

When once corticoid treatment has been instituted for some months, the problem of weaning the patient becomes a difficult one. After such treatment it can be taken that the suprarenal cortex will cease to function. Heavy stimulation with corticotrophin in such cases will produce a temporary rise in corticosteroid output, but even this may lead to exhaustion of the cortex, with symptoms of acute Addison's disease. Abrupt termination of treatment will often lead to severe status asthmaticus, and all patients should be warned of this. Reduction of the maintenance dose when it has been given for six more months must be very gradual—say, 2½ mg. of prednisolone every 2-3 weeks. In many cases the patient must be prepared to continue on maintenance corticoid therapy for life. For this reason it is obviously a form of treatment rarely advisable for children, who will, however, tolerate short courses well.

Long-acting corticotrophin given intramuscularly is an alternative form of treatment which is not complicated by suprarenal suppression. It has the disadvantage that it must be given by injection and that obesity like that in Cushing's disease, with increase of several stones in weight, often develops. In rare cases sensitization to the animal proteins which are present as an impurity may occur, with production of anaphylactic shock. Death from anaphylaxis, however, usually follows only intravenous administration of corticotrophin. 20-40 units of corticotrophin may be given daily or on alternate days with benefit, and many cases have been kept relatively free from attacks in this way.

Sedatives

The well-recognized fact that emotional factors play an important part in asthma suggests that sedative drugs may be useful. There is some evidence that sodium amytal or phenobarbitone in small regular doses may help the nervous asthmatic, but their main value appears to be in combating side-effects of sympathomimetic agents. In status asthmaticus paraldehyde 5 ml. intramuscularly, or 2-4 dr. (7-14 ml.) by mouth remains the safest and most effective sedative for use at night. Morphine is contraindicated because of its depressing action on the respiratory centre. Pethidine, though a less effective sedative, is a mild bronchodilator with some depressing effect on respiration; its total effect is to reduce the tidal volume in the majority of cases. It is, however, reasonable to give it in association with nalorphine (4 mg.) when discomfort is great and other treatment has failed.

Conclusion

In conclusion it may be said that drug therapy, though valuable in asthma, should never be used as an excuse for avoiding the careful investigation of the important precipitating factors in each case, nor should the use of drugs replace measures to improve the general health. The recognition of allergic sensitization, emotional stress, or infection, and their treatment, are always of primary importance, and may lead to long-lasting relief that drugs cannot achieve. In particular the use of corticoids as the first choice of treatment cannot be deprecated too strongly.

The wise administration of bronchodilators is a useful accessory to other forms of treatment. They help to give the patient confidence in relieving symptoms, and may help to break an "asthma habit." Sometimes, because of our ignorance of the underlying pathogenesis, they may provide the only effective treatment available. In the same way corticoids may be used to prevent attacks of status asthmaticus or to control them when they have developed, and in a few cases may convert a disabled, unhappy patient into a relatively normal person capable of carrying out a full day's work.

It must be remembered that the objective in treating asthma to-day is to teach the patient to control and live with his disease. To do this intelligently he must be taken into the doctor's confidence and given some explanation of the rationale of the treatment recommended.

ORAL PENICILLIN IN GENERAL PRACTICE

BY

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Oral penicillin preparations have been in use for nine years, and yet the value of this method of giving the antibiotic is still the subject of considerable controversy. The reason for this may lie in the fact that oral penicillin therapy is almost exclusively administered by general practitioners rather than by hospital specialists. The former encounter innumerable obstacles in making public their observations, and hence there are few reports on the clinical use of oral penicillin. The paper by Chapple *et al.* (1956) is a notable exception to this.

On the other hand, from our hospitals have emanated a number of reports on the blood levels achieved with different oral penicillin preparations administered to healthy volunteers (Fairbrother and Daber, 1954; Laurance and Alder, 1954; Holborow *et al.*, 1956; Henry *et al.*, 1957; to mention but a few). The scarcity of reports on blood levels in ill patients is remarkable. In any case, blood levels are not necessarily related to therapeutic effect (*Brit. med. J.*, 1953). An article on the use of penicillin in sore throat included the statement that intramuscular penicillin rather than oral antibiotics was commonly used in practice for this complaint (Brumfit and Slater, 1957). In subsequent correspondence I suggested that, on the contrary, oral penicillin was probably used far more in general practice than penicillin by injection (Wheatley, 1957). Through the co-operation of the research committee and members of the Northern Home Counties Faculty of the C.G.P., I have now had an opportunity to verify this statement and to collect further information on the subject from those most intimately concerned with it.

Objects of the Investigation

The objects were to find out how much general practitioners use oral penicillin, for what purposes they use it, and in what form and dosage. It is difficult to assess objectively the merits of this form of treatment, yet I feel that after this length of time general practitioners are unlikely to go on using oral preparations if in fact they are useless.

The faculty consists of some 180 members and associates distributed throughout the four counties—Middlesex, Hertfordshire, Bedfordshire, and Essex. Therefore all types of practice ranging from rural Essex to suburban Middlesex are included in the area, which constitutes a fairly representative cross-section of the country as a whole. These doctors were all circulated with a questionnaire asking the following questions:

1. Do you use oral penicillin? Yes/No.
2. Do you use it for Adults/Children/Both?
3. For which of the following infections do you use it therapeutically? Tonsillitis. Acute otitis media. Pneumonia. Acute bronchitis. Any others? (please state which).
4. Do you use oral penicillin combined with a sulphonamide, and if so, for what infections?
5. What preparation(s) do you use?
6. What is your dosage regime?

	(a) Dose	(b) Interval Between Doses	(c) Average Length of Treatment
Adult units or mg. hours days
Children 0-5 units or mg. hours days

7. Do you consider that oral penicillin as given by you for the infections stated is: (a) Better than, (b) comparable to, (c) worse than penicillin by injection.
8. Will you kindly record over a 20-day period the number of cases for which you prescribe sustained penicillin treatment: (a) orally, (b) by injection.

N.B.—By "oral penicillin" is meant penicillin to be swallowed in the form of tablets, capsules, or mixtures. This does not include penicillin lozenges or other forms of local medication.

Participants were asked to return the forms, whether or not they were oral-penicillin enthusiasts.

Eighty-five (47%) doctors agreed to take part in the investigation and sent in completed questionnaires, with the following results.

Use of Oral Penicillin

Eighty doctors (94%) replied that they used oral penicillin, against five who replied that they did not. Of the 80 doctors using it, 66 (82%) used it for both adults and children and 14 for children only. The number of patients treated orally and parenterally over a 20-day period were summated with the following totals: oral, 1,043 (73%); injections, 379 (27%). So that, for every two cases treated with penicillin by injection, five cases were treated orally.

The number of cases treated with penicillin over this period varied enormously from practice to practice. Thus one doctor treated the staggering total of 92 cases orally and 12 by injection, an average of five cases a day. At the other extreme one doctor treated only one case by injection during the period. Most replies, however, fell in the proportion shown by the total number of cases, with an average of 17 treated during the period. This amounts to almost one case a day, so it is apparent that a considerable amount of penicillin is used in general practice. It must also be pointed out that the survey was conducted during the month of May, which was a fairly slack period, and the figures would doubtless be higher for the winter months.

Infections Treated with Oral Penicillin

The four infections named in the questionnaire were correctly chosen as those for which oral penicillin was most often used, with furunculosis and boils coming very close to them. These and other conditions noted by the participants are shown below. The percentage of doctors treating each condition with oral penicillin is also shown:

Tonsillitis	91%
Acute otitis media	88%
Acute bronchitis	69%
Pneumonia	47%
Furunculosis and boils	44%
Finger infections	20%
Carbuncles, dental sepsis, acute sinusitis, scarlet fever, cellulitis (each)	6-10%
Upper respiratory infections, impetigo, phlebitis, mastitis, erysipelas, cervical adenitis, P.U.O., Vincent's angina (each)	3-5%
Urinary infections, bronchiectasis, acute pleurisy, acute conjunctivitis, acute laryngitis, vaginitis, Bartholinitis (each)	1%

Fifteen doctors volunteered the information that they used an initial "loading" dose of parenteral penicillin in the treatment of pneumonia or other infections if they were severe.

With regard to the use of oral penicillin combined with a sulphonamide, 17 (21%) doctors replied that they used this combination whereas 63 (79%) did not. Those using the combination did so for the following conditions:

Pneumonia	8 (47%)
If penicillin alone fails	5 (29%)
Acute bronchitis, acute otitis media (each)	5 (29%)
Boils and carbuncles	2 (11%)
Acute sinusitis, puerperal pyrexia, and chronic bronchitis (each)	1 (6%)

Choice of Preparation

Some doctors replied that they used more than one of the main varieties of oral penicillin, while some used one kind

for children and another for adults. As a result the figures shown below do not represent percentages of the total numbers replying, but the proportionate figures for the different preparations:

	Children	Adults
Penicillin V (phenoxymethylpenicillin)	52 (65%)	60 (75%)
Benzathine penicillin	29 (36%)	8 (10%)
Penicillin G (benzylpenicillin)	16 (20%)	11 (14%)
Penicillin + probenecid	5 (6%)	3 (4%)
Penicillin V + sulphonamide combination	2 (2%)	3 (4%)
Benzathine penicillin + sulphonamide combination	1 (1%)	1 (1%)
Penicillin G + sulphonamide combination	3 (4%)	3 (4%)

It is seen, therefore, that penicillin V is "sweeping the field," since more doctors used this than they did all the other preparations put together. Three-quarters of the participants used penicillin V for adults, although for children benzathine penicillin still remained fairly popular. This is doubtless due to the fact that penicillin V was first introduced in the form of tablets and capsules, whereas the palatability and stability of benzathine penicillin mixtures had been established before the introduction of the former.

There is no clinical evidence that penicillin V is any more effective than penicillin G in twice the dosage. Certainly the latter, even in twice the dosage, remains less expensive than penicillin V, although the price of this preparation may fall with continued usage. Nevertheless it is obvious from this investigation that penicillin V is almost completely ousting penicillin G for oral therapy. Undoubtedly this is due to the fact that penicillin V is more acceptable to the profession owing to reports of higher and more consistent blood levels after its administration. However, as has already been pointed out, these reports have been mainly on healthy volunteers. There remains a need for a therapeutic trial in ill patients.

With regard to penicillin and sulphonamide combined preparations, it is apparent from the previous section that this form of therapy is not particularly popular. Of those using it, 47% made use of the proprietary combinations available, although it might be thought that the dose of penicillin in these is somewhat on the low side.

Dosage Schedules

The only distinction which need be made between the different preparations is between penicillin V and the others. Since approximately twice as much penicillin V is absorbed as either benzathine penicillin or penicillin G, lower dosage schedules would be expected for the former. Therefore various dosage schedules were tabulated for penicillin V and the others, with the numbers of doctors using each scheme.

The most important results from these tables can be summarized thus: *For children*: 66% of doctors used penicillin V in a dosage of 60 mg. three to six hourly, while 65% used the other preparations in a dosage of 125-187 mg. three to six hourly, which is two to three times the dose of penicillin V. Only 5-6% used an eight-hourly scheme for either preparation. *For adults*: 61% of doctors used penicillin V in a dosage of 125 mg. three to six hourly, which is precisely double the most popular dosage scheme for children. Only 4% used an eight-hourly schedule for penicillin V, and the numbers for the other preparations were too small for analysis.

With regard to duration of treatment, the following results were obtained:

	Children	Adults
3 days	6	4
4-5 "	53 (78%)	47 (78%)
6-7 "	7	7
10 "	2	2

In other words, 78% of doctors favoured treatment for four to five days, without distinction between children and adults.

Impressions of the Effectiveness of Oral Penicillin

The results were as follows:

Better than penicillin by injection	1	} (75%)
Comparable to " " "	59	
Worse than " " "	20	

Of the 25% who considered oral penicillin to be less effective than penicillin by injection, one doctor stated that he was giving up using it orally. Of the others, several added their reasons for continuing to use it, the main one being dislike of giving injections to children. One doctor stated that he was allergic to injection solutions and so could not use them.

It is interesting to compare the dosage schedules used by those doctors who considered oral penicillin to be less effective than penicillin by injection. We can assume that an adequate dose of penicillin V is 60-125 mg. three to six hourly (the smaller dose corresponding to the shorter interval) for children, with double these doses for adults. For other penicillin preparations the doses are double those for penicillin V. We can also assume that at least four to five days' treatment is required for the simpler infections. By these criteria, eight out of these 20 doctors (40%) were using inadequate dosage, which might account for inferior results.

It is also instructive to see whether these 20 doctors were "practising what they preached," by noting whether they treated more cases by injection than by mouth. The results are illuminating: more by injection than orally, 6; more orally than by injection, 8; question not completed, 6. Of those treating more cases orally, the proportion of oral to injection recorded by three of them was very high—namely, 29:2, 92:12, and 7:0. The reason for this apparent anomaly is probably summed up in the words of one of these doctors: "Oral penicillin is only slightly less effective than intramuscular penicillin, a disadvantage greatly outweighed by its greater convenience, particularly with children."

Conclusions and Summary

The Northern Home Counties Faculty of the C.G.P. has some 180 members distributed in all types of practice. Of these, 85 (47%) agreed to answer a questionnaire on the use of oral penicillin in general practice.

It was found that oral penicillin was used by 92% of these doctors, of whom 82% used it for both children and adults and the remainder for children alone. The total proportion of cases treated orally to those by injection over a 20-day period in May was 5 to 2. It would seem likely that these results, coming from such varied practices as they do, are representative of national custom. This being so, it may well be that more penicillin is now given by mouth in this country than by injection.

Of the infections commonly treated with oral penicillin, tonsillitis (91%) and acute otitis media (88%) came first, with acute bronchitis (69%), pneumonia (47%), and minor boils (44%) next. Finger infections accounted for 20% and a large number of other miscellaneous conditions fell into the 1-10% range. These results reflect the common penicillin-sensitive infections met with in general practice, with the exception of severe deep-seated infections, such as carbuncles, which are probably best treated with penicillin by injection.

With regard to the preparations used, it is apparent that penicillin V (75% for adults, 65% for children) is "sweeping the field," although benzathine penicillin in its palatable liquid form still retains a place in the treatment of children (36%). Combined penicillin and sulphonamide therapy would not appear to be particu-

larly popular, only 21% of the participants using it. The indications were for serious infections such as pneumonia or other infections which had failed to respond to penicillin alone.

Dosage schedules used by the participants showed very wide variations. However, 66% of doctors used penicillin V in a dosage of 60 mg. three- to six-hourly for children of 0-5 years and 61% used double this dose for adults. The dose used for other preparations was two to three times the above for adults, the numbers being too small to analyse for children. This would seem to reflect fairly accurately the difference between the amount of penicillin V absorbed from the gastrointestinal tract and that absorbed from other penicillin salts. 78% of the participants favoured four to five days' treatment for the infections listed.

One doctor thought that oral penicillin was better than penicillin by injection; 75% of the participants found the two forms comparable. Of the 25% finding oral medication not as good as injection, 10% were probably using inadequate dosage. More of these doctors continued to use oral rather than injected penicillin, despite their impressions of the relative efficiency of the two methods. This is probably because they found oral penicillin to be effective enough to allow its advantages to overcome any slightly diminished therapeutic effect. However, it is apparent that the majority of general practitioners taking part in this survey were completely satisfied with the effectiveness of oral penicillin therapy.

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ADDENDUM.—Since the above was compiled, two articles have appeared on the clinical use of penicillin V, in chest infections (R. Lamb and E. S. Maclean, *Brit. med. J.*, 1957, 2, 191), and in pyogenic lesions (J. I. Burn, M. P. Curwen, R. G. Huntsman, and R. A. Shooter, *Brit. med. J.*, 1957, 2, 193). These reports confirm the effectiveness of penicillin V by mouth.

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