

the G.M.C. ever revise their rules in this respect, they will, it is hoped, urge the need for stringent safeguards in view of the nature of these methods of mass communication.

It is significant that Prince Philip, in his brief address published last week, made a special reference to ethics. In a different context, Dr. Wilder Penfield, moving a vote of thanks to Lord Adrian at Edinburgh in July, made an urgent plea that the medical profession should return to its old traditional behaviour. "We talk so much of medical science," he said, "that we forget to swear the Hippocratic Oath. We never speak of our ethical code, and many who are not of us are ignorant of its existence." And it is interesting to observe that at a time when voices are heard in Britain urging us to adjust our ethical conceptions to meet popular clamour our colleagues in the land of high-pressure advertising are trying to tighten things up. In the *New England Journal of Medicine* of October 15 is published the George W. Gay Lecture on medical ethics delivered at Harvard Medical School earlier this year by Professor J. Howard Means, a lecture to which he gave the title, "Profession or Business?" "Dr. Means," says an editorial in the same issue, "suggests that medicine is showing an alarming tendency to slip from the plane of a profession into the behaviour pattern of the market place . . . a difference in distinguishing ethical from unethical conduct reflects a general social and economic turmoil." The doctor, Dr. Means writes, "sees chiselers and racketeers boring through the otherwise healthy social organism in a great variety of directions"; and he describes the social pressures put upon the doctor, who "is forbidden by all his ethical tradition to engage in advertising, or to solicit patients, which amounts to the same thing. . . ." With courageous criticism of what he has observed in his own country, he says flatly that "organized medicine should abide corporately by its code of ethics as assiduously as it expects its individual members to do. Any double standard in this regard is intolerable." He sees the great danger of the mass media to the doctor who is pushed into public writing or speaking by the institutions with which he is associated—"hospitals, medical schools, and so forth, which have money-raising campaigns under way and wanting to glamorize what they are doing for the advancement of medical science." He recognizes that some of the material used by the mass media for public education are excellent, adding that "some are dreadful."

Dr. Means, recognizing, too, that the more reputable drug houses have gone a long way to raising their ethical standards, nevertheless points

out the difficult ethical problems facing doctors subjected to the high-pressure advertising methods of so many others. A new and disturbing tendency in Britain is for drug firms to announce to press conferences the alleged virtues of their own preparations, biological or pharmaceutical. They quickly get what they are after—namely, wide publicity in the national press. Patients thereupon bombard their doctors with requests that they should have the alleged benefits of these new preparations. The medical profession is thus placed in an intolerable position. The proper place to publish the results of this or that prophylactic or remedy is the medical press, and the medical press can assess, on the basis of published evidence, the value of the products marketed by pharmaceutical firms. What makes matters still worse is that some medical men are misguided enough to lend themselves to this undesirable method of advertising. It is ironical that at a time when our colleagues in the U.S.A. are trying to stop this "behaviour of the market place" we should be attempting to imitate it.

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### DIURETICS UNLIMITED

Until the advent of chlorothiazide parenteral mercurial diuretics were unquestionably the treatment of choice in cedema due to congestive cardiac failure. Millions of injections of mersalyl were given with a minimum of side-effects or toxic reactions. After intravenous administration sudden death due to ventricular fibrillation occurred in a score of patients, but unresponsiveness, sometimes associated with uraemia, was not uncommon, especially when too stringent restriction of sodium intake was coupled with too frequent injections—an undesirable practice largely imported from the United States. But for the inconvenience of parenteral administration, and the advisability of concurrent treatment with ammonium chloride to prevent hypochloreaemic alkalosis and unresponsiveness, mersalyl might still be the diuretic of choice.

Acetazolamide, though not destined itself for a star position, pointed the way to a new series of potent diuretic agents that are effective by mouth. Being predominantly a carbonic-anhydrase inhibitor, acetazolamide has a self-limiting diuretic action which ceases when excessive loss of bicarbonate (and potassium) in the urine induces a metabolic acidosis,<sup>1</sup> and it can no longer be recommended for the treatment of oedema.

Chlorothiazide is the first oral diuretic to have a potency comparable with that of mersalyl—

2 grammes by mouth being equivalent to about 2 ml. by intramuscular injection. Its ease of administration, flexibility of dosage, and ready acceptance by the patient have brought an understandable and worth-while advance in diuretic therapy. The only important undesirable side-effect has been a tendency to hypokalaemia due to increased urinary excretion of potassium. This loss of potassium has been attributed to the mild inhibitory action of chlorothiazide on carbonic-anhydrase<sup>2,3</sup>; but this cannot be the whole explanation, because excretion of bicarbonate does not parallel loss of potassium, which is severe only when sodium retention by the kidneys is marked. Furthermore, derivatives of chlorothiazide, which appear to have even less inhibitory effect on carbonic-anhydrase than the parent compound, also increase excretion of potassium. The chief importance of loss of potassium lies in the tendency of patients with hypokalaemia to develop digitalis intoxication. This is less likely to occur now that the practice in early clinical trials<sup>4</sup> of giving too much chlorothiazide too frequently has been abandoned in favour of intermittent treatment, combined, if the patient is eating poorly or the oedema takes more than ten to fourteen days to clear, with supplements of potassium on days when the diuretic is not given.

A number of derivatives of chlorothiazide have been introduced recently, and doubtless there are others yet to come. The practitioner is spoilt for choice and may feel somewhat bewildered. The first derivative to be introduced was hydrochlorothiazide,<sup>5-7</sup> and this has been now followed by hydroflumethiazide<sup>8-10</sup> (hydrofluorochlorothiazide). These compounds, on a weight-for-weight basis, are more potent than chlorothiazide, but this is of no great advantage unless there is some superiority over the parent compound in the pattern of diuresis produced. Both hydrochlorothiazide and hydroflumethiazide have little or no inhibitory effect on carbonic-anhydrase, and so it was hoped that there would be no increased excretion of potassium in the urine. This has not proved to be the case with hydrochlorothiazide<sup>11,12</sup> nor, as reported by

Drs. J. H. Jones and J. Verrier Jones elsewhere in this issue, with hydroflumethiazide, which induced a fall in the serum potassium below normal in 16 out of 20 patients treated. Both these derivatives should be given intermittently and supplements of potassium be provided in the same circumstances as are necessary with chlorothiazide.<sup>8,10</sup>

Chlorothiazide, or one of its derivatives, is the diuretic of choice in almost all cases of oedema both for initial therapy and, because of flexibility in dosage, for maintenance treatment. No one particular compound has any outstanding therapeutic advantage over another, and the practitioner is likely to use that with which he personally is most familiar. Other diuretics now come in the "also-ran" category, with mersalyl still of value in the occasional unresponsive patient or in refractory cases to potentiate the action of chlorothiazide.

### BED REST IN ACUTE NEPHRITIS

As scientific knowledge advances, and we rely more on the scientific method than on clinical impression to assess the effects of treatment, so more of our long-cherished beliefs are being questioned and discarded. One of these concerns the value of rest in bed for a wide variety of conditions in child and adult. Until recently few doctors have questioned the rationale of bed rest. Yet it is difficult to understand why it should be thought that a child would recover from any of a wide variety of ailments more quickly if he sits up in bed than if he sits or plays in his bedroom—or any other room if it is warm.

It has long been held that children with acute nephritis should stay in bed until most of the signs of renal disease have disappeared—and that, for many children, meant many weeks in bed. It has long been known that albuminuria often follows severe exertion. E. P. Alyea and H. H. Parish<sup>1</sup> showed that not only albumin but large quantities of red blood cells and casts appeared in the urine of most athletes after rowing, swimming, lacrosse, track events, and football. They suggested that it might be unwise for a person who had had nephritis to indulge in severe exercise. This might be thought to have some bearing on the duration of bed rest advisable in acute nephritis.

<sup>1</sup> Counihan, T. B., Evans, B. M., and Milne, M. D., *Clin. Sci.*, 1955, 13, 585.

<sup>2</sup> Slater, J. D. H., and Nabarro, J. D. N., *Lancet*, 1958, 1, 124.

<sup>3</sup> Matheson, N. A., and Morgan, T. N., *ibid.*, 1958, 1, 1195.

<sup>4</sup> Bayliss, R. I. S., Marrack, D., Pirkis, J., Rees, J. R., and Zilva, J. F., *ibid.*, 1958, 1, 120.

<sup>5</sup> Fleming, P. R., Zilva, J. F., Bayliss, R. I. S., and Pirkis, J., *ibid.*, 1959, 1, 1218.

<sup>6</sup> Havard, C. W. H., and Fenton, J. C. B., *Brit. med. J.*, 1959, 1, 1560.

<sup>7</sup> Platts, M. M., *ibid.*, 1959, 1, 1565.

<sup>8</sup> Edmonds, C. J., and Wilson, G. M., *Lancet*, 1959, 2, 303.

<sup>9</sup> Kennedy, A. C., Watson, W. C., and Cunningham, C., *ibid.*, 1959, 2, 309.

<sup>10</sup> Blagg, C. R., *ibid.*, 1959, 2, 311.

<sup>11</sup> Sackner, M. A., Wallack, A. A., and Bellet, S., *Amer. J. med. Sci.*, 1959, 237, 575.

<sup>12</sup> Bartorelli, C., Gargano, N., and Zanchetti, A., *Schweiz. med. Wschr.*, 1959, 89, 331.

<sup>1</sup> Alyea, E. P., and Parish, H. H., *J. Amer. med. Ass.*, 1958, 167, 807.

<sup>2</sup> Rudebeck, J., *Acta med. Scand.*, 1946, Suppl. 173.

<sup>3</sup> Åkerren, Y., and Lindgren, M., *ibid.*, 1955, 151, 419.

<sup>4</sup> ——— *ibid.*, 1956, 154, 245.

<sup>5</sup> McCrory, W. W., Fleisher, D., and Sohn, W. B., *Amer. J. Dis. Child.*, 1958, 96, 576.

<sup>6</sup> ——— *Pediatrics*, 1959, 24, 395.