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Quantitative determination of aldehydes and ketones in metabolic disorders.

The excretion of ketones other than acetone has been described in a few reports of patients with the ketotic hyperglycinemia syndrome.Our unexpected finding of butanone,2-and 3-pentanone in the urine of Gompertz'patient with methylcrotonylglycinuria led us to modify our gaschromatographic(GC)method to allow quantitative determination.The neutral dinitrophenylhydrazones (up to C_6) are separated by isothermal GC under the following conditions:column 180 cm,2 mm ID with Dexsil 300 3% on 100/120 Supelcoport; N_2 46ml/min,48 psi; oven215°C, injector 250°C,detector 300°C.The limit of detection is appr.100 picomoles,the FID response linear up to at least 10 nmoles injected.We have found that normal children not only excrete acetaldehyde and acetone,but also small amounts of butanone and 2-pentanone.These latter compounds and 3-pentanone are markedly increased in methylmalonic acidemia. Aldehydes and ketones in biological fluids and breath have been neglected up to now. However they might be biologically active and their increase could indicate blocks in the intermediary metabolism.

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A Modern Approach to Muscle Disease.

Recent advances in techniques for muscle biopsy have provided a completely new basis for interpretation of muscle pathology and led to the recognition of a number of new muscle diseases.

Biopsy samples are taken from children of all ages under local anaesthesia, rapidly frozen in liquid nitrogen and sectioned in a cryostat (cold microtome) for routine histological stains and histochemical enzyme techniques. The routine use of two standard histochemical techniques (NADH-Tetrazolium reductase, ATPase) is sufficient for recognition of the two basic fibre types, and of structural changes within the fibres.

Thus selective type 1 atrophy can be recognised in conditions such as dystrophia myotonica, myotubular myopathy with type 1 fibre hypotrophy, and congenital fibre type disproportion. Diseases such as central core disease and mitochondrial myopathies, readily missed on routine histological stains, are also readily diagnosed. Illustrative examples will be shown.

At an experimental level histochemical techniques have also been of value in studying the influence of innervation on normal and diseased muscle.

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Polygraphic sleep studies in subacute sclerosing panencephalitis.

As a measure of the brain's homeostatic functions quantitative analysis of sleep cycles and stages may show more reliably than clinical-neurological investigations changes or progression in the course of generalized central nervous disease. This technique was applied to study the course of SSPE and to provide a neurological parameter in a therapeutic trial with lymphocyte transfer factor. Whole night polygraphic recordings were done in 12 patients with SSPE before and after transfer factor repeatedly over 4 weeks to 1 year. The normal pattern of REM- and NREM-sleep disappeared early in the course of the disease. Disappearance of rapid eye movements showed involvement of mesencephalic pontine structures, absence of sleep spindles thalamic alteration. In 10 patients two alternating states remained, discernible by EEG pattern, heart rate, degree of jerking and degree of correlation between EEG bursts, respiratory phase and heart rate Alternation of these 2 patterns became increasingly rapid and irregular in fast deteriorating cases and were extremely slow in more chronic cases. No cyclic changes were seen in one peracute and in one "burnt out" case. Application of transfer factor had no effect on the deterioration of sleep cycle organization.

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Effects of 2-methyl-1,4-naphtohydrochinone-diphosphate (MNDP) on mitochondrial respiration.

The influence of MNDP on respiratory rate, oxidative phosphorylation and redox equilibrium between respiratory chain cytochromes (cyt) and mitochondrial membrane cyt b_5 was studied by polarography and transmittance differential spectroscopy (BRAUSER 1967). O_2 consumption is enhanced 18µAtO/min.mg protein in the substrate free state 2 and controlled state 4. $K_{1/2}=7.4\times10^{-5}$M. The increased O_2consumption is not inhibited by amytal, malonate, antimycin A; it is inhibited by cyanide. The respiratory rate of isolated microsomes is uneffected by MNDP. These data suggest an electron flow from MNDP to the cyt c-aa_3 region of the respiratory chain. this is confirmed by the lack of oxidative phosphorylation during MNDP oxidation (no influence of ADP, DNP, oligomycin). Spectroscopically an electron flow from mitochondrial membrane cyt b_5 to cyt aa_3 is established, mediated by MNDP. This membrane related redox system may be of clinical relevance: hereditary cyt b_5 reductase deficiency is accompanied by severe mental retardation.