The Treatment of Certain Forms of Tuberculosis with a Combination of Prednisone (or Hydrocortisone) and Antibiotics

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Introduction

A study of the pharmacodynamic effects of rapid infusions of para-amino salicylic acid (PAS) (Fortier and Favez, 1952) had led to the use of cortisone in the treatment of clinically and radiologically recent pneumatic pulmonary tuberculosis (Delaloye and Favez, 1953).

Rapid infusion of PAS¹ in the treatment of active tuberculosis of the lungs has caused radiological improvement which was both more rapid and more extensive than that obtained with antibiotics alone (Favez et al., 1956, A).

Rapid infusion was followed by copious early excretion of free PAS in the urine. The efficacious blood level (above 2 mg./100 ml.) is maintained only half as long as after the usual oral administration. PAS should be in contact with the bacilli for about eight of the 24 hours if bacteriostasis is to be effected. It may therefore be presumed that the unusually rapid absorption of the exudative foci resulting from rapid infusion of PAS cannot be due exclusively to bacteriostasis. These rapid infusions have an adreno-corticotrophic effect (Favez et al., 1954). The superior therapeutic effect obtained by this mode of administration may be correlated with this pituitary adrenal action. It is therefore logical to make an attempt at influencing the pneumatic foci more directly, at least in certain alarming situations, by administration of cortisone, rather than to increase the secretion of this hormone by the intermediary of the hypophysis.

Observations

Forty-two patients have been treated with hydrocortisone and 78 with prednisone since 1952; supplemental findings since obtained have confirmed the preliminary conclusions presented at the time before a meeting of the Société des Médecins de Leysin on October 21st, 1952 (Delaloye and Favez, op. cit.) In the course of the same period similar observations have been

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Cortone, Hydrocortone and Deltacortone graciously supplied by Merck Laboratories, New York, New York.
¹The terms “rapid infusion” refers to administration, within an hour, of a solution of 18.5 g. PAS sodium in 500 ml. distilled water. The product used was Aminacyl for infusion (Wander). Aseptic preparation of this solution without heating, which permits rapid administration without secondary effects, is described in detail in another publication (Favez et al., 1956 A).
made by Quiring et al., (1953) at Basle, Ovedoff & Bensusan (1953) at Capetown. We have since reported on a new series of cases (Aguet and Favez, 1954), whereas personal observations have been published by Houghton (1954) at London and by Even and Sors at Paris (1954).

The first to mention indications for cortisone in the field of pleurisy and pericarditis were Minet et al. (1952) at Lille. As regards the benefit of corticotherapy in tuberculous meningitis, mention should be made of Shane et al. (1952) in Canada and of Barnard (1953) at Capetown. Numerous publications have since confirmed the above mentioned reports [Favez and Aguët (1956)]. Data on dosage adopted since 1955 according to the experience of Gilbert (1954) are presented in Table I.

A salt-free, high-protein diet was prescribed. Patients treated with pred-

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TABLE I
nisone received normally salted food. The protein supply was supplemented with amino-acids in the form of Nesmida broth twice daily.

Routine clinical and laboratory examinations included determination of the temperature, body weight, fluid and compound balance, arterial pressure, Mantoux reaction, radiographic and tomographic findings, examination of the fundus of the eye, determination of bacilli in the sputum, gastric juice and urine, by culture and inoculation into guinea pigs, sensitivity tests, determination of the blood protein, salt and potassium level, electrophoresis, haematological examinations, blood coagulation tests, thrombelastography in some cases, ECG and liver function tests. Only pathological findings are mentioned.

**Overall Results**

a) *Clinically and radiologically fresh pulmonary tuberculosis (108 cases)*

One hundred and one patients (including one suffering from meningitis with coma, one with meningitis and renal tuberculosis with coma and six with diabetes) were given combined treatment with hydrocortisone or prednisone and antibiotics. In all cases the pneumonic foci were absorbed completely or nearly so within four to eight weeks. Trabecular opacities and certain nodular changes as a rule remained. The cavities often remained unaltered during hormonal treatment and did not close until in the course of the following month. Seven patients, including one who also had diabetes, did not receive hydrocortisone until after having treatment by antibiotics and chemotherapy for 10 days (one case), three weeks (two cases), one month (one case) and three months (two cases). In the last four cases the lesions showed gradual aggravation until cortisone treatment was started. The radiological picture showed moderate improvement in two and considerable improvement in two other cases. The two affected with meningitis and in coma at the time of admission returned to normal psychical condition within less than a week. Inoculation into guinea pigs of cerebrospinal fluid (and in one case of urine) had negative results at the end of two to four months. Guinea pig inoculations and cultures made with material from sputum and gastric juice were negative in all cases from the fourth month of treatment on.

b) *Pulmonary tuberculosis in which the radiological findings show lesion changes adjacent to pneumonic foci (12 cases)*

Seven patients were given combined treatment with hydrocortisone and antibiotics. In two, the radiological improvement was poor and concerned only the apparently exudative factors. In the remaining five no improvement was seen. Five received hydrocortisone only after treatment with antibiotics and chemotherapeutics for one month (two cases) or two months (three cases). Only one of these, who was also suffering from diabetes, showed marked improvement; the opacities showed gradual spread until cortisone treatment was instituted.

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1Twenty-three of these showed pulmonary tuberculosis of a miliary type.
Case 1: G. R., a man, aged 64, admitted August 5, 1952, with bilateral, grossly confluent pulmonary foci, predominant on the right (Fig. 1), and specific ulcerative laryngitis. He is cyanotic, dyspnoeic, adynamic and aphonic. The body weight is 32.2 kg. for a height of 5 ft. 2 in. Temperature 39.3° C. Tubercle bacilli are found in the sputum. Average erythrocyte sedimentation rate 47.5 mm./hour; blood pressure 100/75 mm. Hg.; Kolmer-Meinicke reaction weakly positive. Normal ocular fundus. Treatment by intravenous administration of INH (200 mg. daily) is instituted immediately. The general condition deteriorates in the course of three subsequent weeks. Pulmonary lesions spread and spontaneous pneumothorax is seen on the left (Fig. 2). Treatment with cortisone and antibiotics is started. X-ray films a month later show considerable regression of pathological changes (Fig. 3). General findings on discharge (July 13, 1953): the voice is normal, and the pulmonary tuberculosis is stabilized (Fig. 4). Body weight 43 kg. Temperature normal. Repeated cultures and inoculation into guinea pigs show that no tubercle bacilli are present in the sputum. Erythrocyte sedimentation rate 17 mm./hour. The ocular fundus is normal.

Case 2: B. G., a man, aged 39, admitted on January 10, 1953 with bilateral, nodular, infiltrative diffuse pulmonary tuberculosis. He is cyanotic, dyspnoeic, and adynamic. The body weight is 60.3 kg. for a height of 5 ft. 9½ in. Temperature 39.2° C. Tubercle bacilli present in the sputum. Blood pressure 100/50 mm. Hg.; average erythrocyte sedimentation rate 55 mm./hour. Normal ocular fundus. Normal bronchoscopic findings. Treatment with cortisone and antibiotics is instituted immediately and continued for two months. Radiological evidence of the pulmonary foci disappears after two months.
General findings at discharge (August 7, 1958): the pulmonary features are practically normal. Repeated cultures and guinea pig inoculations show that no tubercle bacilli are present in the sputum. The average erythrocyte sedimentation rate is 2 mm./hour. Normal ocular fundus. Weight 55.5 kg.

Case 5: L. E., a man, aged 51. Admitted on March 5, 1953 with bilateral nodular infiltrative diffuse pulmonary tuberculosis. Urinary tuberculosis and tuberculous meningitis. He is unconscious and in a state of alcoholic cachexia. His condition precludes determination of height and weight. Temperature 38.2° C. Average erythrocyte sedimentation rate 10.5 mm./hour. Blood pressure 110/70 mm. Hg.; tubercle bacilli present in sputum. Thymol 14. Pathological galactosuria test. Ocular fundus: exudative chorioretinitis. Treatment with cortisone and antibiotics is instituted. The pulmonary picture has considerably improved six weeks later and his general condition is more favourable. Examination of the ocular fundus reveals almost complete absorption of the exudative chorioretinitis without pigmentary sequelae. Cerebrospinal fluid (initial values) cytology: five lymphocytes/cu. mm. (89); chloride 416 mg./100 ml. (403); glucose 58 mg./100 ml. (45), proteins 30 mg./100 ml. (42); colloidal gold 12 x 0 (111122100000); pressure 10 cm. H2O (16). Queckenstedt sign normal on both sides. Guinea pig inoculations negative. Discontinuation of cortisone treatment is followed by a relapse of nodular infiltrations of the lungs. The cerebrospinal fluid shows pathological values again, although guinea pig inoculations remain negative. Treatment with cortisone and antibiotics is resumed; all pathological changes have disappeared after a month. The pulmonary picture is normal on discharge (June 23, 1954). The cerebrospinal fluid is normal and guinea pig inoculations are negative. Urine: negative inoculation. Repeated cultures and guinea pig inoculations show that tubercle bacilli are no longer present in the sputum. Temperature normal. Average erythrocyte sedimentation rate 14 mm./hour. Body weight 72 kg. Normal ocular fundus. Serum hypoprothrombinemia remains (5 Gm./100 ml). Limited ataxia is shown; he tends to walk with legs spread.

Case 6: P. C., man, aged 40, admitted on May 28, 1958 with nodular confluent foci bilaterally in the upper lobes. Comatose state due to acute tuberculous meningitis. Breathing of the Cheyne-Stokes type. Determination of weight and height not possible. Temperature 37.5° C. Tubercle bacilli in the sputum. Average erythrocyte sedimentation rate 54.5 mm./hour. Blood pressure 138/90 mm. Hg.; normal ocular fundus. Cerebrospinal fluid (cisternal puncture): 70 lymphocytes and 20 polymorpholuekocytes per cu. mm. Chloride 362 mg./100 ml.; glucose 32 mg./100 ml.; protein 55 mg./100 ml. Guinea pig inoculations positive. Treatment with cortisone and antibiotics is started immediately; in addition, 50 mg. INH is administered three times a week by intraspinal injection. He completely regains consciousness within a week, but suddenly shows total paralysis of the left third and fourth cranial nerves. Paralysis shows gradual regression. Slight impairment of coordination is associated with lack of periosteal reflexes in the right arm and generalized hyper-reflexia of the tendons. Lasegue's sign weakly...
positive on both sides. After two months, repeated cultures and guinea pig inoculations show that tubercle bacilli are absent from the sputum. Cerebrospinal fluid: 33 lymphocytes and three polymorphonuclear cells per cu. mm.; chloride 412 mg./100 ml., glucose 41 mg./100 ml., proteins 110 mg./100 ml. Negative guinea pig inoculation. Normal ocular fundus. X-ray findings are satisfactory on the day of discharge (January 21, 1954). Cerebrospinal fluid normal. Guinea pig inoculations negative. Body weight 72.2 kg. as against 57.8 kg. immediately before admission. Average erythrocyte sedimentation rate 21 mg./hour.

Case 6: C. M., woman, aged 40, admitted on November 23, 1955 with tuberculous pneumatic infiltrations in the left upper lobe. The general condition is poor. Body weight 50.1 kg. for a height of 5 ft. 6 2/8 in. Temperature 39° C. The sputum contains tubercle bacilli. Average erythrocyte sedimentation rate 37 mm./hour. Blood pressure 100/70 mm. Hg. Treatment with hydrocortisone and antibiotics is started. A month later the parenchymal opacities have cleared and two months later the pulmonary condition is satisfactory. At discharge (March 31, 1956) tubercle bacilli are absent from gastric lavage, repeated cultures and guinea pig inoculations. Erythrocyte sedimentation rate normal. Normal ocular fundus.

Case 7: P. M., man, aged 54, admitted on March 22, 1956 with pneumatic infiltration on the left lung; cavitation of both upper lobes (Fig. 5). Recent anteroseptal heart infarction; Buerger's disease; diabetes (controlled by 25 U. insulin daily). Normal temperature. Body weight 68.8 kg. for a height of 5 ft. 7 3/5 in. The sputum contains tubercle bacilli. Erythrocyte sedimentation rate 24 mm./hour. Blood pressure 138/80 mm. Hg. Blood sugar level 131-225 mg./100 ml. Slight glucosuria. Abnormal galactose test (normal bromsulphalein test). Van den Bergh test: indirect 0.9 mg./100 ml.; direct slightly positive. Nearly normal ocular fundus. Electrocardiogram findings: typical aspect of recent anteroseptal infarction. Bronchoscopy: numerous secretions in the left bronchial tree of which the mucosa is slightly hyperemic. Hydrocortisone treatment with streptomycin and glucuronolactone-hydrazone is started and continued for two months. The left pneumatic infiltration has been cleared, but the cavitation is still visible (Fig. 6). During hydrocortisone treatment the daily dose of insulin is increased to 50 U. After discontinuation of hydrocortisone treatment, further treatment consists in streptomycin administration, rapid infusion of PAS and INH.

General findings at discharge (September 23): normal temperature; body weight 64.3 kg.; repeated cultures and guinea pig inoculations show that the sputum contains no tubercle bacilli. Average erythrocyte sedimentation rate 34.5 mm./hour. Blood pressure 145/80 mm. Hg. The radiological aspects of the tuberculosis are quite satisfactory. The diabetes no longer requires insulin. Electrocardiogram aspects as usual.
in such cases. Buerger's disease shows considerable improvement although oscillographic curves are flat. This condition is favorably influenced by the hydrocortisone. The ocular fundus is unchanged.

Case 7: B. Y., a woman, aged 19, admitted on June 6, 1955 with infiltration in the right upper lobe (Fig. 7). Tuberculous laryngitis confirmed by biopsy. No bacilli in the sputum (cultures sterile). Normal temperature. Body weight 61.2 kg. for a height of 5 ft. 73/5 in. Average erythrocyte sedimentation rate 84 mm./hour. Blood pressure 120/70 mm. Hg. Ocular fundus normal. Bronchoscopy: slight hyperemia of the mucosa of right upper bronchus which contains some secretion. Hydrocortisone and antibiotics are given. The right upper lobe has cleared after a month (Fig. 8). The laryngitis has almost disappeared. General findings at discharge (September 22): normal temperature, body weight 70.6 kg. No tubercle bacilli in the sputum as shown by repeated cultures and guinea pig inoculations. Average erythrocyte sedimentation rate 10.5 mm./hour. Blood pressure 120/70 mm. Hg. Normal ocular fundus. Minute radiological sequelae (tomogram Sept. 22th).

Case 8: R. C., man, aged 16, admitted on June 25, 1955 with pneumonic infiltration of the left upper lobe; nodular infiltrations in both apices with a cavity in the right apex (Fig. 9). Normal temperature. Body weight 54.5 kg. for a height of 5 ft. 8 4/5 in. Sputum contains tubercle bacilli. Average erythrocyte sedimentation rate 10 mm./hour; blood pressure 135/90 mm. Hg. Bronchoscopy: swelling and hyperemia of the mucosa of the left bronchial tree (biopsy: no tuberculous tissue). Treatment with antibiotics and prednisone (25 mg. daily) is started. Normal diet (salt not forbidden); no water retention. The left upper lobe clears a month later (Fig. 10). The cavity is still present, but closes in the course of the second month. General findings at the end of November: body weight 60.8 kg.; temperature normal; no tubercle bacilli in the sputum as shown by repeated cultures and guinea pig inoculations. Average erythrocyte sedimentation rate 3.5 mm./hour; blood pressure 135/75 mm. Hg.; normal ocular fundus.

Case 9: B. H., a man, aged 45, admitted on September 20, 1955 with infiltration of the right upper lobe. Temperature 38.9° C. Body weight 49 kg. for a height of 5 ft. 6 4/5 in. Sputum contains tubercle bacilli. The average erythrocyte sedimentation rate is 15 mm./hour; blood pressure 110/65 mm. Hg. Normal ocular fundus. Bronchoscopy: moderate secretions in the posterior bronchus of the right upper lobe. Hydrocortisone
and antibiotic treatment is instituted. The right upper lobe clears after a month. Discontinuation of hydrocortisone treatment is followed by hypopotassemia (9 mg./100 ml.), hyponatraemia (296 mg./100 ml.), hypoproteinemia (4.2 Gm./100 ml.); electrophoresis (in per cent); albumin fraction 42.6; alpha-globulin 3.7; alpha-globulin 12.4; beta-globulin 12.9 and per cent gammaglobulin 22.2. Severe pain in the muscle of the legs and phlebitis. Complications are gradually overcome. General findings at the end of November: weight unchanged; normal temperature; sputum still contains tubercle bacilli. Four months later the lung conditions are satisfactory.

Case 10: E. G., man, aged 26, admitted on September 17, 1955. Left-sided pneumonic pulmonary tuberculosis. Temperature 39°C. Body weight 70.1 kg. for a height of 5 ft. 10 4/5 in. Tubercle bacilli in the sputum. Average erythrocyte sedimentation rate 24 mm./hour; blood pressure 125/70 mm. Hg. Normal ocular fundus. Bronchoscopy; hyperemia of the mucosa of the left bronchial tree which contains numerous secretions. Hydrocortisone and antibiotic treatment is started. Defervescence after three days. The left lung is clear after six weeks. General findings at the end of November: body weight 74.5 kg.; normal temperature. Sputum contains no tubercle bacilli as shown by repeated cultures and guinea pig inoculations. Erythrocyte sedimentation rate average 9 mm./hour; blood pressure 140/80 mm. Hg.; normal ocular fundus.

Discussion

Studies made of the properties of cortisone used in the field of tuberculosis are left undiscussed here (Sourdat, 1952; Lurie, 1955; Favez & Aguet, 1956; Aguet & Favez, 1956). However, a survey of the pathological anatomical aspects makes it possible to explain to some extent the discrepancies between earlier assumptions and our own observations.

A brief study of the inflammatory reaction in tuberculosis should permit us to demonstrate that the therapeutic use of cortisone is justified in selected cases of tuberculosis.

It is generally known that tuberculosis enters into the category of inflammatory affections, that is to say, a degenerative stage is followed by an exudative stage, which in its turn may or may not be followed by a proliferative stage. Aschoff's 'lesional dualism', which maintains the existence of two types of tuberculosis—one productive and the other exudative—has been discarded.

The stage of pulmonary degeneration will be left undiscussed; its demonstration is very difficult indeed. Exudation, however, is of great importance; the spongy structure and the rich blood supply of the lungs sometimes permit rapid and extensive invasion of the exudate. The exudate of tuberculous alveolitis is polymorphous, i.e. it is often fibrinomacrophagic or purely fibrinous and exceptionally purulent. The nature and quality of the exudate are determined not only by the intensity of the infection, but also by the specific allergic reactivity of the body. The inflammatory response during the exudative stage is not specific and non-mutilating. The broncho-alveolar structure is intact and restitutio ad integrum is therefore possible.

The condition is changed by the occurrence of caseation; caseation is a true necrosis which may leave the alveolar structure intact but which more frequently results in permanent mutilation (of the area affected). Caseation, whether mutilating or not, always leads to a series of proliferative reactions originating in connective tissue, of mesenchymal or reticular origin: the appearance of epithelioid cells, giant cells (largely from the reticulo-endothelial system), lymphocytes and collagen fibers which may iso-
late the caseous lesion. This connective tissue reaction results in the formation of cicatricial tissue which may secondarily calcify or even ossify. There is no constancy, however, in this relatively favorable evolution. Sometimes the caseous material may soften and liquefy for some obscure reason. The formation of cavities and bronchogenic dissemination, facilitated by the canalicular structure of the lungs, is caused by liquefaction. This brief analysis warrants the conclusion that the prognostic evaluation of the severity of pulmonary tuberculosis primarily depends on the following data:

1) the extent of the initial exudative process;
2) the early caseation which is responsible for mutilating lesions (occurring before absorption of the exudate is possible);
3) an insufficient reaction of the connective tissue preventing isolation and cicatization of the caseous lesion.
4) the liquefaction of the caseous material which gives rise to cavitation and bronchogenic dissemination.

It should be borne in mind that, regardless of the stage of tuberculous inflammation involved, its intensity and quality are not dependent exclusively on the number of bacilli in the lesion. The nature of the reactions depends to a considerable extent on the allergic reaction, the immunity acquired in the course of the inflammation (infection) and natural immunity. This is illustrated by the predominant importance of allergy in the formation of such varied lesions as pure fibrinous alveolitis, caseous necrosis and perifocal inflammation.

An analysis of the possible effect of cortisone on these four aggravating factors seems to lead to the following conclusions:

1) Menkin (1956) has shown that it acts by inhibition of leucotoxin and his most recent works seems to prove that ACTH acts in a similar direct manner by inhibiting the production of exudin in late stages of an acute inflammation (acid exudate). Experimental data tend to confirm this anti-exudative effect of cortisone in cases of tuberculous inflammation.

2) Cortisone is equally important during the proliferative and the healing stage. It inhibits phagocytic activity and the proliferation of fibroblasts in vitro and in vivo, and reduces their collagen fiber production. In this manner it inhibits the progress of fibrosis and the formation of granulation tissue; it retards the cicatricial process. It does not affect fibrous tissue, whether normal or tumorous. It inhibits vascular proliferation which is of greater importance in the healing process. Also, it alters the nature of the collagenous substance by causing polysaccharide changes.

3) The anticatricial activity of cortisone constitutes an untoward effect in tuberculosis because it inhibits the reactions of the connective tissue which permit the isolation of caseous matter and the healing of lesions.

4) Experimental pathology has yet to provide further data on the activity of cortisone as regards caseation and subsequent caseous changes. In this respect, too, it appears to have an unfavorable effect.

In conclusion, it should be pointed out that the evolution of tuberculosis foci in the same lung may differ from one point to another. The term
'autonomie évolutive' (Canetti) would seem to be suitable here. The time
element in the appearance of the proliferative and healing stage is var-
iable. It may never be completely attained: caseous lesions may persist for
years without being completely encapsulated. Clinical and radiological ex-
amination often fail to reveal the pathological condition of a number of
lesions.

The various factors discussed enable us to understand the divergent
opinions on the effects of cortisone on pulmonary tuberculosis. They ex-
plain the success obtained in highly exudative severe cases of tuberculosis
and, on the other hand, the failures and aggravations seen particularly in
those forms in which fibro-caseous lesions dominate the clinical picture.

Apparent recent pneumonic foci are nearly completely absorbed within
the first four to eight weeks under prednisone treatment. Those lesions
that have already undergone some degree of connective tissue organization
are relatively refractory. Cavities as a rule do not close until predni-
sone treatment is stopped in favor of antibiotic treatment. The func-
tional isolation of the cavities during the course of the hormonal treatment
is explained by the biological properties of the cortico-steroids and dis-
cussed in another paper (Aguet and Favez, op. cit.). Large dosages of SM
and INH have been used at the onset of cortico-steroid treatment (re-
sorption of exudate containing bacilli) and after it has been stopped (at
this time capillary walls and fundamental substance have recovered or-
iginal permeability and bacilli have multiplied in lesions) (Lurie, op. cit).
Two developmental stages may be distinguished, viz.: absorption of the
exudative foci, followed by closure of cavities and gradual regression of
nodular elements and gradual or no regression of trabecular changes. The
sequelae of an eventual bacillary spread are not observed. They have been
studied by guinea pig inoculation (urine), examination of the ocular fundus
and thoracic x-ray films regularly during and following hormonal treatment.

One patient transiently showed complications due to cortisone treatment
(Case 9). One, suffering from longstanding tuberculosis, died nine days
after discontinuation of cortisone treatment showing symptoms of acute
right heart insufficiency. Hydrocortisone seemed to be responsible for this
fatal issue. Autopsy showed thrombosis of the left inferior pulmonary
artery. The patient had a haematemesis a few weeks before admission. He
was an alcoholic.1

Diabetes constitutes no contra-indication to cortisone treatment; how-
ever, daily insulin dosage should be adapted for the duration of cortisone
treatment. Water retention did not occur2.

Of the 12 cases of longstanding tuberculosis, five showed a fatal issue
three, four and six months, respectively, after cortisone treatment was
stopped. The patients died of right-sided cardiac insufficiency resulting

1 In this case, as in Case 9, the patient showed signs of disturbed hepatic function.
Data so far obtained seem to suggest that corticosteroid treatment is best refrained
from in the presence of disorders of the liver.
2 The two meningitis patients were given rapid PAS infusions at the beginning of
treatment, without having oedema. The sodium intake was therefore 3.5 Gm. daily.
The absence of water retention is probably explained by the rapid urinary excretion
of sodium in these cases (unpublished).
from widespread tuberculosis. The clinical and anatomical findings suggest that cortisone was in no way involved.

The 108 patients suffering from recent pneumonic tuberculosis who were seen since 1952 are all still alive; the first few, including those most severely affected have resumed work and normal social life three years ago. From the human point of view they would have a particularly gloomy prognosis, despite antibiotic and chemotherapeutic treatment. Four patients showed systematic aggravation in spite of specific treatment; radiological improvement was not seen until hydrocortisone was given in addition to antibiotic treatment. It is interesting to note the evolutionary autonomy of certain inflammatory processes. The large doses of streptomycin caused no neurological side-effects. It may be stated that hydrocortisone and prednisone had a protective effect owing to its antitoxic properties.

The change in general condition was the more marked if the pneumonic foci were more markedly exudative. The pneumonic foci are considerably less rich in bacilli than the longstanding ulcerative lesions. The improvement in general condition in cases of tuberculosis showing a predominance of longstanding multiple ulcerative lesions was less marked. It may be stated that the disappearance of the major symptoms of acute tuberculosis is dependent on the absorption of the pneumonic exudate. The improvement in general condition may well be correlated with the reduction in the toxine content of the exudate as lesions seem to be isolated during corticosteroid treatment. The patient affected with pneumonic tuberculosis is suffering from an inadequate and dangerous defence reaction rather than from changes directly caused by the bacilli. This conception stands apart from the clinical data in that it is observed in a number of acute infection diseases of varying etiology. Pathological anatomical studies have shown that pneumonic tuberculous lesions include changes of unmistakable etiology and a perifocal alveolitis which, at least at the onset, has no specificity. Regression of pneumonic tuberculous foci commences from the periphery inwards and runs parallel with the disappearance of the chief symptoms of the condition. Menkin (op. cit.) has demonstrated toxic metabolites in the exudates. Reilly and Selye studied the functional sequelae of certain pathological processes. Also, it should be borne in mind that a pneumonic exudate tends to undego irreversible connective tissue organization. It is therefore logical to make an attempt at reduction of the inflammatory processes in cases of tuberculosis dominated by exudative foci and characteristic of the reactivity of certain subjects.

The late results of cortisone treatment in tuberculosis are not yet sufficiently well known and its disadvantages have not yet been reduced to such a negligible point, that the adrenocortical hormones can be introduced into the routine treatment of circumscribed tuberculosis. In investigations based on the experimental work of Ducommun (1952) we have shown that an anti-inflammatory effect can be produced without hormones by means of association of chlorpromazine and phenylsemicarbazide (Favez et al., 1956, B); the effect thus obtained is usually comparable to that obtained with cortisone.
Conclusions

Acute pneumonic tuberculosis, miliary, serous affections and especially meningitis constitute an indication for prednisone treatment in addition to specific drugs. The results obtained are undoubtedly superior to those seen after antibiotic treatment alone.

SUMMARY

A description is given of 10 cases selected from a group of 120 patients suffering from active pulmonary tuberculosis. These 120 cases were treated with a combination of hydrocortisone (or prednisone), streptomycin and INH. The results obtained in pneumonic tuberculosis, miliary, and tuberculous meningitis were considerably better than those obtained by specific treatment alone. The importance of inflammatory phenomena in pneumonic tuberculosis is discussed.

RESUMEN

Se describen diez casos tomados de un grupo de 120 enfermos de tuberculosis pulmonar activa. Esos se trataron con una combinación de hidrocortisona o prednisona, estreptomicina y Hain. Los resultados obtenidos en formas neumónicas de tuberculosis y en meningitis tuberculosa fueron considerablemente mejores que los obtenidos por los medios específicos solos.

Se discute la importancia de los fenómenos inflamatorios en la tuberculosis neumónica.

RESUME

Les auteurs donnent la description de dix cas choisis parmi un groupe de 42 malades atteints de tuberculose pulmonaire évolutive. Ces cas furent traités par une association d’hydrocortisone ou “prednisone,” de streptomycine et d’isoniazide. Les résultats obtenus dans la pneumonie tuberculeuse et dans les méningites tuberculeuses furent considérablement meilleurs que ceux obtenus par le traitement spécifique seul. L’importance des phénomènes inflammatoires dans la pneumonie tuberculeuse est discutée.

ZUSAMMENFASSUNG

Es wird eine Beschreibung gegeben von 10 aus einer Gruppe von 120 an aktiver Lungentuberkulose leidenden Patienten ausgewählten Gruppe. Diese Fälle wurden mit einer Kombination von Hydrocortison oder Prednison, Streptomycin und INH behandelt. Die bei pneumonischen Tuberkulose-Formen und bei tuberkulöser Meningitis erzielten Resultate waren beträchtlich besser als die durch spezifische Behandlung allein erzielten. Es wird die Bedeutung des entzündlichen Phaenomens bei der pneumonischen Tuberkulose-Form besprochen.

BIBLIOGRAPHY


