series of patients in the U.S.A. with promising results, and Drs. J. Mackinnon, D. E. Anderson, and G. Howitt report in this issue of the journal (p. 243) a controlled trial of the drug. They found that almost twice as many patients were improved by catron as by a placebo, and in some the improvement was remarkable. The incidence of side-effects was small. The mode of action of these drugs is not yet known, and it is important to bear in mind that even such symptomatic relief as they may give probably does not affect the underlying coronary arterial disease. Management of this must not be forgotten.

Thus, tactful and careful handling of the patient is still the most important factor in the management of angina. Correct use of trinitroglycerin is of the greatest importance, but long-acting vasodilators at present in use are disappointing and probably of little value. Perhaps one of the monoamine oxidase inhibitors will prove useful in giving symptomatic relief, though it is too early to define their place in therapy.

PRIMARY HYPEROXALURIA

Primary hyperoxaluria,1,3 also termed calcium oxalate nephrocalcinosis,4 familial idiopathic nephrocalcinosis,5 and familial oxaluria,4 is a rare disease which is characterized during life by the occurrence of a continuous, high excretion of oxalate in the urine, while at necropsy crystals of calcium oxalate monohydrate are found in the kidneys and many organs outside the urinary tract5 (oxalosis6-19). The patients usually come before the doctor in childhood with progressive, bilateral renal calculi, which may be accompanied by calcium oxalate nephrocalcinosis.

Infections of the urinary tract and hypertension complicate the clinical picture; and reports of well-documented cases suggest that death from renal failure at an early age is inevitable. The uraemia may develop insidiously over a period of several years, or may supervene as a relatively acute terminal episode which lasts only a few weeks. It appears that some patients18-19 may present with convulsions in infancy and die after a brief illness; here the diagnosis has been suggested in retrospect by the presence of calcium oxalate nephrocalcinosis and multiple oxalate urinary calculi, but there are no reports of the urinary excretion of oxalate in this type of case. The literature contains references18-19 to cases in which renal calculi and renal failure were accompanied by oxalosis in patients who did not complain of symptoms referable to the calculi until adult life. These may be examples of primary hyperoxaluria in which formation of stone began at an unusually late age, but unfortunately no information is available on the urinary excretion of oxalate. There is no evidence that renal failure due to conditions other than primary hyperoxaluria is ever associated with oxalosis.

The disease can be diagnosed only by determining the 24-hour urinary excretion of oxalate. Several methods are available for measuring small amounts of oxalate,20-27 and a relatively simple procedure suitable for routine clinical use has been described.28 There is a clear distinction between subjects who excrete normal amounts of oxalate (less than about 40 mg. (COOH)₂H₂O per 24 hours) and patients with primary hyperoxaluria, who excrete about 100-400 mg. (COOH)₂H₂O per 24 hours. Other investigations have not shown any characteristic abnormality except for the blood uric acid, which, it has been suggested, may be raised disproportionately to the degree of renal failure present.5 But further work is needed before this can be accepted as other
than an incidental finding. Although oxalosis is the characteristic post-mortem finding in primary hyperoxaluria,\textsuperscript{2,7} it has not proved possible to follow its development during life. Examination of the eyes with a slit lamp and aspiration of bone-marrow have been tried, unsuccessfully, for this purpose. Comparison of specimens of kidney tissue removed at operation and, several years later, at necropsy from the same patient suggests that calcium oxalate is deposited in the parenchyma and interstitial tissue only rather late in the course of the disease.

It appears that primary hyperoxaluria should be regarded as being due to an inborn metabolic error which results in a life-long high urinary excretion of oxalate\textsuperscript{1} and which has a recessive mode of inheritance,\textsuperscript{28,29} though one recent case report\textsuperscript{31} raises the possibility of a variant with a dominant mode of inheritance. It is possible that these genetic variants might represent different metabolic lesions both of which result in excessive excretion of oxalate. The isotopic labelling of the urinary oxalate which follows administration of \textsuperscript{13}C-labelled glycine\textsuperscript{32–35} is compatible with the operation of at least the first stage of the oxidative pathway of glycine metabolism

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glycine \rightarrow glyoxylate \rightarrow \text{formate} + \text{CO}_2 \rightarrow \text{oxalate}
\]

in man and lent support to the idea that the metabolic lesion in primary hyperoxaluria might be located within this biochemical system. The further observation that approximately the same degree of isotope dilution occurred between the precursor glycine and the urinary oxalate in two cases of primary hyperoxaluria\textsuperscript{34} and a normal subject\textsuperscript{35} suggests that the fundamental abnormality in the disease may be a failure to degrade glyoxylate rather than excessive metabolism of glycine via glyoxylate.\textsuperscript{34} Such a metabolic lesion need affect only a small fraction of the total daily metabolic turnover of glycine to produce the amounts of oxalate which patients with primary hyperoxaluria excrete.\textsuperscript{38} It has been shown that alimentary absorption of oxalate is not excessive, and there is no evidence for the existence of a primary renal defect in these cases.\textsuperscript{37} No way is known of influencing permanently either the amount of oxalate which these patients excrete or the formation of calculi, though the administration of very large doses of sodium benzoate temporarily lowers their urinary excretion of oxalate.\textsuperscript{37} Urinary infections, which are frequent, require prompt treatment, and the management of the recurrent calculi follows the standard surgical practice where removal of the cause is not possible.

### REPORT ON ADDICTION

Two distinct types of drug addiction have lately caused some public concern. They are, first, the addiction to carbromal and bromvaletone that some people have acquired through taking these drugs in proprietary preparations bought over the counter without a medical prescription, and, secondly, the addiction to anaesthetic gases that has occasionally been reported in an anaesthetist. The Interdepartmental Committee on Drug Addiction\textsuperscript{1} issued an interim report\textsuperscript{2} this week which was confined to discussing these two matters.

Cases of habitation to the two mild hypnotic drugs carbromal and bromvaletone were found to have been "numerically very few, but individually serious." The committee reports that these drugs are merely examples of a variety of drugs acting on the central nervous system which are on sale to the public without prescription and may be dangerous if used injudiciously. The report recommends, therefore, "that in general any drug or pharmaceutical preparation which has an action on the central nervous system and is liable to produce physical or psychological deterioration should be confining to supply on prescription." These two hypnotics are available to the public without prescription because the Poisons Board, lacking sufficient evidence that the drugs were abused, could not support their sale being restricted by the Pharmacy and Poisons Act of 1933. The present Interdepartmental Committee not only thinks their sale ought to be restricted but recommends moreover that "an independent expert body" should be responsible for advising which substances should be supplied to the public only on prescription.

As to addiction to anaesthetic gases, the committee reports on this question only as it affects anaesthetists, of whom there are said to be about 1,500 in Great Britain practising the specialty exclusively. Some stated in evidence that sniffing the gases before administering them was a recognized and indispensable precaution; failure to do this might be tantamount to negligence. The committee agreed with witnesses that to the great majority of anaesthetists this practice does not encourage addiction. In fact, the problem was found to be "very small indeed, but in two known instances throughout the country in 11 years patients' lives have been endangered." The number of cases of such addiction in the same period was thought to be fewer than 20. While advising that anyone addicted to inhaling anaesthetics should not be entrusted with the administration of them, the committee has this to say on the delicate task of handling the problem when it arises:

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1 Members: Sir Russell Eras (chairman), Mr. A. Lawrence Abel, Professor D. M. Dunlop, Mr. Donald W. Hudson, M.P.S., Dr. A. D. Macdonald, Dr. A. H. Macklin, Dr. S. Noy Scott, Dr. M. A. Partridge.

2 Drug Addiction. Interim Report of the Interdepartmental Committee. 1960. H.M.S.O., London. 6d. net.