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In the definitive treatment, a determined effort is made to promote complete re-expansion of the lung to prevent impairment of pulmonary function. If repeated aspirations of the chest fail to release the lung, one resorts to intrapleural instillations of fibrinolytic enzymes (streptokinase and streptodornase) to liquefy the blood coagulum and, if necessary, decortication.

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ACTH, CORTISONE AND TUBERCULOSIS*

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CORTISONE has been shown to inhibit the formation of granulation tissue and to reduce the function of the reticulo-endothelial system. These facts are of importance in the development of resistance to infection and led Spain and Molomut[1] to investigate the effect of cortisone on the development of tuberculous lesions in guinea pigs and their modification by streptomycin. Tuberculous lesions in those animals which received cortisone were less well localized and more widely distributed than in other groups. Animals treated with streptomycin and cortisone did not show the same degree of healing as those treated with streptomycin alone. The theory that cortisone has fibrinolytic activity was disputed as no action on formed granulation tissue was observed. A warning was given that cortisone might cause a flare-up of latent or quiescent tuberculosis in humans. Experiments by Michael *et al.*[2] using albino rats which are normally resistant to virulent human tubercle bacilli showed that cortisone had a marked effect on this resistance and resulted in widespread tuberculous lesions. Hart and Rees[3] have reported similar findings in mice.

Cummings[4] states that cortisone has no effect on the *in vitro* growth and respiration of the tubercle bacillus. Changes in the response to tuberculous infection when cortisone is given are due to alteration of immune reactions in the host. The tuberculin skin sensitivity reaction is frequently lessened in intensity or suppressed during cortisone therapy, but LeMaistre *et al.*[5] found variable changes in hæmagglutination titres and gamma globulins.

The effects of ACTH and cortisone on active cases of pulmonary tuberculosis are variable. Freeman[6] has reported two cases, in one of which a spread of disease occurred whereas there was no change in the other from a radiological aspect. Symptomatically there was marked improvement in both cases with prompt fall in fever, cessation of coughing, reduction of sputum and fall in sedimentation rate, but these symptoms returned after cessation of therapy. The sputum remained positive throughout. Comden and Netzer[7] treated three cases of far advanced fibrocavernous pulmonary tuberculosis and rheumatoid arthritis with ACTH and noted similar symptomatic improvement, with worsening of the pulmonary disease radiologically in one, and no change in the other two cases after 3½ and 6

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months' treatment with ACTH respectively. LeMaistre *et al.*[8] have reported the results of ACTH or cortisone treatment of seven patients with far advanced pulmonary tuberculosis, four with tuberculous laryngitis in addition. The four with tuberculous laryngitis were deliberately selected so that the effect of the hormones on tuberculous lesions might be directly observed. Cortisone or ACTH resulted in abrupt and profound changes in the course of the illness, characterized by defervescence, a sense of well-being, increase in strength and improvement in appetite. Improvement in phonation and disappearance of dysphagia occurred in those with tuberculous laryngitis and there was reduction of laryngeal œdema and exudate. In all patients the improved state was temporary and could not indefinitely be maintained by further administration of hormone. Two of the patients died. Decrease in density of the lung lesions radiologically was observed in five of the patients.

The experimental evidence led the American Trudeau Society[9] to issue a warning against the use of ACTH and cortisone in the presence of tuberculous infection. However, few reports have appeared in the literature in which these hormones caused an exacerbation of tuberculous disease. Bogen[10] has reported three cases in which ACTH apparently resulted in the appearance of active tuberculous disease. In two cases, one with rheumatoid arthritis and the other with periarteritis nodosa, tuberculosis had not been previously diagnosed: in the former, positive sputum associated with pulmonary disease appeared, and in the latter lymph nodes became larger and biopsy showed tuberculous lymphadenitis whereas biopsy prior to starting ACTH had shown changes of periarteritis nodosa. In the third case pulmonary disease had been stable for two years and when ACTH was given for rheumatoid arthritis the sputum again became positive.

Two patients have been admitted to Toronto Hospital for Tuberculosis during recent months in which administration of cortisone appeared to have influenced tuberculous infection adversely. In each case cortisone had been administered at another hospital.

CASE 1

N.W., 31 year old married woman. She had scleroderma, diagnosed 6 years prior to admission, which had run a progressive course resulting in marked changes in the skin of the face, arms and hands. Seventeen months prior to admission pain and swelling occurred in the region of the left shoulder, and the joint gradually became fixed and relatively painless. Successively the left thigh, right thigh and right arm were involved by painful swellings associated with redness and swelling of the overlying skin. Her symptoms were all attributed to scleroderma and dermatomyositis. In April, 1950, she was treated with cortisone, a total of 4.6 gm. being given over a period of twenty-three days. A small tumour previously noted under the anterior fold of the left axilla became larger and fluctuant. Pus was aspirated from this and also from the left shoulder joint from which tubercle bacilli were cultured. X-ray of the left shoulder showed generalized osteoporosis and erosion of the medial aspect of the head of the humerus. Cortisone resulted in moderate improvement in the symptoms due to dermatomysitis but the remission lasted only 2 or 3 months. There have been no further manifestations of tuberculous disease and the left shoulder joint now shows bony fusion after immobilization in a plaster shoulder spica.

CASE 2

L.C., 48 year old married woman. Four year history of chronic ill health characterized by marked loss of weight, transitory arthralgia and swelling of the small joints of the hands, transitory macular rash on the face, fever, recurrent attacks of pneumonitis which did not respond to antibiotics, swelling of the legs, albuminuria, hyperglobulinæmia and left bundle branch block. A diagnosis of lupus erythematosus disseminatus was confirmed in February, 1951 when the presence of the LE phenomenon was observed in the cells of the sternal marrow. At this time the sputum had been repeatedly negative.

During March and April, 1951, cortisone was given in a dosage of 3.4 gm. spread over 30 days. Rapid but temporary improvement occurred in the patient's condition and this was followed by severe toxæmia, remittent fever and mental confusion. Cough and sputum increased and the sputum was positive for tubercle bacilli on smear and culture for the first time. X-ray of the chest prior to starting cortisone showed moderately dense fibrotic changes at the right base, and one month later miliary tuberculosis was present in the lungs. This was later complicated by tuberculous meningitis. Treatment with parenteral and intrathecal streptomycin and oral PAS since June, 1951, has resulted in considerable improvement but the outcome is still uncertain.

COMMENT AND SUMMARY

There is ample experimental evidence that ACTH and cortisone act adversely on tuberculous infection in animals. In view of this the scanty clinical evidence should, in the present state of our knowledge, be considered significant, although it is appreciated that the few reported cases might have followed the course described without the administration of ACTH or cortisone.

The frequency with which latent or quiescent tuberculous infection flares up as a result of ACTH or cortisone therapy is not known. Many patients have now been given ACTH or cortisone for a variety of conditions, and the number in which tuberculosis was activated appears to be very small. The risk, however, remains and it would appear to be inadvisable to give these hormones to patients with active or quiescent

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tuberculosis unless there are clear cut non-tuberculous indications, in which case streptomycin and PAS should also be given. Streptomycin and PAS should be administered during the period of hormone therapy and although there is no available evidence it is probably advisable to continue these drugs for several months after ACTH or cortisone have been discontinued.

ACTH and cortisone have no place in the treatment of tuberculosis and may be harmful.

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ADVENTURES WITH DECAMETHONIUM BROMIDE*

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THIS REPORT is intentionally not an elaborate scientific document. My only wish is to relate some personal experiences with decamethonium bromide, also called syncurine, a relaxing agent familiar to all of you. Allow me to leave aside the chemical formula of decamethonium bromide and the usual clinical reactions; these you know better than I. In this hospital syncurine has been used quite extensively during the last two years (over 4,000 cases). I feel that this drug is of great value and I do not hesitate to use it. For our mutual benefit I will mention only my difficulties in using this drug.

CASE 1

A 53 year old white female was admitted to the hospital for what was thought to be intestinal obstruction. Urine analysis was normal. Red blood count was 3,200,000 per cm. Hæmoglobin 68%. This patient was found to be group A- RH+ and was cross-matched with two pints of blood. She was slightly jaundiced. Pre-anæsthetic medication consisted of morphine 1/6 and atropine 1/150. She was brought to the operating room and at 2 p.m. intubation was easily performed with pentothal and decamethonium bromide (using a mixture of 500 mgm. of 2½% pentothal and 4 mgm. of decamethonium bromide). Anæsthesia was maintained with cyclopropane and a total of 7 mgm. of decamethonium bromide was given over a period of one and a half hours. No obstruction was found. The liver was slightly atrophic and there were 1,500 c.c. of ascitic fluid in the abdominal cavity. Complete respiratory paralysis followed the injection of the mixture of pentothal and decamethonium bromide and lasted 15 minutes. This was considered normal. Respiration was maintained as usual by manual compression of the bag. Relaxation was maintained with decamethonium bromide, 3 more mgm. being injected up to the closure of the abdomen; one c.c. at a time. Oxygenation, blood pressure and pulse were good all times. The last injection of decamethonium bromide (1 c.c.) was followed by complete respiratory paralysis. After the operation was finished, the endotracheal tube was left in place and connected to the gas machine. The patient was then brought to the recovery room and pulmonary ventilation was maintained by myself until the return of normal respiratory activity. Respiratory paralysis lasted two and a half hours. During that period, colour, blood pressure and pulse were completely normal. A total of a 1,000 c.c. of blood and 500 c.c. of 5% G/W were given. No drug of any kind had been given during that period. At 6 p.m. the patient was conscious, breathing normally and ready to go back to her room.

CASE 2

A 66 year old, obese white woman with chronic bronchitis and hypertension was brought to the hospital for repair of a diaphragmatic hernia. Pre-anæsthetic medication consisted of demerol 100 mgm. and atropine 1/150. Anæsthesia was induced with a mixture of pentothal (500 mgm.) and decamethonium bromide (4 mgm.). The mixture of pentothal and decamethonium bromide was injected slowly and cyclopropane was given at the same time. Intubation was easily performed and the maintenance was uneventful. Relaxation was good. There was moderate respiratory depression and assisted respiration was used. The repair of the diaphragmatic hernia lasted two hours. Exploration of the abdomen showed the liver to be very atrophic. A total of 8 mgm. of decamethonium bromide was used, the last c.c. being injected five minutes before the closure of the peritoneum. This was followed five minutes later by complete respiratory paralysis which lasted three and a half hours. The endotracheal tube was left in place and in connection with the gas machine. Artificial respiration by manual compression on the bag was performed until the return of respiratory activity. Blood pressure and pulse were perfectly normal. There was no cyanosis at any time. Patient had an uneventful recovery.

CASE 3

A fifty year old white woman had cirrhosis of the liver and marked ascites. It was thought that an anastomosis of the portal vein to the inferior vena cava might bring some improvement. The preoperative condition was complicated by anæmia, myocarditis and malnutrition. The patient was brought to the operating room at 9 a.m. Because of cardiac irregularities (she had in fact a right bundle branch block) electrocardiographic tracings were done during the operation. Cardiac irregularities were controlled by procaine given intravenously in a 0.2% dilution, the injection being started before the induction of anæsthesia. Induction took place at 9.15 a.m. Two hundred mgm. of 2½% pentothal were injected slowly,

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