The Effect of Iodoacetate on the Developing Chick Metanephros

During the course of an experiment in which the effects of iodoacetate on organs in developing chicks were evaluated[1], it was found that this antimetabolite also profoundly retards, histologically as well as histochemically, the development of the metanephros. Since the kidney is partially functional, during the development, e.g. in amnion metabolism, this adverse effect of the chemical on this organ is thought to be significant. A single dose of 75 µg sodium iodoacetate in 0.5 ml aqueous solution was injected into the air sac of 11 day old chick embryos. After 7 days these embryos were sacrificed and the metanephros was dissected, and the tissue was processed for the histochemical evaluation of succinic dehydrogenase (SDH) as in previous work[1]. Occasionally, lactic dehydrogenase (LDH) was also studied. In each of the 9 pairs of metanephros studied, the injected organ was compared to that of the sham control. The average findings are described below.

The control tissue showed a well developed pattern of the nephron with apparent collecting tubules in both the cortex and medulla. The morphological features of the proximal and distal convoluted tubules are especially distinct with wide lumina present. SDH activity is most intense in the brush borders of the proximal tubules. A strong reaction is seen in the perinuclear and basal areas of the renal cells. However, finer developmental features as lobule formation and the appearance of a solidly packed parenchyma are not evident. On the other hand, the nephrons of the iodoacetate treated tissue are clearly more embryonic in appearance, showing occasional clumps of differentiating tubules and S-shaped pattern of developing convoluted tubules, expecially at the juxtacapsular region. The lumina of the treated tubules are not as large as those of the control tubules. SDH and LDH activity in the proximal tubule of the injected chicks is less than that in the control chicks; some of the treated tissue showed a spotty reaction, some no reaction at all.

In view of the fact that the primary action of iodoacetate is thought to interfere with the glycolytic process of the developing tissue[2], the retarding effect on the development of metanephros could also be interpreted as a disturbance of this metabolic activity.

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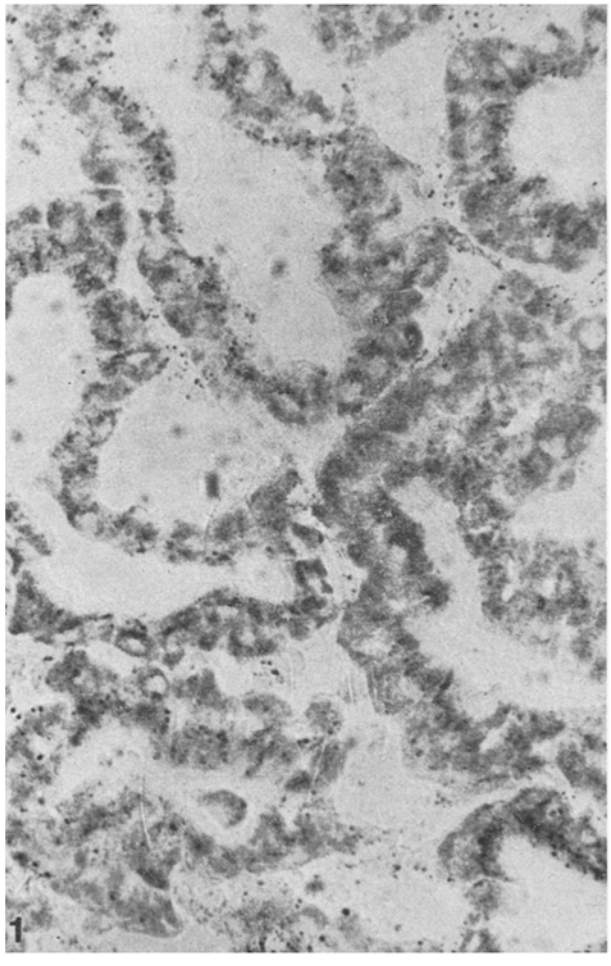

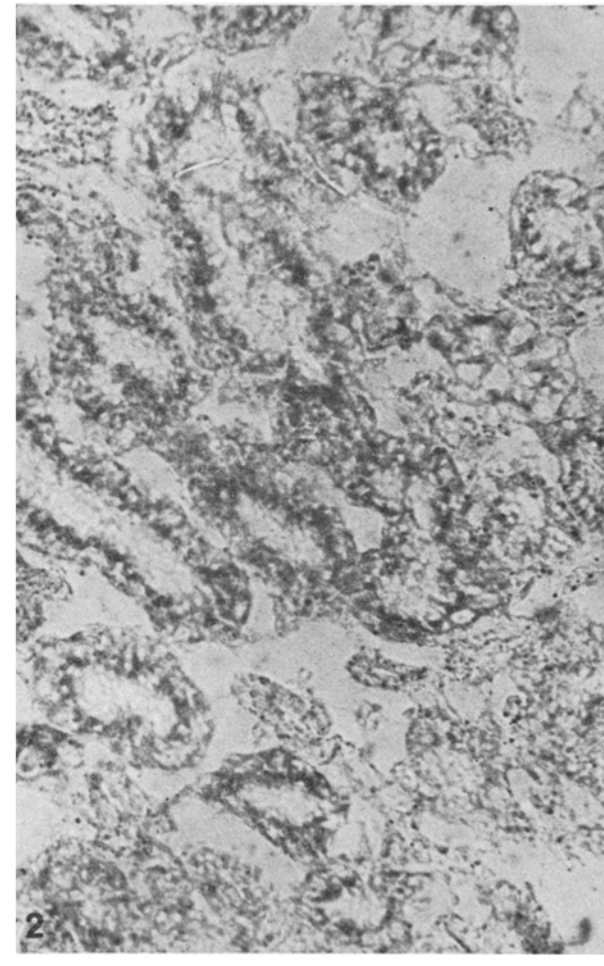

Figs. 1 and 2 are photomicrographs of the metanephros of control and iodoacetate injected embryos, respectively, at 18 days of incubation showing succinic dehydrogenase activity, ×850.

It is known that the differentiation of enzymes is directly related to the development of function[3], and this is especially true with the oxidative enzymes in the metanephros of the rat[4,5].

Résumé. L'iodoacétate retarde histologiquement et histo-chimiquement le développement du métanéphros de l'embryon de poule.

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The Mass and Size of Normal and Activated Macrophages - Studies with a Scanning Interferometer

Physico-chemical stimulation of peritoneal macrophages results in the production of a morphologically distinct population of cells[1–3] which often displays greater functional activity. Activated macrophages may, for instance, exhibit enhanced bactericidal ability[4]. One morphological characteristic of the new, activated population is a greater mean size. This change in cell volume has obvious effects on the relationship between the volume of the macrophage and its membrane surface area. However, it does not provide a complete explanation of the altered volume-to-surface ratio shown by the cells of the activated population[5,6].

The ultrastructural studies of NORTH and MACKANESS[7,8] led them to suggest that the cellular hypertrophy might result from a 'hydration' of the macrophage cytoplasm rather than from an increase in cytoplasmic mass. The present investigation was designed in order to determine whether the increase in macrophage size is accompanied by an alteration in cellular dry mass. To our knowledge the use of the scanning interferometer employed in this study has not been described until now.

Population of normal peritoneal macrophages, together with populations from rats challenged 5 or 8 days previously with a single i.p. injection of Freund's Complete Adjuvant (FCA), were harvested by a standardized procedure[6]. Cells were spotted on to slides to avoid the excessive flattening of cells which accompanies smearing[9]. Fixation was in 10% neutral formalin. Air-dried preparations were scored with a series of lines (1–2 mm apart) to provide reference areas, free of cells, in which the interferometric measurements could be made. Unstained preparations were mounted in water and the cover-slips sealed with paraffin wax.

Estimates of the dry mass of individual macrophages were obtained using a prototype scanning interferometer loaned to this Department by Vickers Instruments, Ltd. The machine is now available commercially as the Vickers M86 combined scanning interferometer and integrating microdensitometer[10]. The instrument measures automatically the integrated optical path difference (IOPD) of individual cells. This parameter is directly proportional to cellular dry mass. Measurements were made using a 100 × water-immersion objective (shearing distance of the optical system, 83 μm) on macrophages bordering the scored areas of the preparations. This simple routine eliminates errors due to 'ghosting'.

Machine fluctuation over long periods was negligible. The IOPD of macrophages in the scanning field were

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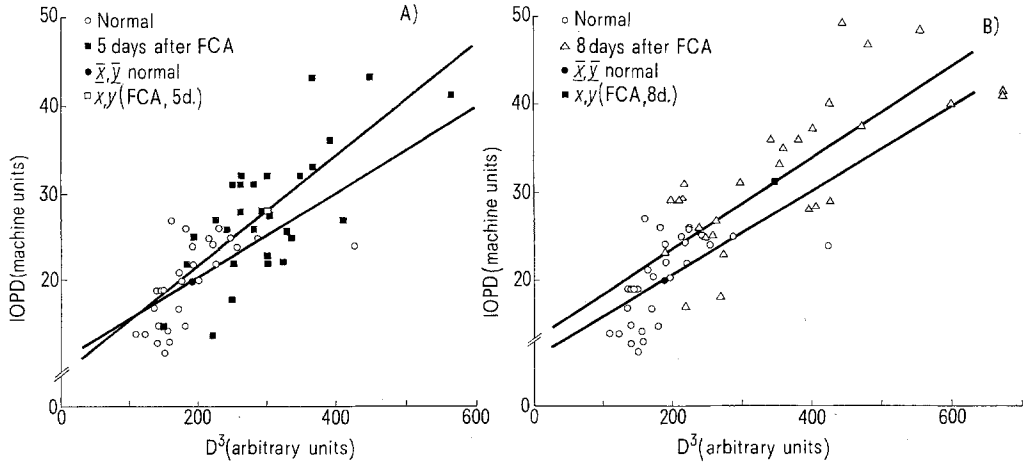

Regression lines for 3 experimental populations of peritoneal macrophages showing the relationship between integrated optical path difference (IOPD) and cell size (D^3). Mean values $\bar{x}$ and $\bar{y}$ are shown. A) Regressions for normal and 5 day-stimulated cells. B) Regressions for normal and 8 day-stimulated cells.