Current Practice

TO-DAY'S DRUGS

ANTIBIOTICS AND CHRONIC BRONCHITIS

A panel discussion on this subject was held on November 12. The members of the panel were Professor L. P. GARROD *(formerly of St. Bartholomew's Hospital, London), Professor* J. G. SCADDING *(Institute of Diseases of the Chest, London), and Dr.* G. I. WATSON *(General Practitioner, Peaslake, Surrey). The chair was taken by a member of the B.M.J. editorial staff.*

Pathogenesis

Chairman: As a preliminary to talking about treatment I think we ought to say a little about the clinical picture and pathogenesis. Professor Scadding, would you like to begin?

Scadding: Well, I imagine that everybody will be familiar with the clinical picture of the chronic bronchitic. It generally starts in adolescence or young adult life with a tendency to cough, especially in the winter and after the common respiratory infections. It's not at this stage disabling, but as time goes on the attacks last longer, and sooner or later the patient finds himself with a persistent cough and off work every winter for a week or a fortnight, perhaps once or twice, or more often. By the time he is 40 or 50 he is breathless into the bargain, with a tendency to wheeze. He may live out a normal span of life, coughing and wheezing, but his life is likely to be shortened by the development of cor pulmonale, generally with a terminal acute infective exacerbation.

Chairman: What about causation?

Scadding: Most people are agreed that in the early stages the bronchi secrete more mucus than normal. The pathological evidence for this is that there is an excess of mucus-secreting cells and glands in the mucosa. Irritation by general atmospheric pollution, and also by smoking, particularly of cigarettes, are certainly important factors in the causation of this. Possibly there is a genetic predisposition. Recurrent respiratory infections play a part in the disabling stage of the disease, though I do not believe these are essential to its early development. In the established disease the common respiratory infections tend to go down to the chest, as the popular saying is, and any infection of the lower respiratory tract takes time to clear up. At this stage bacterial superinfection is important and causes damage, particularly at the level of the periphery of the bronchial tree.

Types of Organism

Chairman: What about the nature of the actual infection? Professor Garrod, do these people always have an infection of the bronchial tree?

Garrod: Yes, after a certain stage. One presumes that the infective element comes in at some interval after the irritant process described by Scadding. Certain bacteria are generally admitted to be associated with this. *Haemophilus influenzae* is the most frequently found, the most clearly pathogenic. The pneumococcus is perhaps the next in importance. It is certainly pathogenic. But I believe there is quite a residue of even advanced cases in which it is not possible to find in the sputum an organism which can clearly be regarded as pathogenic. It may be that some kinds of bacteria which we regard as commensals may be pathogenic in this particular context. *Streptococcus viridans,* for instance. Most of us dismiss this organism as unimportant, but it is of very varied character and may conceivably include individual types which can cause disease.

Scadding: There may be long periods in the life history of the chronic bronchitic when there isn't much to find bacteriologically. The patient has a cough and mucoid sputum, but that's all. It's the exacerbations of the disease in which the sputum becomes purulent that are particularly associated with bacterial infections. And, of course, some patients at a late stage have persistently purulent sputum.

Problems in General Practice

Chairman: Now this clinical syndrome is well known to be very common in Britain. Dr. Watson, would you say it was common in all types of practice?

Watson: I find it rare in my own country practice south of London—compared, for instance, with acute infections. But I am quite familiar with its frequency in town practice. So there must be some obvious element in town which doesn't exist in the country.

Chairman: What is the reason for this? Air pollution?

Watson: Yes, probably *public* air pollution in towns and cities. In the country we only see the effects of *private* air pollution—I mean among smokers.

Chairman: Do you think there is any difference between the clinical picture seen by general practitioners and consultants? Which patients, if any, would you refer to hospital?

Watson: I would imagine a consultant sees the later stages. If you think of chronic bronchitis, like mitral stenosis, as the late stage of early damage, I don't think that I should refer a case of acute bronchitis to a consultant. I should refer a case for his help in the late management of pulmonary failure and heart failure.

Scadding: That's true. The general practitioner will see very many more of the acute infections. The acute respiratory infections in patients who are not chronic bronchitics clear up very well under his care and we as consultants rarely see them. Patients with chronic bronchitis tend to be sent to us for one of two main reasons. It may be, as Dr. Watson says, because they are becoming increasingly disabled. But sometimes a patient is sent in by a general practitioner, saying: "This man has had six or seven attacks of acute bronchitis in the last two years, do you think he is going to become a chronic bronchitic?" All one can do here is to look for evidence of permanent disability. If this is present the patient is on the way to becoming a chronic bronchitic, and the only advice one can give is that he should avoid all occasions of irritating his bronchi, particularly by smoking. If he is exposed to air pollution and it is possible for him to move away from that area, it is a good thing for him to do so. Apart from that, it is important to treat any acute respiratory infection promptly with antibiotics.

Treatment with Antibiotics

Chairman: That brings us conveniently to the question of the use of antibiotics. Is there a case, with a chronic bronchitic of some severity, for giving him routine antibiotic therapy in the winter months? Professor Garrod?

Garrod: I have taken much interest in this, but I have not been directly concerned in any of the large trials in which various antibacterial drugs have been given either

continuously or intermittently. I am aware of the results which have been obtained, and it seems in the first place that sulphonamides, though you might expect them to have some effect on both the most important bacteria, do not seem to be of much use. Penicillin has sometimes been found of value and sometimes not: and when I say value I mean in terms of a reduced number of days off work or days of extreme disability. If penicillin sometimes works and sometimes doesn't, one can only presume that this is associated with the frequency of infection by the pneumococcus, because that is highly sensitive to penicillin, whereas *H. influenzae* is not. The favourite antibiotics for this purpose are the tetracyclines. In all the trials of which I have any knowledge they have had a good effect, whether given continuously or given for special indications, but more particularly when given continuously throughout, say, six months of the winter.

Chairman: What sort of a dose would you consider reasonable?

Garrod: If you are using tetracycline itself, the usual individual dose is 250 mg., and this is better given three times a day; twice is probably not enough.

Chairman: Do you feel inclined to give chronic bronchitics tetracycline or any other drug throughout the winter, Dr. Watson?

Watson: I don't personally give drugs throughout the winter because I am not yet persuaded that these people stay at work any longer on that management than if one treats the very earliest stage of each acute infection.

Chairman: How do you manage to treat that?

Watson: My instruction to a patient who has this liability, and this applies not only to chronic bronchitics but to others liable to chest infections at any age, is that they have some antibiotic by them ready for use. The patient is told that as soon as he feels the symptoms beginning he should produce a specimen of sputum for me, and then start on his antibiotic immediately.

Chairman: Which symptoms and signs particularly?

Watson: Either an increasing amount of cough or the sputum going yellow after having been clear. A person liable to chest infections who starts getting yellow sputum is on the edge of an acute attack.

Chairman: What dose of antibiotics do you use?

Watson: He goes straight on to a therapeutic dose, usually tetracycline, 1 g. a day. I use tetracycline with the vitamin supplement; it costs no more. I always get him to bring me a specimen of sputum.

Chairman: Is this tetracycline being kept in the bathroom cupboard throughout the winter?

Watson: I don't give a man like this tetracycline unless I expect him to have at least three attacks a winter. He is not going to have them for more than a few months.

Chairman: But a few months is quite some time. I mention this because recently there was a leader in a medical journal suggesting it was a mistake to keep tetracycline for any length of time. Professor Garrod, have you any views about this?

Garrod: I certainly have. This was an odd episode in the United States in which out-of-date tetracycline was being stored under damp conditions. It had undergone a peculiar form of degradation which made it extremely toxic. However, the capsules which were responsible for this contained citric acid as an adjuvant to enhance absorption. Unless there is such an acid additive this particular toxic degradation can't occur, and I think I am right in saying there are no tetracycline capsules in England containing citric acid. Of course, that doesn't mean that capsules of tetracycline should not be kept in a bottle in which they are protected from damp, because they can deteriorate in other ways.

Continuous or Intermittent Therapy?

Chairman: There are two slightly different routines for antibiotic therapy. One is to give severe chronic bronchitics tetracycline over several months. The other is the method which Dr. Watson favours, which is to hold your fire until it appears that an acute attack is starting, as diagnosed by a change in the sputum. Professor Scadding, how do you feel about this?

Scadding: In nearly all the well-controlled trials it is found that chronic bronchitics who take small doses of tetracycline throughout the months in which respiratory infections are rife show benefit. They have less time away from work and acute exacerbations don't last so long. Often the *number* of exacerbations is not affected. This suggests that the exacerbations are precipitated by some non-bacterial factor—perhaps a viral infection or smog. But the prolongation of the symptoms, with involvement of the lower respiratory tract, and pus in the sputum are due to bacterial superinfection which can be controlled by the antibiotic.

But perhaps we shouldn't go too far in extrapolating into routine practice the results of a controlled trial based on heterogeneous material. It is quite possible that in all these trials there was a group of individuals who weren't being benefited by this and another group who were. I think there is every reason for individualizing one's approach to the patient. The patient who nearly always has a mucoid sputum and simply gets a purulent sputum during an exacerbation will probably do just as well on intermittent treatment at less cost and with less trouble to himself. Some patients persistently have a purulent sputum which can be rendered mucoid by giving them tolerable doses of tetracycline: 1 g., or even 0.75 g. I agree with Professor Garrod that 0.5 g. is probably quite inadequate. In that sort of a person it is not at all unreasonable to keep him on long-term treatment with a tetracycline in a sufficient dose to keep his sputum mucoid.

Resistant Organisms

Chairman: What is going to happen to the organisms in the patient who is having this continuous antibiotic treatment over the winter? Professor Garrod?

Garrod: If intermittent treatment will serve equally or almost equally well, then it is to be preferred. You give a larger dose perhaps for a much shorter time and the organism has much less chance of getting used to the antibiotic and becoming more and more resistant to it. Long-term treatment on rather smaller doses is exactly calculated to produce increased bacterial resistance in any species capable of acquiring it. And undoubtedly *H. influenzae* can become tetracycline resistant; perhaps slowly and not to any very great extent, but enough to impair the effect of the treatment very seriously.

Watson: Doesn't this come down to the fact that there are very few occasions when there is a true *prophylactic* dose of any antibiotic? An antibiotic is either therapeutic or nothing. Therefore I would ask Professor Scadding doesn't he agree that the choice between continuous therapy and intermittent therapy really depends on how frequently the man gets an acute episode? If after his purulent sputum is cleared to mucoid sputum he goes on

coughing and wheezing and is still disabled, there is probably more to be said for continuous treatment than for the man who only has about four or five acute episodes and clears pretty completely between them.

Scadding: It is really a question of assessing the patient individually. So many complex factors are involved. As regards prophylaxis you *can* give a prophylactic dose against pneumococcal infection, because the pneumococcus is very susceptible and is probably the least capable of becoming resistant of all the pathogens we deal with. Would Professor Garrod agree?

Garrod: Certainly. There is also true prophylaxis in the use of penicillin in the prevention of attacks of rheumatic fever.

Watson: Have you not both mentioned organisms which are extremely susceptible to low therapeutic doses?

Garrod: Yes, that's true.

Scadding: When we come to *H. influenzae* we are in a very different situation. Resistance tends to develop, but fortunately not so easily as in the case of the staphylococcus. In most of the trials in which careful bacteriology has been done—trials of long-term prophylactic antibiotic treatment of chronic bronchitics—it's been found that a small proportion of strains of *H. influenzae*, perhaps 10 or 15%, have shown a significant increase in resistance.

Watson: Would you agree that the man who has four or five attacks and clears up completely has probably not got an endogenous source of infection in his lungs? The man who always produces purulent sputum unless he is on an antibiotic has got a much greater degree of damage—he's got some source of chronic infection. Now I've had a man like this on whom I've done careful bacteriological studies throughout the winter. The predominant organism changed quite often. I would like to hear Professor Garrod say something about the way in which organisms change in patients who are on continuous treatment.

Chairman: Professor Garrod?

Bronchiectasis

Garrod: It's certainly true that in patients predisposed to infection—people with bronchiectasis, for example—if you get rid of one organism they will very probably produce another within a very short time. It depends on the extent of the underlying damage to the bronchial tree.

Scadding: That's very relevant to the present discussion, because some bronchial dilatation develops in the later stages in many cases of chronic bronchitis, and this becomes a factor in the maintenance of the purulent infection of the bronchi. This is a different clinical picture, of course, from the person whose bronchial tree is normal except for localized dilatation in one part of his lung as a result of some single acute damage years ago. But they are both forms of bronchiectasis.

Watson: The other thing which interests me in general practice is how uninfectious the chronic bronchitic usually is. But occasionally he produces an acute episode of disease round the family. And, of course, we all remember, those of us who have been in practice some time, how every now and again a chronic bronchitic turns out to have a tuberculous infection.

Which Antibiotic?

Chairman: Are we all agreed on which antibiotic should be used? Professor Garrod has mentioned tetracycline. There are other so-called broad-spectrum antibiotics. Professor Scadding, do you believe that tetracycline is necessarily the best antibiotic?

Scadding: I think tetracycline is the best compromise between effectiveness and safety. Clinically, there is no doubt in my mind that chloramphenicol is much more effective against *H. influenzae*. But it is not a safe drug, particularly in a disease where you are going to want to use an antibiotic recurrently. A combination of penicillin with streptomycin in full doses is effective in acute exacerbations; but since it has to be given by injection it is not a practical proposition for long-term treatment. Now we have a new drug, ampicillin, whose effectiveness against *H. influenzae* seems to be quite considerable. I should like to hear Professor Garrod's views on that.

Garrod: I entirely agree with what Scadding has said about other drugs. Chloramphenicol does involve a very grave risk to life—it may be a remote risk, but how remote a risk of that kind is anyone prepared to take? So far as this disease is concerned, I think its use is out of the question. Ampicillin looks promising on paper. It should be effective against most of the principal bacteria concerned here, and we have some evidence, from one trial at the Postgraduate Medical School, that its efficacy at least equals that of demethylchlortetracycline. We need to know more about it. I don't think it's been used long enough for us to assess its merits fully.

Watson: I agree that tetracycline is the safest and most effective antibiotic. I would also say that in general no other antibiotic should be used unless laboratory findings point to the necessity. I think this is where, as family doctors, we must work in with the laboratory. If the person is on intermittent antibiotic treatment, which I usually use, a specimen of sputum should be tested at the beginning of each episode. With continuous antibiotic treatment, so long as the patient is improving, I go on with the same antibiotic.

If there's a set-back I check with the laboratory, and I think that is the ideal to be aimed at. In practice to-day it is quite easy for a family doctor to get sputum examinations done. The laboratory pathologists may disagree about the value of the reading in any one sputum examination, but by and large the laboratories can be of great help to family doctors in this respect. As well as that, there's the fascination of watching the biological change. I am seeing an epidemic at the moment of *H. influenzae*. Periodically all the sputum results come back positive for *H. influenzae*, and then I don't see it for weeks and months at a time.

Chairman: What do you do, supposing you have a case on intermittent tetracycline, and this patient suddenly runs an exacerbation in spite of his tetracycline?

Watson: Well, I expect the lab. to help me there and tell me what else to use. If possible I use a bactericidal combination like penicillin/streptomycin rather than a bacteriostatic. Tetracycline is, I gather, mainly bacteriostatic. I think there is much to be said for a penicillin/streptomycin combination, though I believe some people disagree with the combination in the same preparation and they like us to use it separately.

Chairman: Is that so, Professor Garrod?

Garrod: That is a combination of the very greatest value for a few specific indications. I don't as a rule like commercial combinations in which the relative amounts of the drugs are fixed. But in this condition, as Scadding has said, if you can arrange for at least two, and preferably four injections daily, you have a very valuable weapon.

The Acute Exacerbation

Chairman: This rather brings us on to the question of the management of the acute exacerbation of the chronic bronchitic. Presumably everybody agrees that as soon as you get an acute exacerbation you should instantly have the bacteriology and sensitivity tests done. How long is that going to take you?

Garrod: Well, it can be done in 24 hours if the laboratory is prepared to perform sensitivity tests in primary culture. I believe it is possible to do that and get a significant result. Occasionally, of course, you get one that cannot be interpreted and it takes rather longer. But if the matter is urgent it should be possible for a laboratory to report the nature of the infection and its sensitivity to at least a few drugs on the day following the receipt of the specimen. I know this is unorthodox. Some people refuse either to do it or believe that it can be done. But it *can* be done.

Chairman: What are we going to do with the patient in the meantime? Professor Scadding?

Scadding: One can't generalize. It depends very much on how ill the patient is and what sort of treatment he had before. Supposing, for instance, the patient is a known chronic bronchitic, and has been treated with tetracycline either intermittently or perhaps in small so-called prophylactic doses, with an occasional increase for acute exacerbations. If he is very ill, I would certainly, having sent a specimen to the laboratory, start treatment with penicillin and streptomycin straight away while waiting for the result. Theoretically you run into the danger of resistant strains; but in practice the danger of getting resistance before your bacteriological report is pretty low.

Chairman: Professor Garrod, are you prepared to accept that?

Garrod: I would hesitate to support the free use of this combination because in a person with undetected renal insufficiency only a very few grammes of streptomycin can damage the vestibular branch of the eighth nerve.

Scadding: I would agree with that completely. We do examine the urine in our patients, you know! And if we are in any doubt about renal function we have a blood urea done. Fortunately the danger of retaining streptomycin runs parallel with the danger of retaining urea, so that with normal blood urea you're quite safe.

Chairman: Dr. Watson?

Watson: My disagreement with Professor Scadding would be twofold. The first is that in general practice it is difficult to give injections four times a day. I am fairly happy with twice-daily injections so long as I know they are necessary. But I have been brought up not to use streptomycin because most of our chronic bronchitics were children when tuberculosis was still a possibility. There is always this thought in the back of my mind: Is this man tuberculous in any way? Am I ever going to need to give him streptomycin for his tuberculosis? So I keep off streptomycin unles the lab. tells me this is really the only thing I can use. I would start with tetracycline. In an acute exacerbation, if he is not on continuous treatment, he has tetracycline, not less than 1 g. a day, probably 1.5 g. in the first three days. I expect to get the lab. result by 'phone after 24 hours if it contains important information, and in any case by 'phone soon after 48 hours, including sensitivities.

Scadding: Could I say something here? My own remarks dealt only with patients admitted into hospital. They nearly always have had tetracycline by the time they arrive and have failed to respond.

Chairman: Supposing they have been on a low prophylactic dose of continuous tetracycline. Is there anything to be said for increasing the dose of tetracycline heavily in an exacerbation?

Watson: Yes, they usually do respond if you go up to 1.5 g. a day, unless there's resistance, or a fungus infection, or something else entirely irrelevant to the original treatment.

Side-effects

Chairman: You're going to run into side-effects at 1.5–2 g., aren't you?

Scadding: Well, you would certainly run into a higher danger of troublesome diarrhoea. If it remains troublesome diarrhoea it isn't so bad, but if it becomes a resistant staphylococcal enterocolitis then it's extremely dangerous. But you won't get that with the ordinary therapeutic doses for the normal course of five days or so.

Chairman: Does resistant staphylococcal enterocolitis ever occur except in seriously debilitated patients?

Garrod: To my mind the true, often fatal, staphylococcal enterocolitis is rare except post-operatively. I would hardly think it comes into the question here.

Scadding: Oh, I quite agree. I've only seen it in two patients who were gravely ill from other causes and had been treated for a long time with large doses of tetracycline.

Chairman: Is there any special value in parenteral tetracycline for such cases? It's widely used in Germany, I believe.

Scadding: I see no point in it if the patient can take it by mouth—and most of them can.

Chairman: Professor Garrod?

Garrod: It is a very convenient way of increasing the dose and making sure that the blood concentration you want is obtained. Absorption of tetracyclines is rather variable from patient to patient, and if you give the drug intravenously you know it's there.

Watson: I always carry it in my bag but I've never yet used it.

Chairman: When would you send a patient into hospital, Dr. Watson?

Watson: When he is in respiratory or cardiac failure.

Chairman: So you're not really sending him in for an acute exacerbation of chronic bronchitis as such.

Watson: Sometimes, for social reasons, but not medical reasons. I believe that the family doctor, given nursing help at home, can get him over the acute exacerbation unless he goes into cardiac or respiratory failure.

Chairman: Professor Scadding?

Chloramphenicol

Scadding: I think that's a very sensible view. May I go back to the question of the antibiotic treatment of these acute exacerbations? I'd say, with some trepidation in front of Professor Garrod, that I do think there is a place for chloramphenicol in some of these acute exacerbations. I have had experience of a few cases where a nasty acute purulent exacerbation associated with *H. influenzae* failed to respond to anything except chloramphenicol. In those circumstances I am sure Garrod would agree that chloramphenicol is justified, because you

have to balance the probability of cutting short a potentially dangerous acute illness against the admittedly rather remote risk of blood dyscrasia.

Garrod: I absolutely agree. It's entirely a matter of balancing one evil against another. You use chloramphenicol in typhoid fever because it has a substantial mortality if untreated. The same applies to a severe chest infection, particularly in a fairly elderly person whose expectation of life may not be very great in any case.

Watson: And of course in acute infections, where the respiratory obstruction is great, in infants. Could I ask whether the bad reputation of chloramphenicol is based mainly on continuous treatment or acute treatment?

Garrod: Marrow aplasia with chloramphenicol has occurred mainly when the drug has been given for too long. We had two such cases in my hospital before its danger was recognized. But it has also been caused by smaller amounts given for short periods for all kinds of indications. So it has been said that there is no safe dose. That must be accepted.

Prevention

Chairman: Perhaps before we finish we ought to say a few words about prevention. Apart from clearing up the atmosphere and cutting down smoking, is there anything else we can do?

Watson: I think so. I like to believe that the prompt curative antibacterial treatment of acute chest infections in adults and children is equivalent to prophylaxis against chronic bronchitis in the next generation. I would like to hear what the others say about this.

Garrod: I've really no views about this at all. It's a purely clinical problem.

Chairman: Professor Scadding?

Scadding: The question is, do the coughing children develop into chronic bronchitics later? This has never been satisfactorily answered. My feeling is that they probably do not. Some of them, of course, are asthmatics. On the whole, my impression is that the adult chronic bronchitic does not give a history going back to childhood. I'm not saying some of them don't, but the majority of them do not. They started in adolescence or young adult life. Indeed, very often when they started smoking.

Watson: Could a controlled study be made in a clinic where there are a lot of chronic bronchitics? One could perhaps study illnesses, particularly bronchitis before the age of 1, in a group of chronic bronchitics, and compare them, for instance, with people with leg ulcers?

Scadding: It would be very difficult to do it retrospectively. Recollections of childhood are very poor, and when you get back to illnesses in infancy patients haven't even their own recollection. No, the only way of dealing with this problem is a prospective way—following enough of these children who've had repeated infection through into adult life. You want a man who is now young to undertake this so that by the time he's our age he'll be able to give us the answer.

Watson: The trouble is that no family doctor sees both the adult life and old age of the children he brings into the world.

Chairman: What's the answer to that?

Scadding: Back to Methuselah!

Watson: For doctors, at any rate.

ANY QUESTIONS?

We publish below a selection of questions and answers which are of general interest.

Association of Malformations

Q.—*A first child was born with arthrogryposis, congenital dislocation of the hip, and a gross micrognathia with a cleft palate. What are the chances of a similar occurrence in future children?*

A.—This association of malformations is not known to be genetically determined, and the patient may be given a good prognosis for further children.

Factors Affecting Antigen-Antibody Reaction

Q.—*Are there any endogenous or exogenous factors which are capable of suppressing or inhibiting the antigen-antibody reaction in sensitized individuals?*

A.—This question poses questions which cannot easily be answered in a short reply, but details of some of the principles involved can be obtained in the appropriate chapters of a recently published book by Gell and Coombs.[1] There are so many different types of antigen-antibody reactions in sensitized individuals that it would have been helpful to specify a particular mechanism or clinical condition envisaged by the questioner. So far as contact dermatitis is concerned, the ability to become sensitized is probably genetic in the first place, but a disorder of the reticulo-endothelial system, such as leukaemia, the reticuloses, or sarcoidosis, diminishes but does not abolish the antigen-antibody reaction. In various diseases complement is raised or lowered, and this may be a modifying factor in the immune mechanism.

In studies of the antibody deficiency syndrome, particularly the primary type, we see how complicated are the factors of antibody production and inhibition. Basically our allergic reaction depends upon the many factors that determine the availability of the antigen and the antibody. Tuberculin reactions are decreased in conditions of increased lymphatic absorption which occurs in pregnancy, premenstrually, in fever, hunger cachexia, oedema of the skin, and after exposure to sunlight. In tuberculin-type sensitivity injection of tuberculin in increasing doses at short intervals will suppress the reaction—i.e., tuberculin desensitization. A similar effect is seen in the immediate-type reaction—e.g., in pollen desensitization.

In clinical practice the antihistamine drugs suppress or inhibit the immediate-type reaction, which may take several days to return to normal size. Adrenaline, ephedrine, and many other drugs if given just before testing can decrease the reactivity of the skin. The anti-inflammatory steroids have no effect on the immediate-type skin reaction, but they diminish the size of the delayed-type reaction.

REFERENCE

[1] Gell, P. G. H., and Coombs, R. R. A., *Clinical Aspects of Immunology*, 1963, Blackwell, Oxford.

Alopecia Totalis

Q.—*Is there any treatment for total loss of hair which occurred in a woman aged 28 after the death of both her children? Dexamethasone and ultraviolet light have been ineffectual. Clinical examination is negative.*

A.—The prognosis here depends in part upon whether there is a past history or a family history of alopecia. The circumstances of the patient, whether she has any other children, and the support she gets from her husband and relatives in helping her to adjust to her loss are also pertinent to the prognosis. There is, of course, no specific treatment, and steroid therapy seems undesirable. The most helpful measure would be a long holiday with congenial and helpful companions. Otherwise mild tranquillizing measures and purposeful occupation are desirable. Locally, Grenz-ray therapy is harmless and may be stimulating, but massage and vigorous local therapies are to be avoided.