Investigations showed: haemoglobin 12·8 g/dl; white cell count 11·3 × 10^9/l (11 300/mm^3), with 15% eosinophils; blood urea 10·3 mmol/l (62 mg/100 ml); blood glucose 5·4 mmol/l (98 mg/100 ml); and serum sodium 129 mmol(mEq)/l, potassium 5·2 mmol(mEq)/l, and chloride 97 mmol (mEq)/l. Chest and abdominal *x*-ray pictures were normal. Antinuclear factor and thyroid and parietal cell antibodies were absent. The basal plasma cortisol concentration was low and there was no response to prolonged stimulation with tetracosactrin, which confirmed primary adrenocortical failure. Sweat was collected from his back and tested for electrolytes.

Two months after treatment with cortisone acetate and fludrocortisone the patient felt well and had gained weight. The skin over his legs was normal. No local treatment was given for the ichthyosis. Much of the hyperpigmentation was reversible. The sweat test was repeated (see table).

Sweat electrolyte concentrations (mmol/l) before and after corticosteroids

	Before treatment	After treatment
Sodium (normal 51·9 ± 2SD 42·2)	87·0	18·0
Chloride (normal 29·7 ± 2SD 17·7)	71·0	3·2
Potassium (normal 7·5 ± 2SD 3·2)	3·7	16·0

Conversion: SI to traditional units—Sweat electrolytes: 1 mmol/l = 1 mEq/l.

Comment

Clearly the salty sweat and ichthyosis resulted from chronic adrenocortical insufficiency, as both reverted to normal after corticosteroid replacement. Changes in the electrolyte composition of sweat in adrenal disorders are familiar and have been used as an index of adrenocortical function. However, salty sweat in Addison's disease is a remarkable symptom. In this disease the excessive secretion of sodium chloride in sweat is secondary to mineralocorticoid deficiency.

The acquired ichthyosis is more difficult to explain. The hydration of the skin may have been affected by the osmotically more active sweat or by the reduction of dermal blood flow due to chronic hypotension, or by a combination of both. Glucocorticoids may perhaps influence the keratinisation of the epidermis. Ichthyosis also occurs in another endocrine disorder—namely, hypothyroidism.

Salty sweat and ichthyosis may now be regarded as unusual manifestations of Addison's disease.

[1] Fitzpatrick, T B, *Dermatology in General Medicine*. New York, McGraw-Hill, 1971.
[2] Harrison, T R, *Principles of Internal Medicine*, 7th edn. New York, McGraw-Hill, 1974.
[3] Soffer, L J, Dorfman, R I, and Gabrilove, J L, *The Human Adrenal Gland*, p 256. Philadelphia, Lea and Febiger, 1961.
[4] Conn, J W, *Archives of Internal Medicine*, 1949, **83**, 416.
[5] *Scientific Tables*, ed K Diem and C Lentner, 7th edn, p 680. Basle. Ciba-Geigy, 1971.

(*Accepted 24 September 1976*)

University Department of Medicine (II), University of Singapore, Singapore General Hospital, Singapore 3

H L CHAN, MRCP, DIP DERM (LOND), senior lecturer
H M GWEE, MRACP, lecturer

Disodium cromoglycate can inhibit virus-induced cytopathic effects in vitro

Disodium cromoglycate is a potent drug used to prevent attacks of bronchial asthma and seasonal rhinitis.[1 2] It can prevent immune complex-induced exocytosis of histamine granules from mast cells,[3] probably by inhibiting calcium influx at the plasma membrane.[4] It is not known whether the clinical efficacy of the drug lies in this "membrane-stabilising" effect only. A common clinical experience is that exacerbations of asthma are often associated with viral infections of the upper respiratory tract. The possible interference of disodium cromoglycate with virus replication and virus-cell interactions has not been investigated thoroughly.

We report here some findings that may be relevant for planning research on this subject.

Methods and results

Confluent cultures of BS-C-1 cells in Falcon plastic tissue culture flasks or glass tubes were infected with adenovirus 5, echovirus 6, and 7, herpes simplex virus type 1, or Semliki Forest virus in the presence or absence of 10 mg/ml disodium cromoglycate (Lomudal). Replication of the viruses was followed by daily microscopy of the cultures.

Cromoglycate prevented or delayed the appearance of typical cytopathic effects caused by the viruses. The protective effect was dose-dependent in two dimensions, being more pronounced at low multiplicities of infection and undetectable below 1 mg/ml of disodium cromoglycate. Results from a standard infectivity titration of four of the viruses in the presence of 10 mg/ml of disodium cromoglycate are shown in the table. No effect on uninfected cultures was visible in these experiments, but when BS-C-1 cells were passaged several times in the presence of 10 mg/ml of disodium cromoglycate the cells flattened and the rate of cell proliferation slowed down. These effects were fully reversible in 24 hours when the growth medium containing the drug was replaced by normal one.

The drug may not have any direct effect on the viruses, as pretreatment of echovirus 7 virus with 10 mg/ml disodium cromoglycate did not diminish its infectivity. Furthermore, one-step replication curve of Semliki Forest virus in BS-C-1 cells, as studied by plaque assay of virus infectivity, was not changed, despite complete inhibition of the concomitant cytopathic effects in the cultures. On the other hand, agglutination of goose erythrocytes by Semliki Forest virus was inhibited by cromoglycate at concentrations as low as 100 μg/ml. These results suggest that the inhibition of virus-induced cytopathic effects by disodium cromoglycate may be based on preventing the cytolytic effects of the viruses rather than on interfering with the replication of the viruses.

*Effect of disodium cromoglycate on infectivity titration of some viruses in BS-C-1 cells**

Virus	Lowest dilution causing typical cytopathic effects	
	Normal medium	With 10 mg/ml disodium cromoglycate
Adenovirus 5†	10^{-4}	$<10^{-1}$
Echovirus 7†	10^{-4}	10^{-1}
Herpes simplex† ..	10^{-4}	10^{-2}
Semliki Forest virus‡ ..	10^{-7}	10^{-3}

*Cell cultures were washed twice with Hanks's balanced salt solution and refed with Eagle's minimal essential medium with or without 10 mg/ml disodium cromoglycate and supplemented with 3% calf serum, 50 μg streptomycin, and 50 U/ml penicillin. Virus dilutions were added and cytopathic effects were recorded after 3 days' incubation at 37°C.
†Recent isolates.
‡A laboratory strain derived from prototype isolate of SFV, kindly provided by Dr L Kääriäinen.

Comment

The concentrations of disodium cromoglycate required for this cytoprotective effect were about 1000 times those active in "stabilising" mast cell membranes.[3] It would therefore be easy to ignore these observations as an unspecific effect completely irrelevant to the clinical action of the drug. Nevertheless, under 5% of a given inhalation dose of DSCG will be absorbed from the lung, while most of the rest will be either trapped by the upper respiratory tract or transported back to the throat by the ciliary epithelium of respiratory tract, swallowed, and secreted in the faeces.[5] Inhaling several doses of disodium cromoglycate daily, 20 mg each, could result in relatively high concentrations of the highly hydrophilic drug in the thin aquaeous film on the laryngopharyngeal mucosa. This might not protect these tissues from viral infections, but by preventing tissue destruction, high concentrations of cromoglycate could diminish local inflammation and thereby effectively alleviate the symptoms of the disease.

We thank Fisons Ltd, Loughborough, UK, for providing the disodium cromoglycate.

[1] *British Medical Journal*, 1972, **2**, 159.
[2] Backmann, A, Holopainen, E, and Salo, O P, *Lancet*, 1971, **1**, 55.
[3] Orr, T S C, and Cox, J S G, *Nature*, 1969, **223**, 197.
[4] Foreman, J C, and Garland, L G, *British Medical Journal*, 1976, **1**, 820.
[5] Walker, S R, *et al*, *Journal of Pharmacy and Pharmacology*, 1972, **24**, 525.

(*Accepted 16 November 1976*)

Laboratory of Viral Immunopathology, Department of Virology, University of Helsinki, SF-00290 Helsinki 29, Finland

KARI PENTTINEN, MD, professor of virology
ANNE AARNIO, BSC,
TAPANI HOVI, MD, research fellow