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A NEW ERUPTIVE FEVER ASSOCIATED WITH STOMATITIS AND OPHTHALMIA

REPORT OF TWO CASES IN CHILDREN *

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During a period of three months we had the opportunity of observing two cases of an extraordinary, generalized, eruption with continued fever, inflamed buccal mucosa and severe purulent conjunctivitis. The first patient was seen on the tenth day of illness and followed to recovery. The second patient did not come under observation until the twenty-second day after onset of the illness; but the skin lesions at that time corresponded exactly with those of the first case at the same stage of the disease, and a careful description of the eruption as seen in the first week establishes its identity with that in Case 1.

The condition was so unusual and so entirely unlike anything previously observed, that pains were taken to get as many expert opinions as possible from men of wide clinical experience. At the same time, a search was made in the literature of eruptive fevers and allied dermatologic conditions. No diagnosis could be made to correspond with the symptoms and course of the eruption in these two cases and no description was found of a skin condition in any degree comparable.

Figures 1, 3, 4 and 5 will make clear, as verbal description cannot, the nature of the eruption in its several phases. Figure 1 shows the boy on the thirteenth day of his illness. The eyes are swollen shut, exuding pus; the lips are black with crusted blood. The eruption is complete, except for the feet and hands, while on the shoulders, scaling of the horny crusts is already in progress. Figure 3 shows the same boy on the twenty-fourth day. Many of the lesions on the back and chest have already crusted and dropped off; the later lesions of the feet and hands show clearly, but on the arms and thighs there is an exaggerated effect of confluent desquamation due to the liberal use of bland ointments and powder on the skin. In this detail the photograph is somewhat deceptive. Figure 4 shows the same boy on the thirty-third day of his illness. The mouth and eyes are normal; the face, chest and back are practically clear, except for pigmented spots which mark the site of lesions which have crusted and fallen away. Figure 5 shows the other boy (Case 2) eleven weeks after the onset of his disease.

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The sunken, sightless eyes bear witness to the destructive effect of the ophthalmia in this case. Over the whole body may be seen the brownish pink pigmented spots that mark the position of the eruption.

In the uncertainty of diagnosis, each case was treated in isolation with the strong impression in the minds of all that this disease, with its high temperature and profuse eruption, should be considered in the group of infectious, eruptive fevers. There was an interval of a litttle more than a month between the arrival of the patients at Bellevue Hospital and no possible contact could be traced between the families—living, as they were, in widely separated sections of the city. At any rate, no other cases developed; and while the presumption remains that this condition is an infection, there is nothing to indicate that it is spread by immediate contagion.

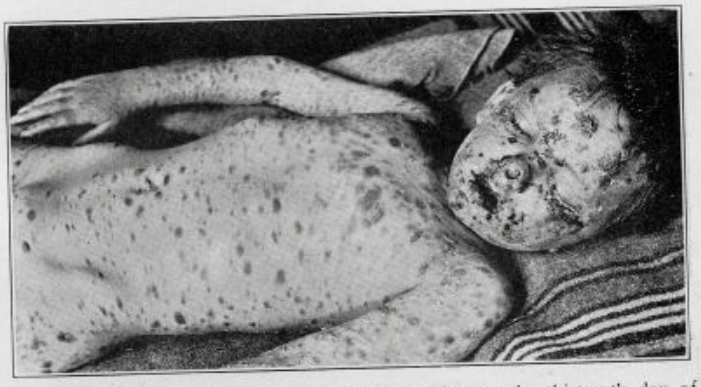

Fig. 1.—Case 1. Nature and extent of eruption on the thirteenth day of the illness.

REPORT OF CASES

CASE 1.—*History.*—H. S., a white boy, aged 8 years, was admitted to the children's service of Bellevue Hospital, May 1, 1922, on the tenth day of his illness. There was nothing significant in the family history; he had diphtheria at 18 months, pertussis at 3 years and measles at 7 years. He had been successfully vaccinated and the tonsils had been removed at 7½ years. His general health had been good until shortly following the tonsillectomy when he was in a hospital for fourteen weeks with a septic temperature, enlarged spleen, jaundice and a blood culture which showed *Staphylococcus aureus* on two occasions. He recovered from this, and was apparently well for two and a half months prior to the onset of the present illness.

Onset of Illness.—Ten days before admission, he complained of a mild sore throat and general malaise. He was not very sick at first, but felt weak and went to bed. The next day he complained of pain in the eyes and did not want to eat because his mouth hurt him. Soon pus was seen running from the inflamed eyes and on the third day reddish spots were noticed on the back of the neck. The body was not examined until the seventh day when the

skin was found to be covered with reddish brown spots; only a few such spots were noted on the face, legs and arms. While at home, the temperature was not taken.

Physical Examination.—On admission the boy was acutely ill with a temperature of 103 F. He was well nourished, mentally clear and cooperative, but was prostrated and unable to open his swollen eyes. The lids of both eyes were edematous and thick pus streamed down the face from the palpebral fissures. There was marked blepharitis marginalis, chemosis and inflammation of the bulbar conjunctiva with haziness of the left cornea. The lips were cracked, bleeding and encrusted. The tongue was swollen, bright red and

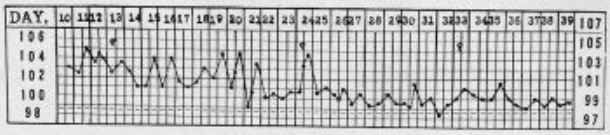

Fig. 2.—Temperature chart of Case 1. P marks the days when photographs were taken.

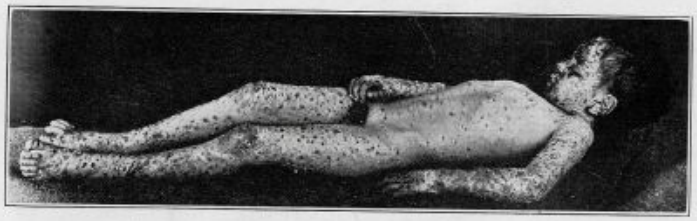

Fig. 3.—Case 1. Twenty-fourth day of the illness.

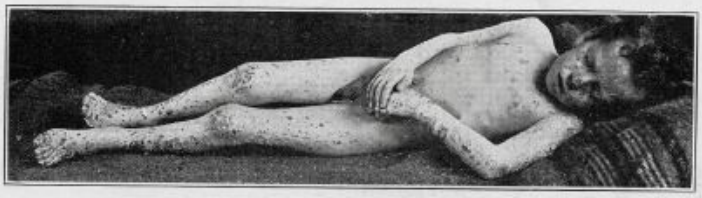

Fig. 4.—Case 1. Thirty-third day of the illness.

fissured, and the mucous membrane of the mouth was inflamed with small bullous lesions which rapidly broke down, leaving a raw and angry surface. The scalp was quite free of any eruption but the face showed large blotches of dried pus, considered secondary to the purulent discharge from the eyes spreading over the papular lesions of the cheeks and forehead.

The trunk, arms and thighs were thickly set with discrete, oval, brownish purple papular lesions, varying in size from 0.5 to 2 cm. in the longest diameter. A few of the largest spots showed a yellowish, dry, necrotic center. There was no vesicle, nor pustule formation; no induration about the papule; no areola and the skin between the lesions seemed to be perfectly normal. The

forearms and legs showed what seemed to be the more recent lesions. These were less raised, of brownish red color, paling somewhat on pressure, and more closely set than were those of the trunk and thighs (Fig. 1).

Careful physical examination disclosed a faint short systolic heart murmur, heard best to the left of the apex and not transmitted. The spleen was palpable 4 cm. below the ribs, and the liver edge could be felt a finger's breadth below the costal margin. Otherwise, there were only normal findings.

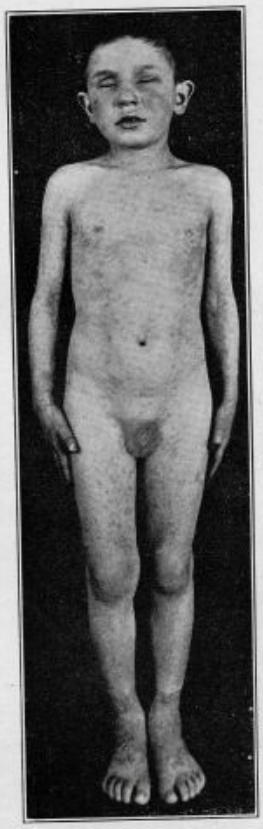

Fig. 5.—Case 2. Eleven weeks after onset of illness. Recovery was complete except for total blindness. Persistent pigmentation shows at the sites of the skin eruption.

Laboratory Examination.—Cultures made from the eyes and throat showed a mixed infection of common cocci and bacilli with no predominating organism and no gonococci. From the necrotic center of one large papule a pure strain of *Staphylococcus aureus* was grown. The blood culture was sterile. The Wassermann reaction was negative.

Blood: The blood count showed 4,000,000 red blood cells with 75 per cent. hemoglobin, and 10,000 leukocytes with 82 per cent. polymorphonuclears and 18 per cent. lymphocytes and transitionals. The blood chemistry was also done and all values were determined to be within the normal range.

Urine: Except for a trace of albumin, which was a constant finding during the period of high temperature, the urine was negative.

Course.—For the next eleven days (from the tenth to the twenty-first day of the illness) the temperature ranged between 101 and 105 F., with a fall to the 100 degree level after the twenty-fourth day (Fig. 2). At each examination the blood showed a definite leukopenia.

During this time there was no complaint of pain or itching or discomfort in the skin lesions. Photophobia and pain in the eyes persisted, but the edema of the eyelids and the purulent discharge yielded to treatment with warm boric acid instillations, dilatation of the pupils with 1 per cent. atropin and the application of 1:5,000 mercuric chlorid in petrolatum twice daily. The right eye cleared rapidly, but the left cornea was already ulcerated and it healed very slowly, with resultant scarring of its lower segment.

New lesions were seen to appear on the skin of the forearms and legs, the palms and soles, for the first week after admission, but none after the eighteenth day since onset. These were at first pale and macular, rapidly becoming firm, dry, purplish papules like those seen on the trunk at the time of admission. Meanwhile, the earliest skin lesions had begun to resolve into

Blood Examination in Case 1

	19th Day	26th Day	37th Day
Leukocytes	4,600	6,700	8,700
Polymorphonuclears	62	52	58
Small lymphocytes	33	45	40
Large mononuclears	3	0	0
Eosinophils	0	2	2

horny, flattened, thick scales, with raised, papery edges. At this stage the fever dropped to its lowest level (Fig. 3).

As the resolution advanced in the same order as the appearance of the lesions, these dry horny scales dropped off from the neck and back, then from the chest and abdomen and thighs, and last of all from the arms and legs, leaving a dull reddish area of apparently normal skin to mark the site of the lesions. There was no instance of pitting or scarring of the skin (Fig. 4).

The inflammation of the mucous membrane of the mouth, lips and tongue subsided within a week of admission. This did not interfere with the taking of nourishment and no gastro-intestinal symptoms were present at any time.

The subsequent history of this case is not especially significant. After a period of normal temperature for two weeks a left otitis media developed; this went on slowly to a mastoiditis for which the boy was operated on June 22. At this time a few crusts still remained on the forearms and feet.

Case 2.—*History.*—S. M., was a Jewish boy, aged 7 years, with a negative family history, who had been always strong and well except for measles at 4 years. He had been vaccinated successfully.

Onset of Illness.—Three weeks before admission, he complained of pain in the eyes and weakness. The next day the eyes were discharging, and a rash was noted on the body which the family physician called "black measles." On the third day of his illness he was taken to the Willard Parker Hospital, where he was found to have a temperature of 103 F., with signs of bronchopneumonia at the right base, a purulent conjunctivitis with great edema of the lids, and a skin eruption of which the tentative diagnosis of erythema multiforme was made. This eruption was described on the third day as being macular, hemorrhagic, with a few papules, with areas of excoriation on the face.

The eyelids were edematous and pasted shut with thick pus, and the mucous membrane of the mouth was practically exfoliated. The boy remained at Willard Parker Hospital for two and a half weeks, with the pneumonia resolving gradually. The temperature ranged from 101 to 104 F. for two weeks, then became irregular at a lower average with an occasional rise to 103 F. The boy was irrational during the first week, and there was great prostration, weakness and loss of flesh. In spite of instillations of boric acid solution and argyrol, corneal ulcers formed, with perforation and abscess formation in both eyes involving all the structures of the globe.

Simple ointments were applied to the skin lesions, which crusted and dropped off the chest and back by the end of the third week.

He was transferred to the Children's Service of Bellevue Hospital on the twenty-second day of his illness, March 11, 1922.

Physical Examination.—On admission the boy was acutely ill, much wasted, with a temperature of 102 F., mentally clear, but totally blind. The lungs showed signs of a resolving pneumonia of the right lower lobe. The eyes were the seat of a panophthalmitis, with destruction of the cornea and lens. Pus was still oozing from the granulating tissue of the shrunken eyeballs.

The skin of the trunk was the seat of irregularly oval pigmentation of a reddish brown color, rather evenly distributed except below the nipples where there were confluent areas. This skin was quite normal in appearance, except for the pigment, and showed no trace of scar tissue.

The arms and legs showed oval brownish red horny crusts, varying from 1 to 2 cm. in the longest diameter without areola or surrounding induration, and without trace of exudate or pustule formation. There was no complaint of pain or itching. Otherwise the examination was quite negative.

Course.—The lung condition cleared slowly with a temperature varying between 101 and 103 F., for a week, then falling to the 100 degree level for eight days. The eyeballs healed by granulation. The skin condition resolved progressively by the falling off of the thick oval horny crusts from the thighs and arms, and, last of all from the feet and soles, each crust leaving to mark its site an area of reddish brown pigment. These areas were identical with the marks found on the back and chest at time of admission.

The family refused to allow blood to be taken for a Wassermann test and insisted on removing him from the hospital fifteen days after admission. Later, this boy was visited in his home and found to be in excellent condition except, of course, for his blindness. With some difficulty consent was obtained for a photograph (Fig. 5).

SUMMARY

1. Two cases have been observed of a generalized cutaneous eruption, not conforming to any recognized dermatologic condition.

2. Both cases occurred in boys, one aged 7, the other 8, coming from widely separated parts of New York City, with no possibility of contact.

3. Both cases manifested a purulent conjunctivitis, in Case 2 going on to panophthalmitis and total loss of vision, and in Case 1 responding to treatment, but leaving a severe corneal scar. The pus showed pyogenic organisms only; no gonococci.

4. A high and continuous fever was present in both cases, explainable in Case 2 by a lobar pneumonia, but in Case 1 without apparent cause other than the skin condition.

5. The eruption showed certain characteristics, identical in each case. The onset was with fever, the rash appearing on the back of the neck

and chest, spreading to the face, arms and legs during a period of about eighteen days, the last lesions to appear being on the soles and palms. At this time resolution of the first lesions began.

The eruption consisted of oval, dark red to purplish macules, separated by normal areas of skin. These became in a few days raised firm papules of brownish purple, from 0.5 to 2 cm. in the longest diameter, without areola, and without subjective symptoms of pain or itching at any time. A few of the largest spots showed a yellow, dry, necrotic center. The lesions on the forearms and shins were smaller and more thickly crowded together. No pustules or vesicles were to be seen. The scalp was at all times free of lesions; but the mouth and lips were intensely sore and inflamed. In Case 1 bullae were noted in the mouth at the end of the first week.

After the third week resolution began in the order of appearance of the lesions. This consisted of a shrinking of the macule to a horny oval of dark brown color, with raised papery edges. From the fourth week these scales dropped off, leaving a faint pigmented area, without pitting or scarring. By the fifth week the chest, face and back were clear, except for pigmentation, while resolution and crusting were still going on on the forearms and legs. Fall of temperature coincided with the period of resolution of the skin lesions.

DIAGNOSIS

1. A skin eruption from drug ingestion is ruled out by careful inquiry which showed that no drugs whatever had been administered in either case.

2. A skin eruption from food poisoning can hardly be considered from the entire absence of gastro-intestinal symptoms in the presence of a high and sustained temperature reaction.

3. Syphilis is to be excluded by the character of the lesions, the age of the children, the negative history, and the negative Wassermann reaction in Case 1.

4. Pemphigus was suggested, from the observation of bullae in the mouth in Case 1. Nothing further in the course of the disease, the appearance of the eruption and its evolution gave any support to this diagnosis.

5. Hemorrhagic measles, as it happened, was the primary diagnosis of the family physician in each instance. Both children had already had measles, in Case 1 at 7 years, and in Case 2 at 4 years. While excusable at the onset, this diagnosis is quite indefensible in view of the distinctive character of the lesion as described.

6. A sepsis with generalized eruption must be considered as a possibility, in spite of the negative blood culture in Case 1. This diagnosis

is suggested by the history of a prior sepsis in Case 1 and might account for the temperature and course and the occurrence of a pneumonia in Case 2. The superficial nature of the lesions, their character and progressive appearance over nearly three weeks and the lukopenia argue against this supposition.

7. Erythema multiforme, from some unknown toxic cause, was proposed as a diagnosis, but this is unsatisfactory from the character and distribution of the lesions, the lack of subjective symptoms, the prolonged high fever, and the terminal heavy crusting.

8. There remains the possibility that this condition represents a distinct disease which has not hitherto been recognized.

Comment.—While the true diagnosis of this condition must be left an open question, the report of these two cases seems justified if only to draw attention to the serious effects to be expected unless the eyes in any similar case receive early and painstaking treatment. The boy in Case 2 is totally blind, while the other boy only escapes with an impairment of vision in one eye. Furthermore, it is hoped that this report may lead to the study of other or similar cases. Quite possibly the observation of this condition in its first stages may clear up the vexed question of its etiology.

Finally, we have been impressed by the striking picture presented by these cases. Here is a syndrome of dramatic onset, with fever, conjunctivitis and cutaneous eruption. The child is prostrated, the mouth and tongue are inflamed and raw, the eyelids are swollen and pus streams from the eyes. There is a course of three or more weeks of high fever, with leukopenia. The eruption, unlike any hitherto described, comes out progressively, for two weeks or more, matures and resolves in horny crusts, in the order of its appearance. The temperature falls with this resolution of the skin lesions. This syndrome suggests strongly an infectious disease of unknown etiology. We believe that this condition deserves to be considered a definite clinical entity.

We wish to express our appreciation of the kindness of Dr. L. Emmett Holt, Dr. John A. Fordyce and Dr. Warfield T. Longcope, who saw one or both of these cases in consultation.