however, but the series was too small to allow of its dismissal. Iproniazid may have a value in severe angina.

The use of a drug with a very high incidence of side-effects tends to destroy the double-blind design of the therapeutic trial, as the clinicians can hardly fail to recognize which is the active drug. In such circumstances conclusions must be particularly cautious, and cannot claim the total lack of possible bias as fully double-blind trials.

With this in mind we would limit our conclusions to stating that we have been unable to confirm any striking value of iproniazid in angina pectoris; that, except in severe cases, it was of no greater efficacy than the placebo; and that even in the severer cases any possible benefit was at best marginal, numbers of such cases being too small, however, to be statistically conclusive.

Side-effects were frequent and troublesome, and were mainly similar to those experienced by others. Toxic jaundice was not encountered.

Summary

A controlled clinical trial of iproniazid in 51 patients with angina of effort is reported.

With the possible exception of its use in severe cases, it was of no greater efficacy than the placebo.

Even in severe cases proof of its value was not conclusive.

Toxic effects were frequent and may sometimes be serious.

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Changing social attitudes towards mental health, the development of an awareness of the benefits that accrue from early treatment, and a growing public confidence in the service which is available are factors probably contributing to the increase in voluntary "boarders" entering mental hospitals in New Zealand. These comments are made in the annual report on mental health statistics which has just been released. The rate of voluntary boarders entering hospital has risen from 13.4 per 100,000 of population in 1938 to 46.7 in 1958—an increase of almost 300%. In the same period the increase in the admission rate for patients was 19.8%. A total of 3,741 people were admitted to mental hospitals in New Zealand in 1958. Of the persons "discharged out-right" from mental hospitals in 1958, 19.8% were in mental hospitals for less than one month, 49.9% were in hospital one month and under three months, and 20.3% were in between three months and six months.

ANTIBIOTIC SENSITIVITY TESTS THE SPECIAL REQUIREMENTS IN OPHTHALMOLOGY

BY

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Little is known of the concentrations that are reached in the conjunctival sac from the application of drops and ointments, but it is established that the intraocular levels reached with penicillin, streptomycin, polymyxin, and neomycin after subconjunctival injection are considerably in excess of the blood levels reached from systemic administration. The usual sensitivity tests, being based on the blood concentrations reached by the different antibiotics on systemic administration, do not give full information for guidance in local treatment, for an organism may be insensitive to a relatively low concentration of an antibiotic and yet respond to a higher concentration. That this is the case with some organisms commonly met with in ocular infection is shown by the findings recorded in the accompanying Table.

It will be seen that in a series of 24 penicillin-resistant strains of *Staphylococcus aureus* found insensitive to disks containing 10 units of penicillin, no fewer than 14 were sensitive to tablets containing 50 units of penicillin, while 22 of the 24 responded to 250 units. (Increasing the concentration does not, of course, affect all organisms. Thus in 69 strains of different Gram-negative bacilli insensitive to 10 units of penicillin, only 4 (all *E. coli*) were found to be sensitive to tablets containing 50 units, and only one more organism, *Proteus vulgaris*, showed sensitivity to 250 units.) Similarly, of 23 strains of pneumococcus, an organism known for its resistance to neomycin, only 3 responded to the standard test of 30 µg. of neomycin, but the incidence of positive responses rose to 17 with 150 µg.; while all the 23 responded to 750 µg. Chloramphenicol,

Sensitivity of Some Micro-organisms in Relation to Different Concentrations of Some Antibiotics

	Staph. aureus (Penicillin- resistant)	Pneumo- coccus	Ps. pyocyanea		Pr. vulgaris and Allied Organisms		E. coli
			(a)*	(b)*	(a)*	(b)*	
No. of strains used							
	24	23	17	8	21	13	10
No. sensitive							
Antibiotic							
Penicillin :							
10 units ..	0	23	0		0		0
50 " ..	14		0		0		4
250 " ..	22		0		1		4
Neomycin :							
30 µg. ..		3	17	8	21	13	10
150 " ..		17					
750 " ..		23					
Chloramphenicol:							
30 µg. ..		23	15		13	1	8
150 " ..						7	
500 " ..			17		18		10
750 " ..						9	
Polymyxin:							
10 µg. ..				0			
50 " ..				6			
100 " ..				8			

* (a)(b) Two different experiments with a different range of antibiotics.

which gave a high incidence of efficacy against Gram-negative bacilli, including *Pseudomonas pyocyanea*, also gave better results when the higher concentrations were used; of 61 different Gram-negative bacilli, 37 were sensitive to tests with 30 μ g.; with tablets containing 150–750 μ g., another 17 organisms proved sensitive, leaving 7 out of 61 unresponsive. The same trend is seen with polymyxin. While none of the eight strains of *Ps. pyocyanea* studied was sensitive to disks containing 10 μ g., six responded to 50 μ g., and all the eight responded to 100 μ g.

These observations help to explain why occasionally a satisfactory result is obtained clinically by the use of massive doses of penicillin subconjunctivally when the organism is reported as penicillin-insensitive. Likewise, control by neomycin of experimental infection by pneumococci is explained by the fact that the dose used (0.5 g. subconjunctivally) gives high concentrations which would be effective against pneumococci which on the ordinary testing might well be reported as insensitive to neomycin.

At present the agents suitable for subconjunctival injection are penicillin, streptomycin, neomycin, and polymyxin (and there is promise in soframycin, of which, however, we have no experience). Streptomycin has distinct limitations in that it is not well tolerated locally and is productive of sensitization. Polymyxin has a limited range of action and is not free from local irritative effects. Penicillin and neomycin are the two agents that can be used readily as a subconjunctival injection, but neomycin is a toxic substance that has to be used with care. Chloramphenicol would be almost ideal for subconjunctival injection, if it were not so insoluble that it has to be used as a suspension of its micronized form, with a maximum possible injection of 0.75 ml. of 15% suspension containing in all some 100 mg. The tetracyclines are entirely unsuitable for subconjunctival use, as they are both insoluble and locally irritative. Information on the relative efficacy of the higher concentrations of these different agents, while it helps in making a choice in any particular case, therefore still leaves considerable problems.

It would seem desirable to establish the following simple routine in reports on the sensitivity of organisms in eye swabs—possibly in all cases, but certainly in infected eyes. One Petri dish should carry six disks or tablets containing the standard strengths for the commonly used antibiotics in ophthalmology: penicillin 10 units, streptomycin 20 μ g., chloramphenicol 30 μ g., tetracycline 30 μ g., neomycin 30 μ g., and polymyxin 10 μ g. A second and third Petri dish would contain the same agents in 5 times and 25 times the concentration. The results so obtained can easily be set out in three columns, giving the clinician clear guidance on the relative efficacy of the different antibiotics in different concentrations for the organism under consideration. A simpler procedure would be to use one Petri dish for penicillin and neomycin, each agent in the three strengths suggested; a second Petri dish would complete tests on other antibiotics in one strength only.

We are indebted to Dr. F. S. Gorrill and Messrs. Evans Medical Supplies for their interest and generosity in supplying specially prepared sensitivity tablets for this study. Dr. S. T. Cowan, of the National Collection of Type Cultures, and Dr. R. I. N. Greaves, of the University Pathology Department at Cambridge, have helped with cultures. We are obliged to Dr. L. Hewlett, of the Royal Eye Hospital, and to Dr. J. Ungar, of Glaxo Laboratories, for advice.

INCIDENCE OF GLYCOSURIA AND DIABETES MELLITUS IN A GENERAL PRACTICE*

BY

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The importance of diagnosing diabetes mellitus early has been recognized for some years, yet many cases are not discovered until the onset of one of the complications of the disease. Joslin *et al.* (1946) stated that the only way to diagnose the disease in its early stages was by more frequent examination of the urine, not only of patients attending for consultation but also of persons who were supposedly healthy. The magnitude of the undiagnosed diabetic population will not be known until attempts have been made to find the true incidence of the disease. Diabetes is not notifiable, hence little information is available regarding its incidence. Tunbridge (1953) estimated that there were 150,000 diabetics in this country, and, because the proportion of the population over 40 years old was rapidly increasing, he estimated that within 20 years there would be half a million diabetics, or nearly 1% of the population. Andrews (1957), in a survey in West Cornwall, found an incidence of known cases of 5.6 per 1,000. In the United States also the disease is not notifiable, but several estimates have been made using data from death certificates which varied from 0.71% (Joslin *et al.*, 1946) to 0.48% (Marks, 1946).

Canvassing a population for cases of the disease gives only the prevalence of those that are known. An estimate of the true incidence depends entirely upon searching for cases as yet undiagnosed. Two surveys have been carried out which demonstrated that in the population there is a reservoir of undiagnosed diabetes (Blotner *et al.*, 1943; Blotner, 1946). In these surveys 45,000 and 69,000 men respectively had their urine tested for sugar, but, as these surveys were limited to men entering the Armed forces, no estimate could be made of the true incidence of diabetes in the population as a whole. The first systematic attempt to estimate the true incidence of the disease in a community was made by Wilkerson and Krall (1947) in Oxford, Massachusetts. Using postprandial blood and urine specimens, they tested 70.6% of the total population of 4,983. The incidence of the disease in the population tested was found to be 1.4%.

The second comprehensive diabetes-detection drive was carried out by Kenny *et al.* (1951) in Newmarket, Ontario. Using postprandial blood and urine specimens, they tested 81% of the population of 4,419 and found 54 cases of diabetes, 21 of them previously undiagnosed; the incidence of the disease was therefore 1.2%. In neither this survey nor in that of Wilkerson and Krall was there any attempt to classify the cases of non-diabetic glycosuria. Other diabetes-detection drives have been reported (Ford, 1949; MacBryde, 1949; Cauley, 1949; Sharkey *et al.*, 1950; Getting *et al.*, 1952; Fox, 1952; Loube and Alpert, 1954; Burn, 1956). Several of these were concerned with particular sections of the population, and in none was it possible to draw any definite conclusions on the true incidence of diabetes.

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