settlement of the pay claim of the other. Though predictions may be falsified, it therefore seems safe to forecast that by the end of September the profession as a whole will accept the reports of the two Joint Working Parties.

The facts and figures of the reports are set out in this week's *Supplement*. The main controversial item in the Council debate was recommendation XV of the Joint Working Party on General Practitioners' Remuneration, which is as follows: "A sum of £1m. per annum should be reserved from the distribution of available money so that further consideration can be given to methods of making the best possible general medical service available to the public. A further Working Party of representatives of the profession and the Health Departments should be appointed to consider this matter." That many members of Council were uneasy about this as a matter of principle is clear from the debate (see *Supplement*, p. 89). What was also clear was that Dr. A. B. Davies had been faced with an appallingly difficult problem and had, with his professional colleagues on the Working Party, found a solution that had made it possible for them to avoid a complete breakdown of negotiations. It is deeply to be regretted that the Ministry side sought to impose on general-practitioner representatives something not in the recommendations of the Royal Commission. Dr. Davies's colleagues in general practice owe him a deep debt of gratitude for the enormous amount of work he has put in on their behalf and for his courage in taking a course that he knew would be open to criticism. And everyone will sympathize with his remark that "perhaps no one in the profession had had to bite his lips more than he had over the so-called 'package deal.'" In the search for clarification of item XV, no one at last week's Council meeting seems to have noticed item iii (b). This begins by saying that there should be no immediate reduction in the size of lists, and goes on: "The question of the future size of lists should be considered by the Working Party mentioned at paragraph XV below." It seems to be worth while drawing attention to this.

Dr. T. Rowland Hill, in his report to the Council, drew attention to certain "blemishes" in the Working Party Report made by the Departments of Health and the Joint Consultants Committee. Among them were the following:

(1) The new consultant joining the service takes ten years to reach his maximum salary. (2) The abolition of weighting meant lack of continuity of responsibility —involving a financial loss and the sacrifice of a principle. (3) The loss of some of the travelling allowances for part-timers. (4) The difficulty of administration involved in the payment of retrospective money to locums. (5) The remuneration of senior registrars of nine and subsequent years' standing—and, indeed, the whole future prospects of senior registrar jobs.

These and other matters the C.C. and S. Committee wishes to raise in future with the Review Body or with Committee B of the Medical Whitley Council. Dr. Hill said that his Committee would waste no time in preparing a report with this end in view. Mr. Enoch Powell, the new Minister of Health, on August 12 sent to the Association a letter on the Review Body (see *Supplement*, p. 71) in which he states that copies of any submissions made to this body by the Government would also be made available to the profession, and vice versa: "In fact, we agreed during our talk that the Ministry of Health would act as a post-box for representations of this kind to the Review Body, and that the correspondence should be open to all parties concerned." After the publication of the Royal Commission Report the B.M.A.'s spokesmen stressed that the profession must have direct access to the Review Body as of right. Mr. Powell's letter does not carry us any further in this respect, noting only that the Review Body "might wish to receive further representations or information direct from either party . . . and it would be for the body itself to decide how far this further evidence would be made known, at once or later, to the other party. . . ." When the Review Body is set up, we hope that it will speedily put the mind of the profession at rest by granting it something to which it attaches the highest importance—the right of direct access.

MODERN TREATMENT OF LEPROSY

The leprosy hospital or settlement used to be a kind of medical slum. Though the unfortunate patients evoked pity, their case was so hopeless that little could be done except nurse them until they died, and even that took painfully long. But the last 20 years have seen great advances. Leprosy has changed from being a hopeless horror to being a relationship between host and invading pathogen that can be successfully challenged, and there is the cheerful conviction that most patients with leprosy can eventually be cured, though it may still take a long time. The fundamental advance during this period has been the introduction of dapsone (diaminodiphenyl sulphone) by J. Lowe[1] and others. This has now become the standard treatment, given in doses

approximating to 300 mg. twice weekly. It has the advantages that it cures most patients in the long run, it never produces resistant bacilli, it seldom produces dangerous complications if given with reasonable care, and it is cheap. Since great numbers of patients must be treated for long periods in poverty-stricken countries, this last attribute is important. All the same, dapsone is not the perfect drug for leprosy, and there have been many attempts to produce drugs which act more rapidly or which are less apt to produce untoward effects or lepra reactions.

In the first place there have been attempts to modify or mask the sulphone molecule by substituting one or both of the terminal amino groups, or by using diaminodiphenyl sulphoxide (which has one less oxygen atom than dapsone).[2] Some of these compounds may have slight advantages over dapsone, but they are not so great as to supplant the parent compound. A more hopeful compound is Ciba 1906 (D.P.T., 4-butoxy-4-dimethyl-amino-diphenol-thiourea). This was first tried by T. F. Davey and G. Currie five years ago and considerable experience has now been gained with it.[3] Briefly, it is given orally as 2 g. daily for an adult. It is slightly more active than dapsone, as judged by the disappearance of bacilli in lepromatous cases. In two to three years signs of drug resistance may appear, so it should not be continued after that period. Its chief advantage is that it is less toxic than dapsone; in particular, it is less harmful to the liver and it has less tendency to provoke lepra reactions or erythema nodosum. Accordingly it is the drug of choice for debilitated patients or for those on dapsone who have complications such as psychosis, neuritis, or the reactions already mentioned. It is rather expensive, especially when the much bigger dosage is taken into account; on the other hand, if it allows treatment as an out-patient instead of an in-patient it may be an economy in the long run.[4] There is some evidence that its therapeutic effect depends on its conversion to a more active metabolite.

The next drug was "etisul" (diethyldithiol *iso*-phthalate), which is somewhat unconventional. Compounds of this type (ethylmercaptans) had long been known to be active against acid-fast bacilli, but their clinical application was hindered by their stench. However, acceptable preparations have been provided by the addition of suitable perfumes, and etisul can now be given twice weekly by inunction over a large area of the body. When given to lepromatous patients in this way Davey[3] found that there was often a remarkable reduction in the number of biopsy specimens of skin, a change in their morphology, and a distinct clinical improvement in the patient. These effects are greater than can be produced by other drugs and they have been confirmed elsewhere. After three to six months signs of drug resistance may appear, and the patients tend to become weary of the treatment. Accordingly this compound is best given in conjunction with dapsone or Ciba 1906, and after three months the etisul is discontinued.

Many other drugs have been tried,[2] but none have been outstandingly successful. Cortisone and related steroids have been found valuable in controlling lepra reactions provoked by dapsone; and unless their administration is unduly prolonged they do not seem to do harm by weakening the body's defences against this infection.

Changes in the morphology of bacilli during treatment with etisul or even with dapsone can be seen in the ordinary Ziehl–Neelsen smear, but they are better studied by the electron microscope.[5 6] When the disease is active and progressing, many of the bacilli are normal in shape and presumably alive, but even at this stage many appear degenerate and are presumably dead. When the disease is regressing, either spontaneously or under treatment, most of the bacilli are certainly defunct. They are corpses of bacilli which the body finds difficult to digest and remove. In Ziehl–Neelsen smears they appear granular and stain poorly; they can be ignored as evidence of active disease. Reactivation of the disease (if it should take place) is preceded by the reappearance of bacilli with normal shape and staining reactions.

Among other aspects of leprosy on which research is proceeding, the nature of the lepromin reaction has been critically reconsidered. It had always been assumed that a positive lepromin reaction was analogous to a positive tuberculin reaction, and that it indicated hypersensitivity of the body induced by the infection specifically to certain chemical fractions of the leprosy bacillus. But now evidence is accumulating[7] that the lepromin reaction may depend

[1] Lowe, J., *Lancet*, 1950, **1**, 145.
[2] Bushby, S. R. M., *Pharmacol. Rev.*, 1958, **10**, 1.
[3] Davey, T. F., *Trans. Roy. Soc. trop. Med. Hyg.*, 1960, **54**, 199.
[4] Garrod, J. M. B., *Leprosy Rev.*, 1959, **30**, 210.
[5] McFadzean, J. A., and Valentine, R. C., ibid., 1960, **31**, 6.
[6] Rees, R. J. W., Valentine, R. C., and Wong, P. C., *J. gen. Microbiol.*, 1960, **22**, 443.
[7] Kooij, R., and Gerritsen, Th., *Int. J. Leprosy*, 1956, **24**, 171.
[8] Wallace, J. H., Elek, S. D., and Hanks, J. H., *Proc. Soc. exp. Biol. (N.Y.)*, 1958, **97**, 101.
[9] Rees, R. J. W., and Wong, P. C., *Nature (Lond.)*, 1958, **181**, 359.
[10] Chatterjee, K. R., *Int. J. Leprosy*, 1958, **26**, 195.
[11] Binford, C. H., ibid., 1958, **26**, 318.
[12] Gunders, A. E., *J. trop. Med. Hyg.*, 1958, **61**, 228.

only on raised sensitivity to almost any foreign substance introduced into the skin. Secondly, great efforts are being made to induce leprosy bacilli to multiply either in laboratory animals or in tissue cultures. Limited multiplication—namely, two to four generations—of the rat leprosy bacillus has been obtained in tissue cultures by J. H. Wallace and colleagues[8] and R. J. W. Rees and P. C. Wong.[9] Material from lepromatous patients has also been inoculated into animals and growth of acid-fast bacilli has been obtained in black mice,[10] in hamsters,[11] and in chimpanzees.[12] The past history of leprosy is strewn with so many premature claims that all reports must be regarded with scepticism until it is proved beyond all doubt whether the bacillus which has been isolated is really Hansen's bacillus or only some previously unrecognized mycobacterium, of which unfortunately there are many. Nevertheless, leprosy has now changed from a subject of despair to one of active, and optimistic, research.

MINOR RESPIRATORY INFECTIONS IN CHILDHOOD

Several recent surveys have been concerned with the prevalence and mode of spread of minor respiratory infections in childhood. The highest attack rate appears to be in the age group 2 to 4,[1] but this is greatly influenced by the extent to which these children mix with children going to school; it is likely to be at the age of 5 to 6 in "only" children.[2] O. M. Lidwell and T Sommerville,[3] working in Wiltshire villages, concluded that the presence of schoolchildren in a household doubled the number of colds experienced by infants under the age of 5. F. S. W. Brimblecombe and colleagues,[4] studying families in Paddington, were equally impressed by classrooms as sources of infection. They considered many possible social and environmental factors in addition, and decided that, once an infection had been brought into a home, its spread within the family depended principally on the degree of overcrowding and, to a less extent, on the adequacy of clothing. Indeed, the propagation of colds and other minor respiratory infections appears to be much more closely related to noisy classrooms and overcrowded homes than to any widespread dissemination of droplet spray.[5] The average number of fresh respiratory infections in schoolchildren has been estimated at five or six each year.[1 4] In seeking an explanation for this massive invasion, we are immediately faced with the enigma of the common cold. Moreover, dozens of new viruses have been isolated from the air passages in the past ten years, many of which have been shown to cause respiratory symptoms. As yet, laboratory tests for specific strains are usually negative in individual attacks, which suggests that more remain to be identified. Undoubtedly these recurring infections derive mainly from the welter of potentially pathogenic viruses to which children are exposed.

The relative importance of natural as opposed to acquired immunity which determines the fall in prevalence after the age of about 7 years remains to be determined. The mechanism of individual susceptibility of "catarrhal children" has been considered by R. Grenville-Mathers,[2] who reviewed 675 children referred to the Harrow Chest Clinic. He found a big increase in respiratory infections when they started to go to school, which persisted until the age of 7, to be followed by a decline in all groups except asthmatics, in whom the frequency tended to persist unchanged throughout childhood. Perhaps more emphasis should be placed on the importance of possible allergic aspects, which clearly influence the pattern and duration of respiratory infections, if for no other reason than to assess the prognosis more accurately.

Attempts to reduce the number of respiratory infections by artificial means have been singularly unsuccessful. They have included ultra-violet irradiation in classrooms,[6] hexylresorcinol in offices,[7] and ultra-violet lamps, oiled floors, and screens between beds in barracks.[8] In the present state of knowledge the most effective means seem to be the sensible management of individual infections and the avoidance of overcrowding at home and in school.

[1] Badger, G. F., Dingle, J. H., Feller, A. E., Hodges, R. G., Jordan, W. S., and Rammelkamp, C. H., *Amer. J. Hyg.*, 1953, **58**, 31.
[2] Grenville-Mathers, R., *Brit. J. dis. Chest*, 1960, **54**, 72.
[3] Lidwell, O. M., and Sommerville, T., *J. Hyg. (Lond.)*, 1951, **49**, 365.
[4] Brimblecombe, F. S. W., Cruickshank, R., Masters, P. L., Reid, D. D., and Stewart, G. T., *Brit. med. J.*, 1958, **1**, 119.
[5] Reid, D. D., *Lancet*, 1958, **1**, 1237.
[6] Spec. Rep. Ser. med. Res. Coun. (Lond.), 1954, No. 283.
[7] Lidwell, O. M., and Williams, R. E. O., *Brit. med. J.*, 1954, **2**, 959.
[8] Macdonald, T. C., Tonkinson, J. D., Porterfield, J., and Dumbell, K. R., *Brit. J. prev. soc. Med.*, 1955, **9**, 33.

PHOSPHATASES IN LEUCOCYTES

A crude subdivision of phosphatases—the enzymes which liberate orthophosphoric acid from many monophosphate-esters—is made on the basis of their optimal activity at varying *p*H. The "alkaline" phosphatases are most active at alkaline *p*H; the opposite applies to the acid phosphatases. The two groups of enzymes differ not only in their *p*H optima but also in their reactions to activators and inhibitors. Thus fluoride inhibits the acid phosphatases but is relatively ineffective with the alkaline enzyme. On the other hand, magnesium ions, which activate the alkaline enzyme, have virtually no effect on the acid enzyme. There are also important differences within the two groups—for instance, between the acid phosphatases from the red cell and from the prostate.

The leucocyte phosphatases—in particular the alkaline enzyme—have been widely studied. Cytochemically there have been two principal techniques. One associated with the names of G. Gomori[1] and H.