

Assessment of the value of a drug in these circumstances presents formidable difficulties, and any conclusions reached on the basis of subjective criteria of this kind need to be treated with reserve. The authors came to the conclusion that haloperidol "deserves a place as an adjuvant to pethidine for routine use in labour," but whether it has any advantages over chlorpromazine in this respect seems impossible to say on the present evidence. On the dosage of 3 mg. intramuscularly no side-effects, extrapyramidal or otherwise, were seen.

DRUGS IN COMMON USE

"Dantyl" (Leo)

"Dantyl" is a mixture of *p*-aminosalicylic acid (P.A.S.), phenyl-*p*-aminosalicylate, and sucrose. Each sachet contains 1 g. of P.A.S., 3 g. of phenyl P.A.S., and 3 g. of sucrose.

Pharmacology.—Phenyl P.A.S., the phenyl ester of *p*-aminosalicylic acid, is broken down after ingestion, and its therapeutic effect in tuberculosis depends on its P.A.S. content and the speed with which this is liberated or absorbed. The serum concentration of free P.A.S. two hours after ingestion of 4 g. of phenyl P.A.S. is less than half the concentration obtained with 5 g. of sodium P.A.S.¹ Detectable amounts of P.A.S. persist in the serum for longer periods with phenyl P.A.S. than with the sodium salt.

Therapy.—It is not known for certain whether the therapeutic action of drugs in tuberculosis depends more on obtaining a high concentration for a short period or a low concentration for a long period. There is some evidence in the case of isoniazid that obtaining high concentrations is important. With phenyl P.A.S., to get peak concentrations similar to those obtained with 5 g. of sodium P.A.S. (about 10 mg. per 100 ml.) ingestion of about 12 g. would be required.¹ The addition of 1 g. of P.A.S. to 3 g. of phenyl P.A.S. increases the peak concentration, compared with that obtained with 4 g. of phenyl P.A.S. alone. The figures given by the makers suggest that ingestion of 4 g. of dantyl gives a concentration two hours later of about 7–8 mg. per 100 ml., a little lower than that obtained with 5 g. of sodium P.A.S. As with other preparations of P.A.S., there is considerable variation between patients.

The dose recommended by the makers is 4 g. of dantyl three times daily. It is usual in this country to prescribe sodium P.A.S. in two doses of 5 or 6 g. each day, based on the results of therapeutic trials in which two daily doses were used. As 4 g. of dantyl appears to give slightly lower peak concentrations than 5 g. of sodium P.A.S., it seems reasonable to give two sachets twice daily rather than one thrice daily. Any difference in tolerance between sodium P.A.S. and dantyl may be less important when this regimen is used.

Side-effects.—It is claimed that phenyl P.A.S. is more palatable and less likely to cause gastro-intestinal symptoms than sodium P.A.S. Although there are no reports of adequately controlled clinical trials to support this, there seems no reason to doubt that some patients may find it more pleasant to drink a sweetened suspension of an almost tasteless powder than to swallow tasteless cachets or granules.

The cost of giving 4 sachets a day is 21s. per week.

REFERENCE

¹ Citron, K. M., and Kuper, S. W. A., *Tubercle (Lond.)*, 1959, 40, 443.

"Metopirone."—In "To-day's Drugs" (June 2, p. 1549) we referred to the recommended dosage of metopirone as 3 g. daily. The manufacturers ask us to state that, so far as the metopirone test is concerned, the dose they now recommend is 750 mg. four-hourly for six doses—i.e., a total of 4.5 g. daily.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Thalidomide ("Distaval") and Foetal Abnormalities

SIR,—Following the recent British Paediatric Association Meeting, I have been encouraged by some of my colleagues to write concerning a principle of treatment which I believe to be of the greatest importance and affecting the present epidemic of thalidomide and other glutaramide-induced micromelia, amelia, and phocomelia in infants.

In many areas paediatricians are having to cope with these distressing cases, and estimates seem to show that there may be 500 to 1,000 of these infants born in this country, up to 3,000 in Western Germany, and more in Australia and possibly elsewhere. Already my colleagues have told me that orthopaedic surgeons are suggesting that the problem of these infants be reviewed at puberty or in a few years' time when co-operation in limb-fitting may be forthcoming. I consider this to be an unfortunate error, because developmental considerations lead me to believe that the optimum success in treatment is obtained if limb-fitting is begun in the early months of life. This should begin with the upper limbs as early as the third or fourth month, which is the normal developmental age for upper-limb approximation and learning. Lower-limb fitting should begin with the developmental age of normal standing—that is, 10 to 14 months. In this way the properly co-ordinated timing of infant learning of body image, balance, and limb and trunk muscle co-ordination can best be obtained. This is, perhaps, comparable to the modern concept of infant learning of speech being best obtained in the deaf child by the early diagnosis and the early provision of a hearing-aid, preferably before 6 months of age.

The future management of this large group of seriously deformed children provides a special responsibility which the country, and particularly the National Health Service, must face squarely. In my opinion and from my experience I consider that the Service must apply itself quickly and energetically, both in time and in making available the necessary facilities and personnel, to tackle this large and distressing problem.

It is, perhaps, not inappropriate, in conclusion, to stress the necessity in the future for tests to be made of the effect on the growing foetuses of experimental animals of new and potent drugs *before* they are made available for human administration. Also the necessity for watchfulness in the administration of drugs to pregnant women, particularly in the early months of pregnancy.

I am grateful to Dr. Smithells for drawing the attention of the British Paediatric Association's conference to the extent and importance of this problem.—I am, etc.,

Kettering, Northants.

ROBERT WIGGLESWORTH.

REFERENCE

¹ Lenz, W., *Lancet*, 1962, 1, 45.

SIR,—In view of the letters in your journal (vide Dr. B. C. Morgan, March 17, p. 792) about the effect of "distaval" (thalidomide) on the foetus, I am