great importance, and a social worker will cover both the patient's home and employment after discharge.

This, briefly, is an outline of the scheme, and it is hoped that many patients who formerly helped to swell the ranks of the unemployed will be returned to work either in the open market or in sheltered employment.

Conclusion

There is no doubt that psychiatry is fast becoming, or has become, an important branch of social medicine. Adequate housing and education, the teaching of the individual how to enjoy his leisure time without becoming bored, and financial security are all important factors in promoting mental health and in preventing relapse of those who have recovered from mental ill-health. The removal of public prejudice against mental disease, and an attempt to make everyone appreciate that psychiatry is a scientific subject, are of paramount importance in the promotion of mental hygiene.

PENICILLIN IN THE TREATMENT OF DIPHtherIA

BY

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Penicillin Sensitivity of *Carynebacterium diphtheriae*

In 1929 Fleming reported that a slightly purified extract of a broth culture of *Penicillium notatum* was active against the pyogenic cocci and rather less so against *Corynebacterium diphtheriae*. This observation was confirmed by Clutterbuck *et al.* (1932) and by Chain *et al.* (1940). Young and Mood (1945) tested six strains for penicillin sensitivity and found all to be inhibited by concentrations between 0.004 and 0.06 unit per ml. In contrast to this Ercoli, Lewis, and Moench (1945) found that over 1 unit per ml. of penicillin was required to inhibit growth. Long (1946b) tested thirty strains and obtained sensitivities between 0.02 and 0.004 unit per ml. It is probable that the size of the inoculum used is an important factor in accounting for these differences, though even if an organism is resistant enough to require over 1 unit of penicillin per ml. to inhibit growth the possibility of successful treatment is not excluded.

Experimental Work on Treatment in Guinea-pigs

Reports on the treatment of experimental diphtheria in guinea-pigs are conflicting, Young and Mood (1945) claiming that infection could be prevented by extremely small amounts of penicillin mixed with the inoculum, and cured by larger doses given as long as 23 hours after inoculation with a larger dose of culture. Ercoli, Lewis, and Moench (1945), on the other hand, state that penicillin had only a negligible action on the course of an infection following a small inoculum.

It would appear that there is not sufficient evidence on which to judge the effect of penicillin on artificially induced diphtheria in the guinea-pig; but even if the evidence were conclusive it is doubtful whether it would be safe to argue from guinea-pig to man. The degree of susceptibility and the lesion resulting from injection of culture in the guinea-pig are not comparable to the naturally occurring disease in man. Further, diphtheria in man is commonly complicated by secondary infection with haemolytic streptococci, Vincent's organisms, and mixed

anaerobes. All these organisms are markedly penicillin-sensitive and are almost invariably present in the disease, though the haemolytic streptococcus is less common than the others.

Penicillin-treated Cases in the Literature

Symons (1945) reported the case of a boy of 13 years who received antitoxin and sulphonamides on the second day of the disease. One day later, as a result of the development of bull-neck and spreading of the membrane, penicillin was administered, 24,000 units being given three-hourly. This was followed by the membrane "separating, disintegrating, and almost disappearing within 24 hours." *C. diphtheriae gravis* and haemolytic streptococci were obtained from swabs before treatment.

Archer (1945) describes the dramatic improvement in the local condition of a patient with "mixed K.L.B., haemolytic streptococci, and Vincent's infection." Diphtheria antitoxin and "antistreptococcal serum" had been given previously without effect. Christie and Preston (1946) refer to two patients both with mixed *C. diphtheriae intermedius* and haemolytic streptococcal infections. Case 1, aged 15 years, had severe pharyngeal diphtheria with a bull-neck. The day of the disease is not given, nor is the state of activity of the membrane. He was treated with antitoxin and a sulphonamide on admission; three days later a petechial rash appeared, and systemic penicillin (100,000 units a day) with an hourly throat spray (500 units per ml.) was started. The throat had almost completely cleared in another two days. Case 2, aged 17, had severe pharyngeal diphtheria of "not more than three days' standing." On admission the patient was treated with antitoxin and penicillin as in the previous case. The membrane separated in two days, though the general condition remained unchanged. Death occurred from heart failure, preceded by immobility of the palate.

Dodds (1946) reported 13 cases treated with penicillin and antitoxin, and 13 controls treated with antitoxin alone. *C. diphtheriae gravis* is stated to have been present in a "high proportion" of these cases, though exact figures are not given; neither is the presence or absence of secondary infection noted. 200,000 units of penicillin were administered daily for two days, followed by 100,000 units daily for three to six days. The conclusions reached were that penicillin "appeared to have been in some degree beneficial in most cases treated," though it "seemed to have little effect on the rate of clearance of the membrane." Symons (1946) reported a further case from which virulent diphtheria bacilli were not isolated.

De, Chatterjee, and Ganguli (1947) describe the successful treatment of 27 Indian children alleged to be suffering from diphtheria, penicillin being administered by three-hourly injections of 10,000 units. Antitoxin was withheld, since the work was undertaken "to ascertain whether the drug can be used in the place of serum," "the risk being minimized by selecting early cases, under the assumption that the child can destroy and/or eliminate a certain amount of diphtheria toxin." Of the 27 cases treated 11 are described as bacteriologically negative; in the remainder the organisms appear to have been identified on morphology alone. In view of the unusually high fever (10 of the patients had temperatures between 102 and 104° F. (38.9 and 40° C.)) it is unfortunate that no indication is given of the presence or absence of secondary infection and, in particular, of haemolytic streptococci. Their cases are classified into four groups. Group I: early cases, bacteriologically positive. Group II: early cases, bacteriologically negative but clinically diagnosed as classical diphtheria. Group III: moderately severe cases, bacteriologically

positive. Group IV: Moderately severe cases, bacteriologically negative but clinically diagnosed as classical diphtheria.

The early cases (Groups I and II) gave histories of from two to six days' illness, the remainder (Groups III and IV) from three to seven days', making it difficult to appreciate the significance of the term "early." Clinical observations are brief, a single word such as "good" or "fair" describing the general condition of the patient, while the word "patch" describes the membrane, its removal being the sole local change recorded in response to treatment. Fuller information will be required before the significance of this can be assessed, but in the meantime the treatment of diphtheria with penicillin without the early adequate administration of antitoxin can only be condemned. The argument of economy cannot carry any weight against the experimental and clinical evidence to the contrary and the considerable risks involved.

Karelitz *et al.* (1947) record the results of treating 80 cases of diphtheria with antitoxin and penicillin; 42 controls were treated with antitoxin alone. The investigation was bacteriologically controlled. The dosage of penicillin employed was 20,000 units three-hourly for one group of patients and 20,000 units two-hourly for a second; a third group was treated by a penicillin spray; while a fourth was given 20,000 units three-hourly with a penicillin spray.

The conclusions reached were that systemic penicillin in this dosage rendered patients bacteriologically negative for *C. diphtheriae* more rapidly than controls treated with antitoxin alone. Toxic complications and the time that membrane persisted were not reduced in the former group, but oedema and soreness were relieved and complications due to pyogenic organisms were less frequent than in the group treated with antitoxin alone. After five days' penicillin treatment 27.5% of patients showed positive throat cultures as compared with 100% of controls. Local treatment alone with penicillin was ineffective.

Personal Observations

The aim in penicillin treatment of diphtheria is the rapid elimination of pathogens, with the prevention of further toxin formation. The evidence available suggests that penicillin is effective in treatment, particularly when secondary infection is present. The work of Karelitz *et al.* shows a substantial reduction in corynebacteria resulting from a dosage of penicillin between 160,000 and 240,000 units a day, though even then 27.5% of patients yielded positive swabs at the fifth day.

In order to judge the most effective dose information is required as to the effects of penicillin in very much larger dosage than has commonly been employed hitherto. Long (1946b) suggested that 1,000,000 units of penicillin were required to eliminate penicillin-sensitive organisms from the throat and gum pockets within 24 hours, and expressed the opinion that less than 500,000 units a day were inadequate in the treatment of diphtheria. Three cases were mentioned in support of this view. It is proposed to describe these cases in detail together with observations on a further three cases. The penicillin treatment and bacteriological investigation were undertaken through the courtesy of Dr. Nathan, medical officer of health for St. Albans, who directed all other details of treatment, including the administration of antitoxin. In all cases daily swabs were taken for more than a month, though the length of time varied from patient to patient.

Case 1

This patient, a man aged 20, was seen at 3.30 p.m. on the fourth day of the disease as judged from his earliest symptom. He was ashy grey, cyanosed, with a massive bull-neck, in pain,

and had severe dysphagia. Breathing was partially obstructed. Fœtor was intense and a thick sputum was being coughed up with difficulty. Adherent membrane with an active spreading edge covered fauces, tonsils, and uvula. The swelling was so intense that it was not possible to view the post-nasal space, larynx, or trachea. The patient had received 20,000 units of antitoxin intramuscularly on the previous day and 80,000 units intramuscularly on the same day. Penicillin treatment was started, a million units being given in the day by three-hourly injection; this was maintained for three days.

On the next day, at 11.30 a.m., the patient was pink in the face and non-toxic, and felt better. The active glistening edge of the membrane had dulled and it was no longer adherent. Fœtor was absent and the bull-neck reduced in size. On the third day of penicillin treatment the patient's appetite had returned, the membrane had separated, and long strands together with altered blood were being coughed up. Obstruction to breathing was a source of continued anxiety, and tracheotomy was considered. The clinical picture was all the more remarkable because the patient felt and looked comparatively well. No complications followed and he recovered. *C. diphtheriae gravis* was isolated in large numbers on the first day of the disease. No haemolytic streptococci and no Vincent's organisms were demonstrated. After this, daily swabs and examinations of membrane failed to reveal any pathogens. (Penicillinase was added to the medium.) The organism was inhibited by 0.02 unit of penicillin.

Case 2

A girl of 13 years was seen on the third day of the disease as judged by the first symptom. She had received 80,000 units of antitoxin intramuscularly. The medical officer of health and the matron considered the prognosis to be hopeless. The patient was very toxic, ashy grey, and collapsed; pain appeared to be intense, and she was delirious, and an adherent early active spreading membrane covered tonsils, fauces, uvula, and palate almost to the teeth. Bull-neck was marked. Penicillin treatment was started, a million units being given in the day by three-hourly injection; this was maintained for three days. The same night the membrane was coughed off intact. When seen by me the next day she appeared to be non-toxic and was mentally alert. There were no complications and recovery was complete. *C. diphtheriae gravis* was isolated in large numbers before treatment and twenty hours after the commencement of penicillin, but not subsequently. The organism was inhibited by 0.02 unit of penicillin, as in the previous case. Haemolytic streptococci were present in large numbers; they were not demonstrated again after treatment had started.

Case 3

A woman aged 32, with severe diphtheria, was seen on the second day as judged by the history, though the appearance of the membrane suggested a later stage of the disease. The patient felt ill and looked toxic, pain was moderate and dysphagia pronounced. Adherent membrane spread from both tonsils on to the faucial pillars to the uvula. (It did not appear to be extending.) Oedema and swelling were marked, and she had a mild bull-neck. 80,000 units of antitoxin had been given intramuscularly. It was decided to try half a million units of penicillin; it was realized that the dose might be too small, since it would be barely sufficient to remove the most penicillin-sensitive organisms from the oral cavity within 24 hours. (The reason for giving the small dose in this case was because I had previously found that patients treated with systemic penicillin began to lose penicillin-sensitive organisms from deep gum pockets when a dose of half a million units was given in 24 hours. The maximum effect was achieved only by giving one million units in that time. As this case seemed less toxic I wanted to try to assess the value of the lower dosage.) One day later the membrane had separated from the left tonsil, but was partly attached to the right. The patient was non-toxic and symptom-free. She recovered, but her convalescence was complicated by immobility of the palate and bradycardia. *C. diphtheriae gravis* was isolated in large numbers from swabs and membrane before treatment. The organisms were also demonstrable in small numbers 24 hours later. A haemolytic streptococcus not belonging to Group A was also present in

spite of the fact that it was markedly penicillin-sensitive. This suggests that the dosage was too low. The strain of *C. diphtheriae gravis* was inhibited by 0.004 unit of penicillin.

Further Cases.—Three further cases have been treated. All were mild, all received one million units of penicillin a day for three days, and in none was I able to demonstrate diphtheria bacilli after the first day's treatment.

Discussion and Conclusions

Though there is agreement that *C. diphtheriae* is penicillin-sensitive, considerable disagreement exists as to the degrees of sensitivity recorded. A possible explanation is the absence of any standard technique for the estimation of sensitivity, and in particular of the size of the inoculum.

The experimental work in animals has produced conflicting results, so that there is little evidence on which to judge the possibility of effective treatment in man.

An attempt has been made to review all the cases of penicillin-treated diphtheria that have been described in the literature at the time of writing. In this country no case of diphtheria without secondary infection appears to have responded to treatment in a convincing fashion. By far the most important observations on this subject are those of Karelitz *et al.*, who, in spite of relatively large dosage (160,000–240,000 units a day), failed to observe any increase in rate of clearance of the membrane or any reduction in the incidence of toxic complications. The value of their report is impaired by their failure to use tellurite media and penicillinase for culture purposes; if they had done so their figures for the persistence of diphtheria bacilli would probably have been from 10 to 30% higher.

The most valuable criterion on which to judge the response to penicillin treatment would appear to be the time taken for *C. diphtheriae* to be eliminated from the lesions, thus excluding the effect of secondary infection. The dose of penicillin employed might reasonably be supposed to be that which reduces this time to the minimum.

Evidence is presented that *C. diphtheriae* can be eliminated in under 24 hours in severe cases of diphtheria with a dosage of 1,000,000 units a day. Though a smaller dose than this would probably be inadequate, a larger dose might be even more effective.

Summary

The available experimental and clinical evidence on the penicillin treatment of diphtheria is reviewed.

Experimental and clinical evidence is brought forward to show that it is possible to remove diphtheria bacilli from the upper respiratory tract within 24 hours.

A plea is made for larger dosage; at least 1,000,000 units a day would appear to be desirable in severe cases.

The value of penicillin is particularly striking in the presence of secondary infection.

The importance of early adequate antitoxin administration is stressed.

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SPLINTS FOR FRACTURED NOSES

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Fractures of the nose are common injuries, but their early treatment is often unsatisfactory because displacement is obscured by haematoma and oedema. If telescoping of the septum does not obstruct the airway and there is no lateral deviation or depression of the bridge-line, no active surgical treatment is required. If any or all of these displacements have occurred, early treatment by the classical Gillies-Kilner (1929) technique of disimpaction and reduction yields excellent results with a minimum of discomfort to the patient. Should the displacement be missed in the early stages serious disability and disfigurement result, which can be put right only by more extensive procedures such as nasal refracture or bone-grafting (Oldfield, 1944).

After reduction of a recently fractured nose a simple type of splint is required such as a "cellona slab" (Fig. 1),

FIG. 1

FIG. 2

FIG. 1.—A "cellona slab" used for splinting a recently fractured nose after reduction.

FIG. 2.—A Safian brace.

a collodion splint reinforced by a moulded lead plate, or a Safian brace (Fig. 2), all of which serve to hold the nose in the correct position until union occurs in the correct alignment. This usually takes place in a very short time. If the bridge-line has been depressed, the "St. Louis method" is indicated (Fig. 3). Nasal refracture is required

FIG. 3

FIG. 4

FIG. 3.—"St. Louis method." Two lateral acrylic struts held in position by two through-and-through mattress sutures.

FIG. 4.—Nasal splint in position.