenocortical-androgenic steroids on admission to the hospital. Exudative components on the initial roentgenogram, before treatment began, were present in all.

Group B: Ten patients with far advanced active pulmonary tuberculosis. Ages ranged from 31 to 64 years. The known duration of tuberculosis varied from one to 15 years. All of them had cavitation with positive sputum, and had received antecedent chemotherapy for varying periods prior to the initiation of the new therapy schedule, and had reached a clinical and radiologic "stalemate." Two had thoracic surgery performed at an earlier date (one thoracoplasty subsequently followed by lobectomy with complicating broncho-pleural and pleuro-cutaneous fistulas; and one simple uncomplicated thoracoplasty).

Group C: Ninety-seven patients with comparable disease were observed for two years. They served as "controls," although they were not observed concomitantly with the steroid-treated groups. However, the same criteria of response were applied to them as to those receiving steroid adjuvant therapy.

METHOD OF STUDY

Evaluations and determinations were made in all instances prior to, during the institution of the experimental regimen and for at
EFFECT OF STEROID SUPPLEMENTS IN TUBERCULOUS PATIENTS

At least three months after its discontinuance.

The following pertinent clinical notations recorded were: fever, weight, blood pressure, cough and sputum, bleeding tendency, peptic ulcer history, development of euphoria and other untoward effects of therapy. A postero-anterior chest roentgenogram was taken at monthly intervals. Laminograms were obtained when warranted to determine more accurately the presence or absence of residual cavitation. The other laboratory tests included were: (a) Mantoux test using 1:1000 O.T. (monthly); (b) blood count (weekly); (c) urinalysis (monthly); (d) blood sugar and urea (monthly); (e) sputum examinations (three specimens) or gastric lavages (two specimens) monthly for smear and culture; the standard oral glucose tolerance test, using 100 grams of glucose (monthly) and with specimens of blood and urine drawn before, one-half, one, two, three and four hours after the glucose was administered; (g) total serum protein (monthly); (h) serum globulin distribution patterns — serum mucoprotein determination (modification of Winzler technique) (normal values 40-80 mg. per cent); zinc sulfate turbidity (Kunkel technique) (normal values 4-8 units); acid precipitable globulin (Greenspan technique) (normal values 4-8 units). These tests were done at monthly intervals with the exception of the zinc sulfate turbidity test which was repeated every two weeks during the time adrenocortical-androgenic steroids were being administered.

METHOD OF TREATMENT

(A) Chemotherapy of Tuberculosis: The new cases of tuberculosis (Group A) without previous chemotherapy all received equal parts of streptomycin and dihydrostreptomycin.
cin sulfate (Distrycin) (1 gram intramuscularly twice weekly) and isoniazid (INH) 300 mg. daily in three divided doses. The old retreatment cases of tuberculosis (Group B) continued with whatever combination of drugs they were receiving when the supplementary adrenocortical androgen therapy was introduced. These latter patients were receiving the following drugs: cycloserine and INH—three cases; INH and para-aminosalicylate (PAS)—two cases; Distrycin and INH—one case; viomycin, INH, PAS—two cases; viomycin, Distrycin, INH, PAS—two cases; Thus, INH was administered to all patients in this group in combination with one or more other chemotherapeutic agents. All of these patients (Group B) were maintained on the same chemotherapy in their poststeroid therapy observation period.

(B) Adrenocortical Therapy: All of the 20 patients received the same dosage schedule for 12 weeks. The steroid used was prednisolone (Delta-Cortef) 15 mg. three times daily orally for three days, then 10 mg. t.i.d. for the next three days, then 5 mg. t.i.d. until the tenth week; tenth week—5 mg. b.i.d.; eleventh and twelfth weeks—5 mg. daily. On termination, the patients received 80 units ACTH intramuscularly daily for three consecutive days.

(C) Androgen Therapy: All of the 20 patients received the oral testosterone preparation, fluoxymesterone (Halotestin), in the dosage of 5 mg. daily for the duration of adrenocortical therapy (12 weeks). The androgen was added for these reasons: (1) to counteract the possible gluconeogenic effect of the steroid; (2) to lessen protein catabolism and (3) to minimize the development of osteoporosis with the prolonged use of steroid therapy.

(D) Associated Therapy: During this same 12-week period, all patients were placed on a salt poor diet (about 3 grams) and given potassium chloride 3 grams daily.

Results of Treatment

After the termination of the adrenocortical-androgenic regimen, all of the 20 patients were followed closely for at least three months and some for as long as 20 months. The average follow-up observation period was 11.5 months.

(A) Clinical Findings: (1) Fever: All of the patients in Group A had temperatures of 100°F. or higher on admission. In nine the fever subsided within three to 14 days after onset of combined therapy. None of the cases in Group B was febrile just before institution of treatment. One patient in this latter group developed fever about ten days after institution of steroid supplements with roentgenologic evidence of increased infiltration on the right side (impression of nontuberculous pneumonitis). The steroid combination was interrupted for two and one-half weeks during which interval tetracycline (1.0 gram daily) was given. Complete regression of the above x-ray findings occurred. The therapy was then re-instituted.

(2) Weight: Nine patients in Group A gained weight (maximum 20 lbs.) during the regimen. Their weight remained stationary or increased after the discontinuance of the adrenocortical-androgen schedule. Of the ten patients in Group B, five who showed a somewhat stationary or declining weight curve for varying periods before steroid therapy, gained three to ten lbs. during the treatment and maintained this advantage afterwards.

(3) Cough and Sputum: A significant diminution in these symptoms occurred in nine patients of Group A; a similar improvement was noted in three cases of Group B during treatment, but return to the previous status was observed subsequently. Two patients in Group B, who had bronchospasm associated with their pulmonary tuberculosis, showed definitely less dyspnea during adrenocortical-androgen steroid therapy, but dyspnea recurred after this therapy was stopped.

(4) Blood Pressure: This remained within normal limits in all 20 cases. No essential change was noted during the therapeutic regimen or afterwards.

(5) A sense of increased well being was elicited in nine patients of Group A and five of Group B during treatment.
(B) Roentgen Findings: Group A: During the 12-week period of adrenocortical-androgen steroid therapy, eight of the ten cases revealed moderate to marked roentgenologic regression of infiltrative disease, with definite closure of the cavity in two instances. This status continued afterward. Two cases showed closure of cavity in the post-therapy phase and in another case it was questionable. One other patient had lobectomy performed for residual cavitation about three months after completion of the steroid therapy, with conversion of the sputum postoperatively. Two showed regression of cavity during therapy and no significant change post-therapy, but both refused surgical intervention. One case revealed no change in cavity during therapy, but did show an increase subsequently at the time of a superimposed myocardial infarction. Finally, one, in whom clinical diabetes was evidenced during the course of therapy, had extensive bilateral exudative and cavitary disease. She exhibited fever, weight loss and progression of disease during treatment with the outlined regimen. Death occurred 10½ months after the regimen was discontinued. Whether the diabetes would have manifested itself without steroid therapy is, of course, impossible to know.

Group B: During adrenocortical-androgen steroid therapy, two cases revealed slight regression of infiltration, one of them in cavity size as well. Two other cases showed slight shrinkage of cavities. However, the roentgenologic improvement in these four cases was of little clinical significance. Five cases showed a stationary radiologic course during and after therapy. One patient exhibited an increase in cavity size during treatment which receded after ward. Two of the ten cases died (both with large terminal hemoptyses) 13½ and 20½ months after discontinuance of steroid therapy.

(C) Other Laboratory Findings: (1) Sputum and Gastric Lavage Tests: Five patients in Group A showed conversion on culture during the therapy period and this status continued subsequently. One, in whom previous reference was made as to questionable cavity closure, had negative sputum examinations during therapy, one positive culture post-therapy which subsequently converted. Three had positive sputum on smear or culture or both before, during and after therapy. The one subjected to lobectomy converted her sputum postoperatively. In contrast to this, the bacillary examination of one patient in Group B became negative. This occurred during the second month of adrenocortical-androgen steroid, and remained negative during the entire observation period. No other conversion on smear and/or culture was noted in the remaining nine cases.

(2) Mantoux Test: No significant variation occurred in the size of the tuberculin reaction observed during or after treatment with the steroids as compared to the pre-therapy reaction.

(3) No significant variations were observed in the peripheral blood count, urinalysis, blood urea and total serum protein determinations.

(4) Glucose Tolerance Test: This was considered normal if the blood sugar returned to 120 mg. per cent at the end of two hours, and if it did not rise above 180 mg. per cent during the period of the test. With the criterion, seven of the 20 patients (35 per cent) demonstrated a reduced tolerance for glucose prior to the institution of steroid-androgen therapy. Five (25 per cent) of them continued to show this reduced tolerance during and after steroid treatment. One patient was abnormal only during the therapy phase and reverted to a normal tolerance at the end of the therapy. Another, who had been abnormal, became normal throughout the therapy period and afterward. In these two cases, the reversion coincided with improvement in their disease state. When the successive glucose tolerance curves obtained for each patient are plotted together, one observes several types of response: (a) all curves remain within normal or abnormal limits; (b) the pretreatment curve is essentially normal, but after the first month of exposure to steroids, the greatest depression in glucose tolerance occurs. This gradually returns to normal as
the steroids are reduced or withdrawn (Fig. 1); (c) the tolerance for glucose is increasingly depressed during the observation period, and returns to normal after the steroids are terminated (Fig. 2).

Of the 13 patients who demonstrated a normal tolerance initially, six remained normal during steroid administration; the remaining seven became abnormal during this therapy, and three of them revealed abnormal tolerance even after the steroids had been withdrawn.

(5) Serum Globulin Distribution Patterns: Alteration in the serum proteins by chronic disease is well known. The elevation of the serum globulins is most apparent, since these comprise the protein components associated with resistance to infection, including the antibodies and the acute phase reactants. Greenspan demonstrated that an estimation of the alterations in globulin patterns could be made by the determinations of the serum mucoprotein, the acid precipitable globulin and the zinc sulfate turbidity which reflect the alpha-globulin, the alpha-2-plus beta globulin, and the gamma globulin fractions respectively (Fig. 3).

(a) Serum mucoprotein determinations: Fourteen of the 20 patients (70 per cent) had elevated serum-mucoprotein levels before the steroid-androgen regimen was started; six of those 14 remained abnormal during and after steroid therapy, while return to normal levels occurred in the post-therapy phase in the other eight cases. Six of the 20 patients, had, initially, a normal serum mucoprotein level. Three of these became abnormal during steroid-androgen therapy and this persisted afterward. In general, there was a fairly good correlation as shown previously between the height of the serum mucoprotein levels and the extent of the clinical and radiologic findings. Regression of disease was usually associated with return to normal levels. There was no difference between serum mucoprotein changes observable in the pa-

![Figure 2: Successive glucose tolerance curves taken at monthly intervals before (curve 1), during (curves 2, 3 and 4) and after (curve 5) prednisolone, fluoxymesterone therapy in one patient. This illustrates another type of response to the steroids in which glucose tolerance is increasingly depressed, and returns to normal only after steroids are withdrawn.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21366/)
tients receiving steroids and those in group C (controls).

(b) Acid precipitable globulin: This is a measure of the acute phase reactants and comprises the alpha 2-plus beta globulin components. In the present study, 16 of the 20 patients had a high acid precipitable globulin which persisted throughout the steroid and post-steroid observation periods in 14. Similar results were obtained in the control group of patients. The steroids did not appear to influence the pattern of response of this serum protein component.

(c) Zinc sulfate turbidity: Prior to the institution of steroid-androgen therapy, 15 patients demonstrated an elevated zinc turbidity, three were normal and two subnormal. During the steroid therapy period, 18 returned to normal or subnormal levels. Ten of these dropped to below normal, but reverted to normal or elevated values when the steroid was withdrawn. This depression of gamma globulin during steroid administration, reflected by reduced zinc sulfate turbidity, and the consequent rise after withdrawal, appeared to be rather characteristic. This is demonstrated in Fig. 3 in which the mean values of the serum globulin obtained for Groups A and B (steroid treated) are compared with the mean values of patients in Group C (non-steroid treated controls).

(6) Sputum Bacterial Sensitivity Studies: Six patients in Group A and five in Group B had sputum sensitivity studies prior to the start of steroid-androgen therapy. It is interesting to note that in three of these six cases in Group A, partial or complete resistance to streptomycin was reported, although these patients had never received this antibiotic previously. They were sensitive, however, to INH and showed no evidence of bronchogenic spread during steroid therapy. The diabetic who died showed organisms sensitive to INH throughout, with partial resistance to streptomycin and to cycloserine (in the post-steroid phase). The latter drug had been added to the antibiotic regimen when her condition showed further deterioration. Of the five cases studied from Group B, organisms sensitive to INH were noted in four and to cycloserine in one, before steroidal therapy. Organisms resistant to streptomycin were found in one and to cycloserine in three patients. One of them showed an increase in cavity size during steroid therapy which later receded.

(7) Untoward Effects Which May Be Attributable to the Steroidal Therapy:

(a) Moon facies of slight to moderate degree was noted in five cases.

(b) Slight hirsutism developed in three women.

(c) Acne occurred in three women with increased libido in one of them.

All of the manifestations (a, b, c) disappeared within two months after adrenocortical-androgen therapy was discontinued.

(d) Some dyspnea and fever of several days' duration developed soon after steroid-androgen therapy was started in one woman in Group B. No reduction in the discharge of exudate from a pleuro-cutaneous fistula was observable. Another patient developed a superimposed nontuberculous bronchopneumonia.

(h) Electrocardiograms were taken in all 20 cases during and after therapy. Six cases showed high peaked T waves consistent with possible hyperkalemia during treatment (two in Group A and four in Group B). The serum potassium was within the upper limits of normal in four and elevated in two of these cases. The T waves reverted to normal after steroid-androgen therapy was stopped. Serum sodium and serum chlorides in these six patients were normal. The ECG configuration may have been influenced by the administration of potassium chloride during the period of steroidal therapy.

Comments and Conclusions

Steroids have been used in tuberculosis on the assumption that they may help to counteract some of the reactions to the infection which may themselves be harmful to the host. These agents may modify or suppress deleterious host responses to infection in such a way that the antimicrobial drugs are better able to control the infection. The intensity and quality of the inflammatory response to a tuberculous infection does not depend exclusively on the number of bacilli in the
lesion, but on the extent of the allergic reaction as well, the natural immunity of the host and the immunity acquired in the course of the infection.

Another possible advantage of combined steroid and antibiotic therapy is the apparent synergistic action of corticoids and isoniazid. Isoniazid appears to retard the inactivation of steroids by the liver. In addition, it has been observed that although the allergic response of the patient to the tubercle bacilli is suppressed, the formation of circulatory antibodies may not be inhibited (agglutination titer of Middlebrook-Dubos). Thus, corticosteroids may permit the multiplication of tubercle bacilli by interfering with immune mechanisms, but at the same time, accentuate the bactericidal effect of isoniazid.

However, exposure of patients to exogenous corticoids carries with it the possibility of several physiologic derangements which must be considered. An increased incidence of reduced glucose tolerance has been noted in association with tuberculosis. Increased andrenocortical activity with resultant elevated corticoid levels usually accompanies disease states in an attempt to counteract the stress imposed by the disease. When such hyperadrenal activity exists, some interference with normal carbohydrate metabolism may often be demonstrable, as a result possibly of the anti-insulin action of the adrenal steroids. Thirty-five percent of the 20 patients in this study demonstrated a reduced tolerance to glucose even before administration of steroid therapy. It would appear that in normal individuals the increased demand for insulin imposed by the elevated corticoid levels is met adequately. However, a patient whose pancreas has an inherently reduced capacity may demonstrate decreased efficiency in handling carbohydrate during periods when steroids are elevated beyond levels for which they can be compensated.

Increased gluconeogenesis from protein cannot fully explain the reduced glucose tolerance, glycosuria and ketosis observed. Certainly in the present study little demonstrable action could be ascribed to the androgenic "nitrogen sparing" steroid in preventing the corticoid inhibition of carbohydrate tolerance. It is possible that there are other metabolic derangements associated with increased levels of corticoids. One of the significant differences between "pancreatic" and "steroid" diabetes is in the response of serum inorganic phosphate to induced hyperglycemia. The expected decline in phosphate is not seen in the diabetes of pancreatic origin. In contrast to this, there would appear to be no interference with the peripheral utilization of carbohydrate in "steroid" diabetes since the normal fall in serum phosphate is observable in patients receiving steroids even though their tolerance for glucose appears to be impaired. Similarly, in the present study, no alteration in the expected fall in serum phosphate was observable, although the glucose tolerance was reduced, indicating that the reduction in tolerance was probably related to the endogenous and exogenous increase in steroid levels. During adrenocortical therapy the incidence of reduced glucose tolerance rose to 70 per cent. This effect of the steroids appeared to be reversible in most instances, in as much as some reduction in tolerance for glucose was seen in only 30 per cent of the 20 cases at the end of the observation period. It is possible that the administration of adrenocortical steroids may convert a potential or "latent" diabetic into a "florid" diabetic with consequent aggravation of the underlying tuberculosis.

The variations in serum mucoprotein in tuberculosis have been reported by a number of investigators. Elevated serum mucoprotein is generally found in patients with extensive involvement, during acute toxic manifestation of their disease. Schaffner, et al. demonstrated the consistent elevation in gamma globulin in most patients with tuberculosis. The measurement of zinc sulfate turbidity was found useful for estimation of serum gamma globulin in tuberculous patients. The serum mucoprotein, zinc sulfate turbidity, and acid precipitable globulin fractions gradually return to normal levels as the disease status of the patients improves with chemotherapy. Although supplementation with steroids does not appear to alter the
serial values obtained for serum mucoprotein or acid precipitable globulin, 90 per cent of the patients in the present study experienced a reduction in zinc sulfate turbidity to normal or subnormal levels during the period of steroid therapy (Fig. 3). This depression of gamma globulin by the corticoids, and consequent rise after withdrawal appears to be characteristic. It may be associated with the general suppressive action of adrenal steroids on lymphoid tissue and antibody globulin synthesis, and emphasizes the importance of adequate antimicrobial therapy during period of corticoid administration.

Keeping in mind these considerations, the basic problem for the clinician still remains as follows: is there a definite place for adjunctive adrenocortical steroids used with or without androgens in the treatment of tuberculosis? Reports in the literature would indi-
cate that: (1) in experimental tuberculosis, adrenocortical agents exercise a harmful ef-
fect;41 (2) pre-existing tuberculosis (not in-
frequently undiagnosed) can be re-activated
by corticoids administered for other condi-
tions;41 (3) these steroids are helpful in comb-
ating hypersensitivity reactions to antimicro-
bial therapy in tuberculous patients;41,48 (4) there is a preponderance of opinion that favors the combination of adequate che-
motherapy with adrenocortical hormones in
cutely ill febrile patients with extensive pre-
dominantly exudative bronchopneumonic dis-
 ease, miliary and meningeal tuberculosis and in acute tuberculous serositis involving the pleura, pericardium or peritoneum.47 One
recent article concludes that "combined ste-
roid and antimicrobial therapy is, at present,
the best form of treatment of all patients with
active pulmonary tuberculosis."48

In the evaluation of results, a distinction
must be made between patients with recent,
acute forms of tuberculosis previously un-
treated with antibiotics, and patients with
chronic, active disease who have reached an
apparent clinical and radiologic "stalemate"
after a prolonged course of present-day anti-
tuberculosis therapy. A distinction must also
be made between symptomatic and objective
signs of improvement; the former may often
appear to be dramatic in patients treated
with steroid adjuncts. Of more fundamental
importance, however, is the degree and rap-
idity of radiologic regression with cavity
closure and sputum conversion.

Results in our two groups totalling 20 pa-
tients (though small in number, they were
closely followed) can be summarized as fol-
loows:

Group A (ten cases previously untreated
with chemotherapy):

Symptomatic improvement — afebrility
within two weeks in 100 per cent of cases
after initiation of the combined steroid-anti-
microbial therapy, weight gain in 90 per
cent, significant reduction in cough and sput-
um in 90 per cent.

Objective improvement — moderate to
marked roentgenologic regression of infil-
trative disease in 80 per cent, definite cavity
closure in 50 per cent (in one of the five cases,
this was accomplished by resectional surgery),
questionable residual cavitation in one case,
regression in cavity size in two, increase in
cavity size in two. Sputum conversion oc-
curred in 70 per cent. One patient died 10½
months post-therapy. She was a newly dis-
covered diabetic who showed clinical and
roentgenologic deterioration prior to, during
and subsequent to therapy with steroid sup-
plements and antibiotics. Incidentally, her
lack of resistance to the disease appeared to
be revealed also by an apparent hypogam-
maglobulinemia (zinc sulfate turbidity test)
before such therapy. It is of interest to men-
tion here that the only death in 30 tuber-
culous cases treated with chemotherapy and
adrenocorticoid hormone in another reported
series,49 occurred in an originally undiagnosed
diabetic patient.

Group B (ten chronic cases previously
treated with specific antibiotics):

Symptomatic improvement — weight gain
(slight to moderate) in 50 per cent, increased
sense of well being, 50 per cent; temporary
relief of bronchospasm, 20 per cent; tempo-
rary reduction in cough and sputum 30 per
cent.

Objective improvement — 40 per cent re-
vealed slight regressive radiologic changes of
little clinical significance, cavity closure in
none, unchanged radiologic findings in 50
per cent and temporary increase in size of
cavity 10 per cent (during steroid therapy).
Sputum conversion was found in none. Two
patients died with massive hemoptyses, but
this occurred many months later in the post-
therapy observation period.

We have compared the results obtained in
the 20 patients treated with steroids with the
97 "control" patients. Our current beliefs
are as follows: (1) in chronic tuberculosis
where apparent maximum improvement has
been achieved with antimicrobial therapy,
the concomitant administration of adreno-
cortical steroids is not of real value and is
potentially hazardous. Superimposed nontu-
berculous pneumonia (especially staphylo-
cal) and aggravation of the underlying tuber-
culosis, in particular, must be considered as
possible complications. The euphoria and
weight gain seen in some of our patients can be achieved with an androgenic supplement alone; (2) the routine initial use of adrenal-cortical agents in conjunction with chemotherapy for the previously untreated, so-called “garden variety” type of active pulmonary tuberculosis appears unnecessary and may lead to unexpected side effects; (3) the use of adrenal-cortical steroids (together with adequate chemotherapy) should be considered: (a) in patients with hypersensitivity or allergic reactions to one or more of the antibiotics, unresponsive to simpler measures. Desensitization with gradually increasing antibiotic dosage, in conjunction with steroid therapy can be accomplished often; (b) in acutely ill patients with miliary and meningeal tuberculosis; in acute tuberculous pneumonia and acute serous membrane involvement. Even within this category, proper selection of patients rather than routine use for all is desirable. The dosage schedule of steroids should be “tailored” to the individual case and in relation to the acuteness of the clinical condition. The duration of such therapy should be short—perhaps a few weeks, rarely longer than two months.

SUMMARY

Does combined adrenocortical-androgen steroid therapy potentiate the patient’s response to chemotherapy for pulmonary tuberculosis? An attempt was made to evaluate this in a group of 20 patients. All had active disease, one-half never had previous antimicrobial therapy (Group A); the other half had apparently reached the maximum benefit of such therapy (Group B). Adrenocortical-androgen therapy was given to all in a uniform manner for 12 weeks together with chemotherapy for tuberculosis. In addition to the usual clinical, radiologic and sputum examinations, ancillary studies pertaining to glucose tolerance and serum globulins were made in these patients prior to, during and after the discontinuance of the steroids. The data collected were compared with a comparable group of patients studied previously who did not receive steroids. Untoward side effects and results of treatment in both groups are recorded three to 20 months (average 11.5 months) after cessation of the steroid drugs. Three patients died and the causes are cited. In the patients studied, the addition of the adrenocortical-androgen supplements did not appear to produce significant potentiated effects above and beyond what we have seen chemotherapy alone do. However, some weight gain occurred in about 50 per cent of the patients. This response can often be achieved in such patients with an anabolic steroid preparation alone, without resorting to the more hazardous use of adrenocortical steroids. The pros and cons of such adjunctive treatment are discussed and indications for their use in tuberculosis are suggested.

RESUMEN

Se pregunta si la terapeutica combinada adrenocortical-androgenos intensifica la respuesta del enfermo a la tuberculosis pulmonar. Se hizo un intento para valorar esta posibilidad en 20 enfermos. Todos tenian enfermedad activa, la mitad (grupo A) no habian sido previamente tratados; la otra mitad (grupo B) habian alcanzado el beneficio maximo del tratamiento antimicrobiano. Se dio el tratamiento de esteroides a los dos grupos de manera uniforme por 12 semanas juntamente con quimioterapia antituberculosa. Ademas de los habituales estudios clinico, radiologico y examenes de esputos se hicieron otros estudios auxiliares como tolerancia de glucosa, globulinas en el suero, antes durante y despues de interrumpir el tratamiento de esteroides. Los datos reunidos se compararon con los de un grupo de enfermos estudiados antes de quienes no se usaron los esteroides. Los efectos indeseables y resultados del tratamiento en ambos grupos se registraron durante 3 a 20 meses (media: 11.5 meses) despues de la interrupcion de las drogas. Murieron tres enfermos y se mencionan las causas. En los enfermos estudiados el agregado de suplementos de adrenocortical-androgenos no parecio producir efectos potenciados significantes mas notables que lo observado con la quimioterapia sola. Sin embargo, hubo cierto aumento de peso en aproximadamente 30 por ciento de los enfermos. Esta respuesta puede obtenerse a menudo con una preparacion anabolica de esteroides sin recurrir al uso mas azaroso de los adrenocorticoides. Se hace una discusion de las ventajas y desventajas del tratamiento adjunto y las indicaciones de el se sugieren.
RESUME
Le traitement associé adrénocorticoïde-androgènes renforce-t-il la réaction du malade à la chimiothérapie pour tuberculose pulmonaire? L’auteur a essayé de l’estimer dans un groupe de 20 malades. Tous avaient une affection évolutive, la moitié d’entre eux n’avaient jamais eu de traitement anti-microbien antérieur (groupe A); l’autre groupe avait apparemment atteint l’effet maximum d’un tel traitement (groupe B). Le traitement adrénocorticoïde-androgènes fut donné à tous d’une manière uniforme pendant 12 semaines, associé à la chimiothérapie antituberculeuse. Outre les examens habituels cliniques, radiologiques et bactériologiques, des études complémentaires furent faites concernant la tolérance au glucose et les globulines du sérum chez ces malades, avant, pendant et après cessation des stéroïdes. Les éléments réunis furent comparés à un groupe semblable de malades antérieurement étudié, qui n’avaient pas reçu de stéroïdes. Les effets secondaires fâcheux et les résultats du traitement dans les deux groupes sont unregistrés pendant une période de 3 à 20 mois (moyenne 11,5 mois) après cessation de la thérapeutique stéroïde. Trois malades moururent et les causes en sont indiquées. Chez les malades étudiés, l’addition de produits adrénocorticaux et androgènes ne semblait pas produire d’effets marqués de renforcement en dessous ou au-delà de ce que provoque la chimiothérapie seule. Cependant, une certaine gain de poids survint dans environ 50% des malades. Cette réaction peut souvent être acquise chez de tels malades avec une préparation stéroïde anabolique seulement, sans faire appel à l’emploi plus dangereux des stéroïdes adrénocorticaux. Les arguments pour et contre un tel traitement supplémentaire sont discutés et l’auteur suggère les indications de leur emploi en tuberculose.

ZUSAMMENFASSUNG

Bei den untersuchten Patienten schien die zusätzliche Behandlung mit Nebennierenrinden-Androgen keine beträchtliche potenzierte Wirkungen auszuüben, die über das hinausgehangen wäre, was wir unter Chemotherapie allein haben zustande kommen sehen. Immerhin gab es einige Gewichtsanstiege in ungefähr 50% der Kranken. Diese Reaktion kann jedoch auch oft bei derartigen Kranken erreicht werden mit einem Stoffwechsel-Steroid-Präparat allein, ohne, daß man zu dem etwas gefährlicheren Gebrauch von Nebennierenrinden-Steroiden greifen müßte. Das Für und Wider solcher zusätzlichen Behandlung wird diskutiert und Indikationen für deren Einsatz bei der Tuberkulose vorgeschlagen.

Complete reference list will appear in the reprints.

PRIMARY PULMONARY LYMPHOGRANULOMATOSIS
A case of malignant lymphogranulomatosis with primary site in the lungs is described. Initially, pulmonary tuberculosis and then lung abscess were diagnosed since both radiologic appearance and clinical symptoms imitated these two clinical entities. Scalene node biopsy gave the correct diagnosis. Hemoptysis as well as a large cavity in one lung encountered in this case are unusual manifestations of primary pulmonary lymphogranulomatosis.