HERPES SIMPLEX STOMATITIS IN CHILDREN: ITS CLINICAL PICTURE AND COMPLICATIONS AS SEEN IN CAPE TOWN*

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Stomatitis is defined for the purposes of this paper as an infection that involves the tongue, the gums, and the mucous membrane of the hard palate, cheeks and lips. Angular stomatitis and cheilosis from deficiency diseases are not included under this heading.

The various types of stomatitis seen in children include: (1) herpes simplex stomatitis; (2) thrush or monilial stomatitis; (3) Vincent's stomatitis; (4) catarrhal stomatitis due to systemic disease, drugs or trauma; and (5) noma or acute gangrenous stomatitis of the mouth due to pyogenic organisms in severely debilitated children.

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PICTURE OF HERPES STOMATITIS

Clinical Description

Ulcero-gingivo-stomatitis caused by the herpes simplex virus is probably the commonest cause of stomatitis in childhood.[1,2] Clinically it has the following characteristics: The age incidence is between 1 and 6 years. The symptoms are mainly those of refusal to eat because of painful mouth. Along with this there is general malaise and fever. The children are extremely restless and unhappy. On examination, small

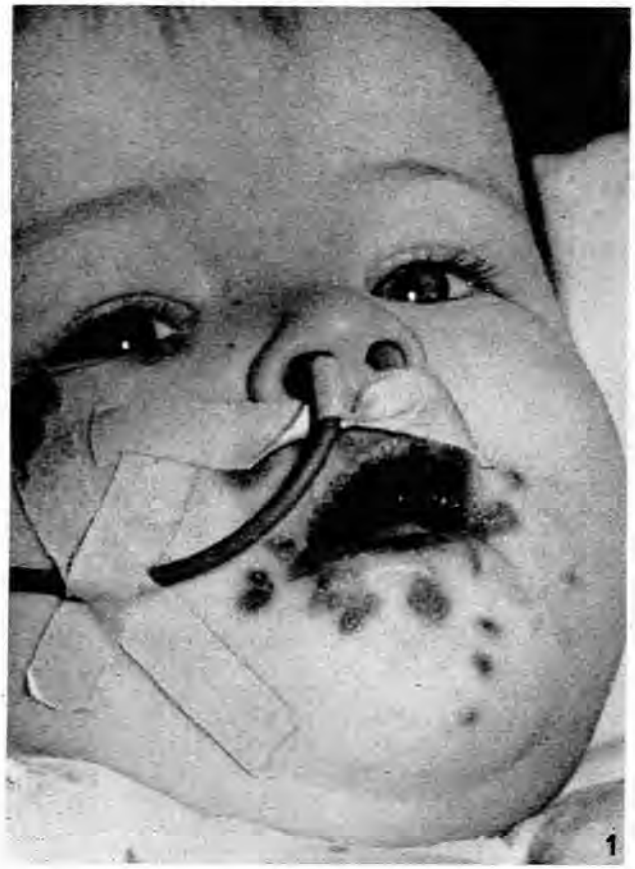

Fig. 1

herpetic lesions are frequently present on the lips and face (Fig. 1). Inside the mouth the initial lesion is a vesicle which is seldom seen because it ruptures early. The ulcer that results is quickly covered by a greyish-yellow membrane and this frequently resembles a plaque. The lesions can be found on the tongue, the palate, and the mucous membrane of the cheek and lips. They vary in size but are usually between 0·3 and 1 cm. in diameter. The gums are swollen and red and extend down between the teeth. They bleed easily on being touched by a spatula. Frequently there is a submental or submandibular adenopathy.

Clinical Course

This lasts from 10 to 16 days after the onset of symptoms and no treatment is at present known that will shorten this course. During this time the mouth continues to be extremely painful and usually there is a persistent pyrexia which may rise to 105°F. The severity of the systemic reaction thus sometimes seems to be out of proportion to the local lesions in the oral cavity. On recovery there is complete resolution of the lesions without scarring.

Epidemiology[3]

At birth, infants have a passive immunity to herpes simplex infection. This immunity disappears by the age of 6 months, after which the infants become susceptible to primary infection with the virus. It is generally believed that about 90% of primary herpetic infections are sub-clinical, while in the other 10% of infections there is a manifest clinical state in the form of stomatitis which occurs most frequently between the ages of 1 and 3 years. A non-clinical carrier state exists as well and is more common in children from 7 months to 2 years of age (20%) than in adults (2·5 %). For this reason patients with clinical herpes usually give no history of contact with herpes infections.

Following the primary invasion of the virus both in clinical and subclinical infections there is a rise of antibody titre in the serum. The virus, however, remains established in the host but becomes latent. In certain susceptible individuals there are recurrent attacks of herpes simplex stomatitis. These attacks occur at times of stress such as generalized systemic disease, emotional upsets, menstruation, sunburn, etc. The ulcero-gingivo-stomatitis infection seen in children usually represents the primary infection with herpes simplex virus.

Differential Diagnosis

1. *Thrush.* This occurs in particular in children under the age of 1 year. It is characterized by small milky-white lesions on the tongue and the oral mucous membrane. The mouth looks red and inflamed but there is no true ulceration and the gums are not affected as in herpetic stomatitis. There is as a rule no adenopathy or lesions on the face. Thrush responds rapidly to therapy with 1% gentian violet or 'mycostatin'.

2. *Vincent's stomatitis.* This is more difficult to differentiate since so many cases of herpetic stomatitis have secondary infection with Vincent's organisms. However, Vincent's stomatitis is rarer in children than in adults. It is characterized by severe halitosis, and the gums tend to be retracted rather than hypertrophied round the bases of the teeth. Treatment with penicillin will cause resolution of the symptoms within a couple of days.

3. *Catarrhal stomatitis* due to systemic disease, drugs or trauma must be differentiated on the history.

4. *Noma or gangrene of the mouth* is a gross condition. It is very rarely seen in this country.

HERPES SIMPLEX STOMATITIS IN CAPE TOWN

During the last 4 years, 121 cases of herpes simplex stomatitis have been seen in the wards of the Red Cross War Memorial Children's Hospital and the paediatric wards of Groote Schuur Hospital. An analysis of these cases is presented in Table I. It will be noted that the mean age was 20 months, which

TABLE I. ANALYSIS OF CASES

Hospital	*Number of cases*	*Mean age*	*Male*	*Female*	*European*	*Non-European*	*Malnourished*	*Deaths*
Red Cross Hospital	81	20 ± 13 months	44	37	16	65	55 (E=4)	26
Groote Schuur Hospital	40	20 ± 13 months (excluding 3 European children aged 7, 8 and 10 years respectively)	21	19	14	26	24 (E=2)	7
Total	121		65	56	30	91 (75%)	79 (65%)	33 (27%)

E=European.

TABLE II. ANALYSIS OF DEATHS

Hospital	*No.*	*European*	*Malnourished*	*Confirmed by autopsy*	*Autopsy negative*	*No autopsy*
Red Cross Hospital	26	1	25	13	5	8
Groot Schuur Hospital	7	0	6	3	1	3
Total	33	1	31 (94%)	16 (49%)	6 (18%)	11 (3%)

agrees well with what is described in the literature. The sex incidence showed an equal distribution between males and females. Of the cases 75% were non-European. The majority of the children (65%) were malnourished, i.e. they conformed to the clinical diagnosis of kwashiorkor or marasmus, or weighed less than 65% of the expected weight for their age. The death rate was 27% which was surprisingly high. An analysis of the deaths is shown in Table II. From this it can be seen that all except 2 deaths occurred in grossly malnourished children. Even the one European child who died suffered from protein malnutrition. In almost half (49%) of the 33 deaths there was autopsy evidence of generalized herpes simplex infection.[4] In these children there was a high incidence of coma or convulsions, hepatomegaly, and bleeding tendency or purpura (Table III). In cases that recovered a bleeding tendency was noticed in only 1 and convulsions in 3.

TABLE III. CLINICAL FEATURES OF PATIENTS WHO DIED

Cases	*Age range*	*Coma or convulsions only*	*Bleeding tendency or purpura*	*Convulsions and bleeding tendency*	*Large liver*
16 proved cases	9 - 24 months	11 (69%)	7 (44%)	4 (25%)	12 (75%)
17 unproved cases	11 - 30 months	3 (17%)	5 (29%)	0	8 (47%)
Total 33		14 (42%)	12 (36%)	4 (12%)	20 (60%)

Treatment

All patients received antibiotics and supportive therapy with intravenous fluids where indicated. Gamma globulin in large doses was given to 17 severely-ill children, of whom 9 died. It is therefore not possible to say whether it had any beneficial effect. It is probable that the gamma globulin was given too late, i.e. after generalized dissemination of the virus had taken place. In view of the general state of shock and collapse that precedes death and the frequent occurrence of adrenal necrosis[4] it was thought that cortisone might be beneficial. It was given to 7 patients where generalized spread of the virus was suspected clinically. Of these, 6 died.

DISCUSSION

The clinical features of the series of cases of herpes simplex stomatitis reported in this paper conformed in most respects to what is well described in the paediatric literature. This applies in particular to the age incidence, 1 - 3 years, and the preponderance of infections among the lower socio-economic groups. In a study of the Pretoria Bantu population Coetzee[5] found that, at birth, high antibody levels (passively transferred from the mother) were present in 100% of cases studied. Between the ages of 3 months and 5 years there were a variable number of negative sera but at 6 years 100% of the population again had high antibody levels. Universal primary infection in Pretoria therefore occurred before the age of 6 years. It would seem that the pattern is similar in Cape Town and would account for our seeing so few primary infections among lower socio-economic groups after that time. The 3 older children with herpes stomatitis in our series were all Europeans of higher economic status.

Generalized spread of the herpes virus with a fatal outcome has been described by several authors. It sometimes occurs in children with eczema and is known as Kaposi's varicelliform eruption. All reported deaths have been in the neonatal period apart from this type and 2 cases reported by Zuelzer and Stulberg[6] in 1952. In the series reported in this paper, it is of interest that there were 16 cases aged 9 - 24 months in which generalized spread of herpes virus was proved at autopsy.† The cause of this high incidence of fatal generalized herpes simplex infection in Cape Town is obscure. It is tempting to suggest that severe malnutrition, which was an almost universal association with these fatal cases, favours the generalized spread of the virus.

SUMMARY

Stomatitis resulting from herpes simplex virus infection is the commonest form of stomatitis in childhood between the ages of 1 and 6 years. Symptoms are sometimes severe enough to warrant hospitalization. A series of 121 cases at 2 hospitals in the Cape Peninsula has been analysed. Thirty-three of these cases died and, in 16 of these, generalized herpes simplex infection was found at autopsy. The relationship of severe malnutrition in the form of kwashiorkor or marasmus to generalized spread of herpes simplex virus with a fatal outcome is discussed.

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† See article by Dr. D. McKenzie on p. 133 of this issue.