A FATAL CASE OF MUSTARD GAS POISONING

BY

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There have fortunately been no opportunities of seeing the fatal effects of mustard gas on human beings in this country since the last war; therefore it may be of interest to record my observations on a family who became contaminated with mustard gas, and the post-mortem findings on the one patient who died.

History of Case

Some boys entered a W.D. area and found a few mustard bombs which had exploded and been left covered with bleach powder. They threw stones at them, and one burst into flames, giving off smoke to which a boy aged 8 was exposed for several minutes. Later, when the flames were extinguished, he picked up the bomb and in so doing scattered some of the contents on his jersey and trousers. This was a white powder consisting of bleach mixed with the remains of the liquid mustard in the bomb. The boy returned home about an hour later complaining that his arms and legs were burning. His mother states that the exposed parts of his body, not face, looked as if they were severely sunburnt. She stripped and washed him and put him to bed. She washed his jersey, but the other clothing was left hanging in the room where the mother and four children were sitting for an hour or so before going to bed.

About two hours later the boy started vomiting, as did the other members of the family, and all complained of intense pain and irritation of the eyes. By the next morning five members of the family were suffering from severe conjunctivitis, and the boy had blisters on his penis and thighs, while his elder brother, who shared a bed with him, also had blisters on his thigh and arm.

Clinical Record and Treatment

The mother and four children were immediately admitted to hospital. The originally contaminated patient was suffering intense discomfort from his eyes; they were watering profusely, and he was quite unable to open them. The penis was swollen and blistered, as were the inner parts of the thighs, while an area of erythema extended over the forearms, abdomen, and thighs. The blisters were aspirated and cod-liver oil applied to the burnt areas. The eyes were irrigated with normal saline every two hours, 10% sulphacetamide (albicid) drops were instilled every four hours, and 1% atropine drops were put in twice a day until full dilatation was obtained.

During the next 24 hours further blisters developed, spreading peripherally from the original burns and also on the buttocks, which rapidly became very raw. Vomiting ceased, but was replaced by an irritable cough. The respirations rose to 40 a minute, the temperature to 101.2°, and pulse to 140; the boy was restless and delirious, and incontinent of urine and faeces. This stage continued for about 36 hours, with alternating periods of lucidity and delirium. He began to show signs of pulmonary congestion, and was given sulphathiazole tablets. Frequent irrigation of the eyes was discontinued 24 hours after admission, and the exudate merely washed out before putting in the sulphacetamide and atropine drops.

Three days after admission his general condition improved; he was rational and no longer incontinent, and took his food and drinks well. There was slight oedema of the cornea, and the conjunctivitis was still very marked, though he was now able to open his eyes.

The burnt areas, chiefly of first and second degrees, were clean, but the erythematous areas on the legs, arms, abdomen, and chest were gradually extending and being replaced by blisters. The cough was very troublesome at times, chiefly tracheal in type, and a few crepitations were heard at the lung bases. There was some nasal catarrh but no sputum. Inhalations of menthol compound on a Burney Yeo mask gave some relief. The temperature all this time was fluctuating between 98 and 101°, but the general condition was improving, and sulphathiazole was discontinued on the sixth day after admission, 23 g. having been given. At this stage his non-protein nitrogen and urinary calcium were normal, and a sternal puncture showed no abnormal cells.

A blood count taken on the fifth day showed 13,000 white cells per c.mm. with 88% polymorphs, but two days later this had dropped to 3,800, when the sulphathiazole was discontinued. From this date the white cell count and also the haemoglobin fell rapidly and the temperature steadily rose. The boy became very irritable and particularly resented exposure of his skin to the air. The pulmonary signs increased and he appeared to have difficulty in clearing mucus from his trachea.

His abdomen became very distended and tender, especially on the right side. His white cell count on successive days was 13,000, 7,600, 3,800, 1,200, 600, 200 per c.mm., and at this stage the 200 cells were made up of polymorphs 12%, monocytes 14%, lymphocytes 26%, pathological lymphocytes 48%. Blood transfusion had been considered when the agranulocytosis developed, but was not done as it meant cutting down through burnt tissue. However, as four or five injections of 10 c.cm. of pentnucleotide had no effect it was decided to start continuous blood transfusion, and between the eighth and tenth days three pints of fresh blood and one pint of glucose-saline were given. On the eleventh day his abdomen was less distended and tender and the bowels were acting. The temperature was, however, 104°, respirations 30, and the cough was very troublesome. Mentally he was bright, he was drinking well, and his kidneys were acting normally. His condition, however, steadily deteriorated during the next 24 hours, with increasing difficulty in respiration, and he died at 2 a.m. on the twelfth day after the accident.

Remainder of Family

The mother and three other children were suffering from acute conjunctivitis on admission. They all responded well to treatment with sulphacetamide and atropine, and their eyes were almost normal within a week.

One of the boys who had shared the patient's bed had blisters on the thigh and forearm, and during the next week these extended, his penis became blistered, and a well-marked erythema developed on the bathing-drawers area. A very troublesome cough started on the fourth day but soon cleared up. On the sixth day he vomited and complained of abdominal pain, about the same time that his brother also had acute pain due to a duodenal ulcer. The pain in this case, however, subsided in about 24 hours. Another boy, who also shared the bed, had acute conjunctivitis and developed blisters on the buttock and perineum that, although remaining clean, took eight weeks to heal.

Three other members of the family—girls aged 5 and 12 and a boy aged 2—were admitted about a week later with severe coughs, and the two youngest developed a bronchopneumonic condition. These were in bed when the contaminated boy came home, and presumably were affected by vapour from the clothes the following morning.

Several members of the family showed a definite reduction in their white cell counts, which were taken on the tenth day. The majority were from 4,000 to 6,000 per c.mm., though one boy had a count as low as 2,800. In the course of a week all these counts increased by 2,000 or 3,000, coincidentally with an improvement in the general condition.

Post-mortem Examination (Dr. Eric Gardner)

A well-built boy with extensive first-, second-, and third-degree burns on the body, some healed and the remainder healing satisfactorily.

Brain: 55 oz.—rather severe congestion superficially and on section. Pharynx congested. Membranous ulceration of larynx and a membranous tracheitis and bronchitis, seen also in section of lung in larger bronchi with some peribronchial consolidation. Right lung: Lower lobe—massive collapse superficially, centre of lung aerated; upper lobe—similar to a less extent; solid oedema of lower lobe. Left lung: Similar condition of collapse but less extensive. Heart: Vessels, valves, and myocardium normal to naked eye. Stomach: Mucous membrane congested. Duodenum: Ulcer 1 cm. in length; ulcerated completely through mucous membrane on to muscular coat. Jejunum and ileum: Mucous membrane congested, fading out in ileum. Caecum: Area of ulceration finger-print size. Colon: Slight congestion. Liver: 36 oz.—smooth; terminally congested. On section, pattern blurred and surface glazed (cloudy swelling). Spleen: 4 oz.—swollen; firm and deeply congested. Kidneys: 8 oz.—deeply congested; surface veins prominent; capsule adherent in patches. Cortex—radial lines of congestion; pelvis congested and oedematous. Patches of congestion in ureters. Adrenal glands oedematous; bladder normal. Section of tibia: Red bone marrow pale; considerable pallor in head and upper end of shaft. Vertebrae, deep brownish colour on section.

Summary.—A membranous ulcerative laryngitis and a membranous ulceration of the main air tubes of the lung had led to a massive collapse of that organ—the immediate cause of death. Further changes were noted in the glands of the body and in the bone marrow, consistent with and consequent upon the changes in the blood. The cause of death was: (a) agranulocytosis; (b) multiple burns from mustard gas.

Summary of Microscopical Examination of Tissues
(Prof. G. R. Cameron)

Severe pulmonary oedema and haemorrhage, with macrophage infiltration, acute desquamative bronchitis and bronchiolitis, slight peribronchitis—no bronchopneumonia; acute desquamative tracheitis with false-membrane formation; acute ulcerative laryngitis with false-membrane formation; acute ulceration of first part of

duodenum; cloudy swelling, congestion, cast formation in kidneys; cloudy swelling and early necrosis in liver; distension of spleen with red corpuscles; depletion of lymphoid tissue in spleen, mesenteric, inguinal, and pre-aortic lymph glands, with lymphoblastic proliferation; disappearance of granular polymorphonuclear leucocytes and myelocytes from bone marrow.

Comments

The outstanding features in this case are:

1. Terminal pulmonary oedema and haemorrhage, both of which appear to have developed within the last one or, possibly, two days of life, judged by the relatively slight cellular reaction in the lungs.
2. Acute bronchitis and bronchiolitis, which must be grouped with the laryngitis and tracheitis, since all show the same degree of inflammatory change and epithelial damage. These changes are of longer standing than the pulmonary oedema and haemorrhage, and are to be attributed to inhalation of mustard vapour.
3. Ulceration of the duodenum (and of the caecum) of some days' duration—probably at least a week; it is certainly not terminal.
4. Depletion of lymphocytes, with lymphoblastic proliferation, suggests a longer process—i.e., is not terminal.
5. Haemorrhages in the adrenals.

The mild degenerative changes and slight necrosis of liver and kidneys are difficult to separate from post-mortem change—a source of error which has to be seriously considered here, since the necropsy was delayed for about 30 hours. However, the presence of granular and "calcium" casts in the kidneys is evidence of some damage to these organs during life. These changes do not, however, suggest sulphathiazole poisoning if the findings described in monkeys with this drug (Climenko and Wright, *Arch. Path.*, 1941, **32**, 794) are applicable to man.

Discussion

In the boy's case the contamination was due partly to mustard vapour and partly to a mixture of liquid mustard and bleach powder. The contamination of the family was due to vapour given off from the boy's clothing, which was hanging in the living-room.

In the war of 1914–18 it was found that the majority of mustard gas casualties were due to *vapour*. These were caused not by inhaling the gas directly on the field of battle, but by a contaminated man going into a billet or dug-out, whereupon the liquid contamination on his clothing 'evaporated', resulting in a high concentration of vapour in a confined space, which caused many casualties indirectly among hitherto unaffected and uncontaminated men. This is well illustrated in the present case, for one individual was contaminated by liquid and seven others became vapour casualties indirectly. The obvious warning is, *Never take contaminated clothing into a confined space.*

Initial Symptoms.—Apart from the burning sensation of the skin in the contaminated boy, *vomiting* was the first symptom in all the patients. This is now well recognized clinically in mustard gas poisoning, and is followed a few hours later by irritation of the conjunctiva.

Burns.—The burns were chiefly of the first and second degrees. It does not seem to matter greatly what treatment is used for these, so long as attention is paid to *strict asepsis*. According to those who have had most experience, acriflavine emulsion, liquid paraffin, tulle gras, etc., will all give satisfactory results, and it is suggested that the treatment which is most readily available and understood by the nursing staff should be used. It is important to aspirate the blister fluid under aseptic precautions in the early stages, and to preserve as much of the blistered skin as possible. In this connexion amyl salicylate limits the effusion, but is expensive, is not always readily available, and is irritating to the scrotum and face; on the whole, therefore, it is not applicable to large numbers of cases. Fomentations should not be used, nor should tannic acid, as recent work has shown that when a large area of burnt skin is tanned there is a possibility of absorption of tannic acid, giving rise to liver-cell necrosis (personal communication from Prof. Cameron). That fresh patches of erythema and blisters continue to develop for seven to ten days is a well-established clinical fact, and is not, as is sometimes thought, due to reinfection. Healing of the burnt area

is often very slow. One of the boys with a second-degree burn about 3 in. by 2 in. on the perineum took eight weeks to heal, although there was no secondary infection.

Eyes.—Miss Ida Mann, in a personal communication from the Nuffield Laboratory of Ophthalmology, classifies the clinical signs of mustard gas burns of the eyes into four grades as follows:

Group 1: Very Mild.—Lids and sometimes conjunctiva red, cornea clear. Sometimes slight oedema of the lids and lacrimation. No photophobia. No treatment required.

Group 2: Mild.—In addition to the above there is superficial corneal haze, lacrimation and/or discharge (profuse), photophobia and/or blepharospasm. Treatment consists in keeping the eye clean, using mydriatics and only non-irritating antiseptics. Do not bandage the eye; reassure the patient, as there is a large element of fear. Recovery should take place in one to three weeks, and is complete.

Group 3: Severe.—In addition to the above there is deep corneal haze—(a) without new vessel formation, (b) with new vessel formation. Treatment is on the same lines as with Group 2. The case takes several weeks to recover, and if Group 3 (b) there may be relapses and prolonged disability, with final recovery.

Group 4: Very Severe.—As above, but with iritis, copious and prolonged discharge, and inability to open the eyes for a period of weeks or months. Partial recovery follows in about nine months. There is a risk of ulceration following prolonged degenerative processes, occurring after five to ten years. Treatment is by mydriatics, cleanliness, and non-irritating antiseptics.

The present case would appear to fall into Group 2 or Group 3 (a). Discharge was not a feature and there was not much corneal haze. In all cases intensive irrigation is irritating and harmful. A non-irritating antiseptic would seem to be indicated when secondary infection is present. Mydriatics relieve the pain and spasm.

Trachea and Lungs.—Tracheitis is an early symptom, and should be relieved by inhalations. An irritable cough starts on the second to fourth day, and bronchitis or pulmonary oedema develops, or the condition gradually subsides in a few days. The usual remedies are applicable here.

Blood.—The obvious question of the cause of the agranulocytosis was whether it was due to the sulphathiazole, of which the patient had received 23 g., or whether it was due to the mustard gas. I understand from Prof. Cameron that this condition was recognized in the last war as an occasional sequela of mustard gas poisoning and that much experimental work has confirmed its importance. The post-mortem findings did not suggest that the agranulocytosis was due to the sulphathiazole, and the fact that some of the other cases which had no sulphonamide also showed a marked diminution in their white cell counts eight to fourteen days after the contamination strongly suggests that the mustard gas was the causative agent. The question naturally arises whether sulphonamides should be used in dealing with mustard gas cases, and investigation of this problem is urgently required. It is known that mustard has an affinity for lymphoid tissue, and the relatively greater proportion of this tissue in children may make them especially susceptible.

Intestinal Ulceration.—Ulcers of the duodenum are well known as a textbook complication of burns, although I believe they must be relatively uncommon. This is probably due to the fact that patients often die before the ulcer has time to develop. The symptoms of pain and tenderness on the right side of the abdomen with general distension were obviously due to the ulcer found after death. A similar ulcer was present in the caecum. Haemorrhage and acute ulceration of the mucosa are, however, commonly found in experimental mustard gas poisoning.

Convalescence.—Convalescence tends to be prolonged, and good nourishing food, with extra milk and especially an excess of vitamin C, is important. The vitamin C should be given in large doses of 500 mg. 12-hourly for three doses, followed by 50 mg. twice a day, proportionately less being required for a child.

I was fortunate in being able to call upon the expert knowledge of Capt. K. Hill, R.A.M.C., in treating these cases, and to have the opportunity also of discussing them with Prof. G. R. Cameron and Surg. Lieut.-Cmdr. G. Foss, R.N.V.R. My thanks are due to all of them for their expert assistance, to Miss Ida Mann for her classification of eye cases, and also to Dr. E. Gardner for his post-mortem report.