Octanoate also inhibited the uptake of glucose and pyruvate by the perfused rat heart[10,11]. When hearts were perfused with both glucose and long chain fatty acid, the formation of triglyceride was increased[12], probably accompanied by a decrease in the tissue concentration of free fatty acid. It is not, however, known whether glucose could encourage the formation of triglyceride from octanoate.

It is attractive to postulate that the accumulation of free intracellular fatty acid is toxic to heart function, for example, by inhibiting oxidative phosphorylation[13]. This could explain (i) the effect of a very high concentration of fatty acid (2·8 mM octanoate) on the heart; (ii) the decreased efficiency of contraction of the isolated atrium when exposed to 2 mM hexanoate as sole substrate[14] and (iii) the effect of very high circulating concentrations of long chain fatty acids on the rhythm of the infarcted heart, because uptake of free fatty acid by the ischaemic segment is proportional to the circulating concentration[15], while oxidation of free fatty acids is probably reduced on account of hypoxia[2]. Furthermore, since completion of this report, high but not low perfusate concentrations of a long-chain fatty acid, linoleate, have also been shown to be toxic to the perfused rat heart[16].

The experiments reported here show that fatty acids in high concentrations can be toxic to the normal heart and can result in decreased contractility and rhythm disturbances.

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[1] Shipp, J. C., Opie, L. H., and Challoner, D., *Nature*, **189**, 1018 (1961).
[2] Evans, J. R., *Canad. J. Biochem.*, **42**, 955 (1964).
[3] Randle, P. J., *Ann. Rev. Physiol.*, **25**, 291 (1963).
[4] Opie, L. H., *Amer. Heart J.*, **77**, 100 (1969).
[5] Oliver, M. F., Kurien, V. A., and Greenwood, T. W., *Lancet*, i, 710 (1968).
[6] Gupta, D. K., Young, R., Jewitt, D. E., Hartog, M., and Opie, L. H., *Lancet*, ii, 1209 (1969).
[7] Kurien, V. A., Yates, P. A., and Oliver, M. F., *Lancet*, ii, 185 (1969).
[8] Opie, L. H., *J. Physiol.*, **180**, 529 (1965).
[9] Opie, L. H., *Amer. J. Physiol.*, **209**, 1075 (1965).
[10] Randle, P. J., Newsholme, E. A., and Garland, P. B., *Biochem. J.*, **93**, 652 (1964).
[11] Garland, P. B., Newsholme, E. A., and Randle, P. J., *Biochem. J.*, **93**, 665 (1964).
[12] Opie, L. H., Shipp, J. C., and Evans, J. R., *Amer. J. Physiol.*, **205**, 1203 (1963).
[13] Falcone, A. B., and Rose, L. M., *Biochim. Biophys. Acta*, **105**, 233 (1965).
[14] Siess, M., Müller, K., and Peter, U., *Arzneim.-Forsch.*, **18**, 1245 (1968).
[15] Owen, P., Thomas, M., and Opie, L. H., *Lancet*, i, 1187 (1969).
[16] Henderson, A. H., Craig, R. J., Sonnenblick, E. H., and Gorlin, R., *Cardiovasc. Res.* (in the press, 1970).

Electron Probe Microanalyser Localization of Lead in Kidney Tissue of Poisoned Rats

ATTEMPTS to explain the morphological changes of the kidney induced by lead poisoning have been concerned chiefly with nuclear and cytoplasmic inclusions[1,2]. Cytoplasmic inclusions have been shown to contain Fe (ref. 1), but the composition of nuclear inclusions remains a subject for debate. It is still not clear whether lead is deposited within the kidney and some authors deny a direct action of this element in favour of a mechanism of indirect action through vascular changes[3]. Fortunately, the problem of detection of metallic localizations within the kidney is amenable to direct observations with the electron probe microanalyser, an instrument ideally suited to the purpose, with a detection limit of about 10^{-15} g and a spatial resolution of about 1 μm (ref. 4).

Kidney tissue was taken from Sprague–Dawley rats fed for 72 weeks on 1 per cent lead acetate solution[5]. Conventional paraffin embedded sections were made, mounted on pure silicon wafers, and the paraffin removed by xylene. Such sections, about 20 μm thick, were suitable for pathological purposes. Numerous glomeruli and normal and dilated tubules could be clearly defined under the microscope. In the electron probe (CAMECA), lead was readily found within cortical tubules in granules of differing shape and size. Fig. 1 shows a typical localization within a kidney tubule. Notable concentrations of calcium and phosphorus were found to be associated with the lead. Other elements were probably also present, but the chief constituents of the granules were lead, calcium and phosphorus. The scanning X-ray images (Fig. 1) also showed that calcium and phosphorus, in contrast to lead, appeared weakly throughout the tissue comprising the tubules.

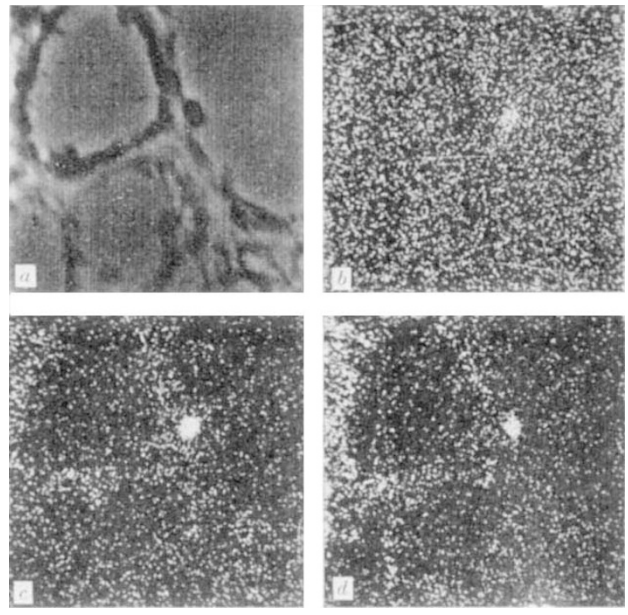

Fig. 1. Electron beam scans of rat kidney tissue, showing location of lead, calcium and phosphorus. Accelerating voltage 35 kV, specimen current 10^{-7} A. Each scan covers the same area of 100 μm × 100 μm. *a*, Specimen current; *b*, lead; *c*, calcium; *d*, phosphorus.

These observations lend support to recent electron microscope work[5] which suggested that lead poisoning is associated with lead–protein complexes. In that study lead was identified by a careful extraction process on many whole kidneys which isolated a quantity of inclusions sufficient for chemical analysis. Our work, in addition to localizing the lead, shows that calcium and phosphorus are co-deposited with the lead in these complexes, a result consistent with the hypothesis of the importance of lead–protein complexes.

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[1] Galle, P., and Morel-Marager, L., *Nephron*, **2**, 273 (1965).
[2] Blachman, S. S., *Bull. J. Hopkins Hosp.*, **58**, 384 (1936).
[3] Fishberg, A. M., *Hypertension and Nephritis*, 606, fourth ed. (Leo and Febiger, Philadelphia, 1939).
[4] Carroll, K. G., *In Vivo Techniques in Histology* (edit. by Bourne, G.) (Williams and Wilkins, Baltimore, 1967).
[5] Goyer, R. A., May, P., Cates, M. M., and Krigman, M. R., *Lab. Invest.* (March, 1970).