With higher doses (HC-3 1400 nmol/kg or TPHC-3 700 nmol/kg) there was little change in the plasma choline concentration or in the respiration within the first hour. About 60 min after a repeated dose of either drug the animals began to show signs of progressive respiratory distress, which was followed by a continuous rise in plasma choline concentration. The terminal choline concentration was from 8–10 times greater than basal values (about 12 nmol/ml). The increase in choline concentration was greatest in those animals whose respiration was most severely affected.

Since the rise in plasma choline was always secondary to respiratory difficulty it appears that it was a consequence of hypoxia rather than the result of a primary effect of the hemicholinium on the entry of choline into tissues.

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Effect of hydrocortisone and indomethacin on changes in LDH isoenzymes in skin after thermal injury

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After a mild thermal injury of 60° C for 1 min to one hind limb of cats and rabbits there are changes in the total lactic dehydrogenase (LDH) activity and in the proportion of LDH-1 in the skin of the injured limb (Lewis, Lowe, White & Worthington 1970; Lewis, Peters & White 1971). At 2 h the concentration of total LDH activity is significantly below control level whereas 6 h after the injury the activity is significantly raised. At 2 h the proportion of isoenzyme LDH-1 activity expressed as a percentage of total LDH activity is significantly raised to 181% of normal but returns to normal during the following 12–24 hours.

In the present experiments the anti-inflammatory drugs hydrocortisone (100 mg, 10 mg and 1 mg) and indomethacin (50 mg, 5 mg and 1 mg) were administered by close arterial injection over a 30 min period immediately after the injury. Although the fall in the concentration of total LDH activity 2 h after injury was not affected even by the highest doses of the anti-inflammatory agents, the increase in total LDH at 6 h, and the increase in the proportion of LDH-1, were significantly reduced. Thus the increase in total LDH activity to 126% of control level as a result of injury was significantly inhibited by all doses of hydrocortisone and by indomethacin (5 mg and 1 mg). The rise in the percentage of LDH-1 to 181% 2 h after injury was inhibited by all doses of both anti-inflammatory drugs.

Although it is not yet clear what role these enzyme changes play in the inflammatory process, the present findings indicate that the inhibition of increased LDH activity and particularly of the change in isoenzyme pattern in the skin might constitute an important aspect of the action of steroid and non-steroid anti-inflammatory agents.

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