Treatment with methyl thiouracil, 100 mg. twice daily, was begun and considerable clinical improvement followed. After two weeks she complained of "difficulty in focusing her eyes," and her doctor noted that she had horizontal nystagmus to right and left. The dose of thiouracil was reduced to 100 mg. once a day during the next week, but she stated that she felt "light-headed" and that everything she looked at "seemed to be jumping about." After another four days she developed such intense vertigo that she could not stand or even sit up in bed unless she kept her eyes closed, and any attempt to get up and move about caused nausea and sickness. Gross nystagmus was present in all planes. Thiouracil was stopped and the more severe symptoms subsided during the next three days, but she remained unsteady and immediately became sick when she tried to walk. At no time was there any headache or skin rash, and apart from the symptoms described above she felt quite well.

Her general condition was good and the signs and symptoms of thyrotoxicosis were definitely improved—pulse 100, exophthalmos much less noticeable, skin normal, and no complaint of feeling hot. She was in fact very pleased with the effect of treatment and most anxious to continue to take the thiouracil in case symptoms should return. The only abnormal finding in a full examination of the central nervous system was a very coarse nystagmus in all planes. Romberg's sign was negative and the ocular fundi and tympanic membranes were normal. The condition of the heart and the blood pressure were unchanged, except that a few extrasystoles were noted.

During the next three weeks she gradually improved and was able to go out if accompanied. She still found reading difficult. Her thyrotoxic symptoms, however, increased again, and partly on this account and partly because of the unusual effects of the thiouracil treatment she was sent to Professor Himsworth. He agreed that the development of nystagmus could, in reason, be attributed only to the thiouracil, but could neither recall having encountered a similar case himself nor, in spite of wide inquiry, both in this country and abroad, find anyone else who had done so. He advised surgical treatment for the thyrotoxicosis without delay.

The patient was admitted to hospital on May 24, 1949; and on June 3 subtotal thyroidectomy was performed by Mr. John Griffith. During the first week after operation nystagmus increased, but by the fourteenth day, when the general condition was excellent and the pulse rate had become stabilized between 70 and 80, it became less marked and she made no complaint of visual disturbance. She was then discharged from hospital.

Sections of the excised gland were examined by the pathologist (Dr. R. W. Johnson), who reported that the appearances were typical of thyrotoxicosis.

When last seen, on July 15, 1949, six weeks after operation, she looked and felt well and had gained a stone (6.4 kg.) in weight. Nystagmus, however, was still present, being most marked when she looked to right and left, but also when the eyes were raised upwards. She said that she could read without difficulty but that "things jumped about" when she looked to either side. Apart from the nystagmus, examination of the central nervous system was negative as before, and there was no evidence of cardiovascular sclerosis or ear disease.

COMMENT

When thiouracil produces toxic effects they are generally manifest on or about the fourteenth day after the beginning of treatment. In the present case visual symptoms and nystagmus appeared at this time. These receded again with omission of the drug. There is therefore strong presumptive evidence that this was an effect of thiouracil. The absence of history or physical signs of disease of the central nervous system or of vascular sclerosis makes any alternative explanation improbable.

It might be suggested that the particular sample of thiouracil used contained an impurity which could be held to blame; some of the tablets were therefore sent to the manu-

facturers for analysis, but they were found to be in every way normal pure samples of methyl thiouracil.

In the circumstances it is of course impossible to give a prognosis, but as four months have elapsed since thiouracil was discontinued and signs and symptoms are still present it seems unlikely that complete recovery will now take place.

Acknowledgment is due to Dr. Fitzgerald Frazer for permission to publish these notes of his patient and for his own careful records of the case while she was under his care. I have also to thank Professor Himsworth for his interest and advice.

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Fulminating Staphylococcal Pneumonia Treated with Massive Doses of Chloramphenicol and Penicillin

Fulminating staphylococcal pneumonia has in recent years shown itself to be a rapidly fatal condition despite penicillin therapy. We have recently encountered a case following influenza B infection in which the organism was resistant to penicillin. Early treatment with chloramphenicol was instituted, but the patient's condition deteriorated rapidly; however, with increased dosage he recovered after a critical illness.

CASE REPORT

The patient was a male nurse aged 39. His first symptoms were those of a severe febrile cold. After four days he developed a slight pain in the left side of his chest. During the next six hours this increased to such an extent that breathing became difficult; it was at this stage that he attended the casualty department of University College Hospital.

Physical examination showed a severely ill man with marked respiratory distress, temperature 100.6° F. (38.1° C.), pulse 100,

FIG. 1.—Radiograph taken on March 22.

respirations 26. Movement on the left side of his chest was considerably reduced and rhonchi were widespread. Radiographs of his chest taken at that time (March 22, 1950) showed consolidation in the anterior and middle basal segments of the left lower lobe (Fig. 1). A diagnosis of aspiration pneumonia was made, and after blood and sputum had been collected for laboratory examination he was given 2.5 g. of chloramphenicol

followed by 0.25 g. four-hourly. This drug was made available as part of an investigation into the treatment of aspiration pneumonia. Later, when it became obvious that this was in fact a case of penicillin-resistant staphylococcal pneumonia, the supply was maintained by the Ministry of Health.

During the first 24 hours of treatment there was a great deterioration in the patient's condition. He showed an ashen-grey cyanosis, his temperature reached a maximum of 102° F. (38.9° C.), and the physical signs in his chest indicated rapid spread of the pneumonic process. The left side did not move at all on respiration, the percussion note over it was stony dull, and breath sounds were inaudible. Radiographs at this stage showed (March 24) the left hemithorax to be completely opaque, but with no evidence of mediastinal displacement (Fig. 2). A report of the sputum culture described a predominant growth of *Staphylococcus aureus*, resistant to penicillin and moderately sensitive to chloramphenicol.

FIG. 2.—Radiograph taken on March 24.

FIG. 3.—Radiograph taken on August 8.

In view of this report and of the patient's poor response to chemotherapy, the dosage of chloramphenicol was doubled and crystalline penicillin, 1,000,000 units three-hourly, was started; the patient was placed in an oxygen tent.

For 24 hours his condition remained critical, but thereafter he made steady, if slow, improvement. His temperature fell by lysis to normal in 14 days. Within 10 days of his admission radiographic evidence of resolution appeared and three weeks later was almost complete. He received in all 43 g. of chloramphenicol. Complement-fixation tests for influenza showed a titre of 1/4 for influenza B on admission and a titre of more than 1/128 six days later. Fig. 3 shows the radiographic appearance on August 8.

DISCUSSION

In the great influenza pandemics of 1889 and 1918-19 the staphylococcus was only occasionally found in fatal cases, although in localized outbreaks a high incidence was reported (Netter, 1892; Chickering and Park, 1919). In the smaller epidemics of recent years it has been found in a considerable proportion of the more serious cases (Stuart-Harris *et al.*, 1938). Wollenman and Finland (1943) and Stuart-Harris *et al.* (1950) have commented on the failure of fulminating cases to respond to chemotherapy.

The present case appeared on admission to be one of a moderately severe aspiration pneumonia. It was only after 24 hours on conservative doses of chloramphenicol that the condition gave rise to anxiety. At this stage he presented the prostration, respiratory distress, and ashen-grey cyanosis typical of a fulminating case of staphylococcal pneumonia. There seems to be little doubt that, without the very large doses of chloramphenicol and penicillin used, he would have succumbed to his infection within 48 hours of his admission to hospital.

SUMMARY

A case is described of fulminating staphylococcal pneumonia, secondary to influenza B, successfully treated with chloramphenicol and massive doses of penicillin.

Reference to the literature suggests that the association of influenza and staphylococcal pneumonia is an extremely fatal one.

I wish to thank the Virus Reference Laboratory, Colindale, for carrying out the complement-fixation tests for influenza, Professor M. L. Rosenheim for permission to publish this case, and Dr. J. D. Nabarro for advice in preparing the manuscript.

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The Ministry of Health states that more blood was given to hospitals in England and Wales during the June quarter this year than in any three months since the war. Gifts totalled 128,392, making over 250,000 in the first half of this year. Over 35,000 new donors joined the National Blood Transfusion Service in the quarter. Blood consumption is 50 times what it was in 1938 and is still mounting. To meet these increasing demands without calling too often on existing donors, at least 200,000 more enrolments are needed. There are now 388,000 registered donors—a gain of 10,700 in the quarter and the highest total since 1945.