without ever losing one's patience or temper. The problem is not then likely to be long-lasting. It will disappear—only to be replaced by a completely different problem which, one hopes, will be more easy of solution.

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TREATMENT OF HYDROFLUORIC ACID BURNS

BY

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Burns caused by hydrofluoric acid are largely confined to workers in special industries, and it is unusual for a case to appear in a burns unit which is not near an industrial area. Knowledge of hydrofluoric acid burns, and their treatment, thus tends to be restricted to industrial medical officers. Nearly all the work published on the subject has appeared in industrial medical journals, and little in the more widely read medical press. The effects of such burns, however, are of so peculiar a severity that it may be worth while to give an account here of my own experience of a single case, and in that connexion to discuss what is known of their nature and their treatment.

Chemistry of Hydrofluoric Acid

Hydrofluoric acid is an inorganic compound of hydrogen and the element fluorine. Fluorine occurs in nature as fluorspar (Derbyshire spar, blue-john), which is a crystalline fluoride of calcium. Agricola described it in 1530 and named it "fluor," from the Latin verb "to flow," as it melts at red heat. The crystals exhibit a bluish glow when light falls upon them. This effect has led to the more general description of the phenomenon as "fluorescence."

Crude hydrofluoric acid was first prepared about 1720 by an unknown English glass-worker. Priestley and Scheele in 1771 discovered that fluorspar was a salt of lime and a peculiar acid. They distilled fluorspar with strong sulphuric acid in a glass vessel, and obtained a vapour which corroded the flask. Meyer in 1781 and Wenzel in 1783 distilled fluorspar with strong sulphuric acid in iron and lead vessels, and obtained what must have been fairly pure hydrofluoric acid. Ampère in 1810 was the first to suggest that the acid was a compound of hydrogen with an unknown element, which he called "fluorine." Fluorine itself, a member of the halogen group of elements, was first isolated by Moissan in 1886 by electrolysis of potassium fluoride in an excess of anhydrous HF.

Hydrofluoric acid is chemically a weak acid; its degree of dissociation is small compared with that of the strong mineral acids; but its power to attack silica and silicates makes it of great industrial importance.

The fluorides, or salts of hydrofluoric acid, differ strikingly from the salts of the other halogens. Whereas silver bromide and silver chloride are very insoluble,

silver fluoride dissolves readily in water. On the other hand, calcium fluoride and magnesium fluoride are insoluble salts, and this fact plays a vital part in the treatment of fluoride toxæmia and hydrofluoric acid burns. Fluorides also tend to form complex compounds such as silicofluorides and fluoraluminates. Sodium fluoraluminate, or cryolite, is important in the extraction of aluminium from the ore (Partington, 1946).

Hydrofluoric Acid in Industry

Hydrofluoric acid has many uses in industry. Its capacity to dissolve silica is used (1) in foundries, for removing sand from castings; (2) in glass works, for etching and frosting glass and removing tool marks from cut glass; (3) in the pottery and china industries, for removing spots in the glaze; (4) in the graphite industry, for removing siliceous impurities; (5) in the manufacture of ashless filter paper. In breweries it is used for cleaning pipes, as it destroys yeasts and thus restrains secondary fermentation. It is used as a bleaching agent in the manufacture of cane chair-seats. Hydrofluoric acid fumes are given off in the manufacture of superphosphates for fertilizers.

Toxicity of Fluorine Compounds

The toxic actions of fluorine compounds fall into three groups—acute poisoning, chronic poisoning, and local effects. Acute and chronic poisoning have been reviewed extensively by Roholm (1937), Greenwood (1940), and others. The present paper is concerned with the local effects. A few fatal cases of fluoride burns have been reported, but in these there was no evidence of fluoride absorption.

Many fluorine compounds have corrosive action on the skin. The HF molecule would appear to be the active agent, and any acid-reacting solution of fluorides, bifluorides, or fluosilicates is corrosive (Roholm, 1937). Most of the published cases of burns are due to hydrofluoric acid itself.

Hydrofluoric Acid Burns

Ever since its discovery hydrofluoric acid has been known to cause deep, slow-healing, painful burns. Lesions may be produced by exposure to the acid vapour or to its aqueous solution in various strengths. Repeated exposure to the vapour may lead to ulceration of nasal and oral mucosa, bronchopneumonia, and oedema of the lungs; there may be conjunctivitis; the cuticles may be attacked, causing suppuration and loss of the finger-nails (Eulenburg, 1876; quoted by Prosser White, 1934). The concentrated vapour may burn the skin (Schuermann, 1937).

The aqueous solution causes burns, the severity of which depends on the strength of the solution and the length of time it is in contact with the tissues. One outstanding feature of burns by hydrofluoric acid is the excruciating pain which they cause. When the acid is in weak solution the onset of pain may be delayed for an hour or more. A burn from anhydrous hydrofluoric acid is felt immediately (Gehrmann, 1948).

Exposure of the skin for a minute or two to a weak solution of the acid, or momentarily to a strong solution, produces a blanched slightly oedematous weal, with subsequent crust formation in about four days. The crust separates in a week, when the subjacent area will be found to have healed (Paley and Seifter, 1941; Gehrmann, 1948; Thelwall Jones, 1939).

In more severe burns there is a greyish-purple discoloration of the skin with a surrounding red, oedematous area. Blisters containing sero-purulent fluid are raised on the skin. Beneath the skin there is deep destruction of tissue, which is responsible for slow-healing ulcers. It appears that the horny layer of the skin acts as a barrier to the weaker solutions, but once this barrier has been passed, though the skin is not dissolved, the necrosis of tissue beneath is surprisingly extensive (Fredenhagen and Wellmann, 1932).

Thelwall Jones (1939) reported a series of twelve cases. In these he drew attention to the following outstanding points: (1) the intense pain of the burn, which may be delayed for several hours, but which in the absence of treatment may persist for several days; (2) the tough coagulated area of skin at the site of the burning; (3) the progressive destruction of tissue beneath the skin, which may continue over a period of several days.

According to Roholm (1937), as stated above, the active agent is the intact HF molecule, which is capable of penetrating intact epidermis.

Treatment

The various treatments which have been suggested for hydrofluoric acid burns are based on three principles: (1) dilution and washing away of the acid; (2) neutralization of the acid with weak alkalis; (3) precipitation of the acid as insoluble fluoride. A pamphlet issued by the National Council of the Pottery Industry recommended washing under running water. This was to be followed by immersion for one minute in weak ammonium carbonate solution. The area was then to be washed in water and re-immersed in ammonia, the process being continued for about ten minutes. The use of ammonia has the disadvantage that the ammonium fluoride formed breaks down to ammonium bifluoride, which itself is corrosive.

Ziener (1935) recommended immersion in a saturated solution of sodium bicarbonate. Schlick (1911) showed experimentally that the toxic action of sodium fluoride was neutralized by the simultaneous administration of calcium chloride.

Fredenhagen and Wellmann (1932) treated hydrofluoric acid burns of the hand by massaging a cream of magnesium oxide and glycerin into the surface of the burn. The paste was reapplied frequently and kept in contact with the burn for several hours. They tried the injection of a 20% solution of magnesium sulphate into the burned tissue, and reported one successful case. They suggested, on theoretical grounds, that a 10% solution of calcium gluconate would be a better agent to inject, though its action would be slower. Schuermann (1937) tried the injection of 10% calcium gluconate solution in a case of burning by the vapour of hydrofluoric acid. He gave it intravenously, however, and reported it to be without benefit. Thelwall Jones (1939) reported success with the injection of calcium gluconate into and under the coagulum of the burn. Paley and Seifter (1941), who carried out a series of controlled experimental hydrofluoric acid burns in rats, reported beneficial results from the injection of calcium gluconate into and under the burn.

Thelwall Jones (1939) drew up a scheme of treatment. This is now the basis of the emergency treatment of burns in many factories where the acid is in use. The main points in this scheme are: (1) emphasis is laid on

the need for immediate treatment as soon as the burn occurs; (2) the burned part is immediately washed or immersed in a warm saturated solution of sodium bicarbonate; (3) after the washing a cream of magnesium oxide and glycerin is massaged into the surface of the burn; (4) *as soon as possible* a 10% solution of calcium gluconate is injected into and under the coagulum of the burn; further dressings of magnesium oxide cream are then applied, being renewed night and morning for five to six days.

The injections of calcium gluconate are given in the hope that fluoride in the tissues will be inactivated by precipitation as insoluble calcium fluoride. It is uncertain whether such a simple chemical reaction actually occurs in the tissues, but the injection gives immediate relief of pain when adequately carried out, and prevents the extensive necrosis seen in untreated cases (A. Lloyd Potter, personal communication). Gehrmann (1948) points out that the lesions of finger-tips and nail-beds are particularly painful, and that local analgesia is necessary to allow the injection of calcium gluconate to be given. The nails can then be opened to release tension. He also recommends soaking of the burned part in 70% alcohol and ice. This is believed to close lymph channels and retard penetration of the acid beneath the horny layers of the skin. It relieves pain and may promote diffusion of fluorides from the tissues into the alcohol.

Case Report

The patient was a woman employed in the manufacture of glass measuring-tubes. On these she etched the graduations, using a 60% aqueous solution of hydrofluoric acid as the etching medium. The work was done in fume cupboards in a quiet part of the factory, so that there was little likelihood that the worker would be distracted from the routine. Rubber gloves and apron were worn. The tubes to be etched were mounted on brackets in the fume cupboards. The acid was contained in a wax dish and was applied with a rubber applicator. Each cupboard was closed between applications by means of a foot pedal. Alongside the worker was a sink with running water in which the gloved hands were washed after each application.

In some way the right glove became perforated without the worker's knowledge, and a quantity of acid entered the glove. It is uncertain how long it was there before she noticed pain in the hand, but it was thought to be about four minutes. The glove was then immediately removed and the hand washed in a warm saturated solution of sodium bicarbonate. Magnesium oxide paste was massaged into the hand and fingers, and she was taken to a neighbouring hospital, together with a copy of Thelwall Jones's instructions, for injection of calcium gluconate solution. The burn was there seen to involve the whole hand. Thus the injection of calcium gluconate into and under the coagulum must have presented a formidable problem. After the injection, magnesium oxide cream was again applied. The pain was not relieved by the treatment. The following morning she was stated to be in great pain, morphine being required to give relief. The hand was grossly swollen, as were the fingers, and the burned skin was white and insensitive. The appearance suggested complete ischaemia of the digits, possibly due to vasospasm.

The patient was transferred to this unit, where she arrived about 20 hours after the accident. The hand presented a startling appearance. The pain was severe, and seemed to be situated deep in the palm. The fingers were insensitive to touch, were grossly swollen, and were a dirty grey. They appeared completely bloodless. The palm, which was insensitive to touch, presented a large grey blister, which was opened and found to contain sero-purulent fluid. This was collected and tested for fluoride,

with a negative result. The blister was snipped away. The fifth, fourth, and third fingers, the tip of the index finger, and the tip of the thumb were grey and necrotic. It was possible to snip into the pulp of the middle finger without pain. The tissue was coagulated and necrotic right down to bone. The lateral side of the index finger and most of the thumb had escaped the acid. The medial side of the index finger had suffered a partial-thickness burn of the skin. The back of the hand had a patchy, partial-and-full-thickness burn of the skin (Fig. 1). It was obvious at this stage that

the three medial fingers were necrotic, the condition being probably due to deep penetration by the acid. The depth of penetration of the palm was uncertain, but there was at least full-thickness destruction of the skin (Fig. 2). Further calcium gluconate was injected and magnesium oxide cream was applied, more as a gesture of despair than in the hope of doing any good.

FIG. 1

FIG. 3

FIG. 2

FIG. 4

On the sixth day after the accident the whole of the slough on the palm of the hand was excised under general anaesthesia. It extended down to palmar fascia, but the latter was

FIG. 5

FIG. 6

largely intact and healthy bleeding tissue was reached. An immediate split-skin graft was applied to the palm. The fingers were left at this stage, as there seemed to be less necrosis than was at first feared. It was believed that more digital tissue might be saved by waiting for clear demarcation.

The palmar graft took surprisingly well, and exercises to thumb and index finger were begun on the tenth day after the accident.

On the 38th day the demarcation of the sloughing tissues was clear (Figs. 3 and 4). The necrotic portions were all removed and the stumps were closed with the aid of split-skin grafts. Healing was almost complete in 60 days from the accident (Figs. 5 and 6). The hand was tender at first, but function steadily returned to the useful claw formed by the index and thumb remnants. The wide mobile palm, ensured by the early excision and grafting, is proving a great asset.

Discussion

This case reveals the crippling lesions which may result from the action of hydrofluoric acid on the tissues of the hand. Until such a case has been seen it is difficult to realize that such extensive latent destruction is occurring under an apparently superficial lesion. The extreme penetrative power of hydrofluoric acid and the deep necrosis which it causes are not yet adequately explained. They are clearly not due merely to its acid properties, since solutions of other mineral acids much stronger in this respect do not produce comparable lesions. Lloyd Potter suggests that there may be some special action of the fluorine ion on living tissues. Compounds containing fluorine have long been known to act as protoplasmic poisons (Roholm, 1937; Greenwood, 1940); and it is quite certain that organic compounds containing this element, in particular the fluoracetates, have a specific and intensely poisonous action on certain vital enzyme-systems (Peters, 1950). It would appear, indeed, that a more direct and detailed biochemical study of the nature of the action of hydrofluoric acid on tissues and their constituents might yield information which would throw light on its extraordinary penetrative power *in vivo*.

The first-aid treatment of hydrofluoric acid burns is most important. The early and thorough injection of calcium gluconate into and under the coagulum is imperative. A general anaesthetic would have been necessary for adequate injection in the case I have reported. It would therefore seem justifiable to amend the instructions for treatment as follows: "Injection of 10% solution of calcium gluconate into and beneath the coagulum of the whole burned area, under local or general anaesthesia, as required."

It must be borne in mind that the injection of calcium gluconate solution, or indeed of any other fluid, into the tissues of the fingers can produce sufficient pressure to endanger the circulation and may lead to necrosis.

Once the active progress of the burn has been controlled there is much to be gained by early excision of the slough and application of free grafts. In the present case the area of the palm where the slough was excised and a skin graft applied was virtually healed within 14 days of the accident.

Summary

Attention is drawn to the fact that little is known generally of hydrofluoric acid burns and their treatment. The literature on the subject is confined to industrial medical journals.

The chemistry and toxicology of hydrofluoric acid are reviewed.

A severe case of hydrofluoric acid burns of the hand is reported and treatment is described.

Some modification of the treatment of hydrofluoric acid burns is suggested, and the early excision and grafting of the lesions are urged.

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TWO TYPES OF DIABETES MELLITUS, WITH AND WITHOUT AVAILABLE PLASMA INSULIN

BY

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The sensitive technique of assay of small amounts of insulin described by Bornstein (1950) was used by Bornstein and Trewhella (in press) to investigate the plasma insulin content of 11 diabetics. It was found that three had available insulin and eight had none.

We have now investigated the available plasma insulin content of two different types of human diabetes which have been suggested on clinical grounds to be due to (1) lack of insulin and (2) factors other than lack of insulin (Lawrence, 1951).

The first type is generally young and is characterized not only by hyperglycaemia but by rapidly developing *ketosis* and severe weight loss, and requires insulin to live. The second type consists largely of middle-aged obese females with similar grades of hyperglycaemia and glycosuria, but with *no ketosis* and no important loss of weight. Their diabetes is easily controlled by low diets without insulin, particularly if weight is reduced.

Technique

Five patients of each type have been tested immediately after diagnosis and before any treatment. They drank 50 g. of glucose instead of breakfast, and two hours later venous blood was collected in a heparinized

syringe and immediately centrifuged, and 1 ml. of plasma was injected into each of six alloxan-diabetic, hypophysectomized, and adrenalectomized rats. The fall in the true blood glucose of the rats one hour after plasma injection was determined.

The results are read from a standardization curve previously obtained from the same rats with re-crystallized Novo insulin. The method proved sensitive from 1/20,000 to 1/2,000 of a unit of insulin (0.05 to 0.5 milli-unit), according to the formula $E = 67.48 + 41.85 X$, where X is the $\log_{10}$ of the dose in milli-units/100 g. rat. The results are expressed briefly in the Table.

Group 1: Severe, with Ketosis

Patient:	1	2	3	4	5
Sex and age ..	M 32	F 52	F 9	M 28	M 42
Weight (kg.) ..	46	56	25	41	54
Blood sugar mg./100 ml.	431	382	406	268	318
Glycosuria ..	++++	++++	++++	++++	++++
Ketoneuria ..	++++	+	++++	+	++
Mean change in blood sugar ..	+1	-3	-3	0	-2
Standard deviation	±6	±9	±7	±6	±7
Plasma insulin milli-units/ml.	0	0	0	0	0

0 = below lower limit of the assay.

Group 2: Obese, no Ketosis

Patient:	6	7	8	9	10
Sex and age ..	F 35	F 47	F 53	F 46	M 57
Weight (kg.) ..	79	69	75	85	83
Blood sugar mg./100 ml.	292	381	312	311	232
Glycosuria ..	++++	++++	++++	++++	++++
Ketoneuria ..	0	0	0	0	0
Mean change in blood sugar ..	-28	-30	-22	-25	-23
Standard deviation	±19	±9	±6	±8	±8
Plasma insulin milli-units/ml.	0.26	0.29	0.19	0.24	0.20

It seems clear from these results that available plasma insulin is absent and present respectively in these two different types of diabetes. The difference might be due to grades of severity of the same process, but this seems unlikely in view of the widely differing clinical picture. Further tests may show an intermediate content of plasma insulin, but it is to be noted that in the previous series reported no intermediate types were found. The technique opens wide possibilities for research into the nature and aetiology of "diabetes."

We are indebted to Dr. Hallas Mölder, of the Novo Therapeutic Laboratories of Denmark, for crystalline insulin free from the glycogenolytic factor and to Messrs. Boots Pure Drug Company, Ltd., for their research grant for expenses.

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Ethylene oxide is being increasingly used commercially as a fumigant, and a recent Home Office pamphlet (*Fumigation with Ethylene Oxide: Precautionary Measures*, H.M.S.O., February, 1951, price 6d.) outlines the risk of explosion and of poisoning by this not unpleasantly smelling gas. A method of detecting low concentrations of the gas is described, and the wearing of respirators by operators working in pairs is essential during the airing period. First aid consists principally in removal to the open air, artificial respiration, and administration of oxygen.

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