ERUPTIONS FROM BROMIDES AND IODIDES.

*A Portion of a Lecture on "Drug Eruptions."*By H. RADCLIFFE CROCKER, M.D., F.R.C.P.,
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[WITH COLOURED PLATE.]

It is an unfortunate circumstance sometimes attending our therapeutic efforts to alleviate or cure disease that by the action of the drugs we employ we may unwittingly produce disorders of various organs which may lead to consequences as serious as the original disease itself, and, if the drug be persisted in, may even have a fatal result. The skin lesions thus produced are not the least important of such disorders, and are included under "drug eruptions," or the more high-sounding title of "dermatitis medicamentosa."

Even when the eruptions are not dangerous in themselves their diagnosis is often highly important, as they may simulate serious diseases, such as measles, scarlatina, or rōtheln, and, more rarely, variola, vaccinia, and syphilis, as well as many skin eruptions which are usually due to other causes.

A large number of drugs may produce an eruption after their ingestion. Nevertheless, drug eruptions are decidedly uncommon. In nearly all cases there is either an idiosyncrasy on the part of the patient or there is renal or cardiac disease present, which interferes with elimination, or the dose is large, the medicine long continued, or there is a combination of these factors.

In some persons a very small dose of certain drugs—for example, quinine—will invariably produce an eruption, and if the dose be increased or the medicine continued, the extent and form of the rash may be much aggravated, a partial erythema becoming general or changing into a vesicular eruption, or a vesicular rash may become bullous or pustular. Various forms of eruption may be excited by drugs, but only the pigmentation produced by arsenic or nitrate of silver, and the eruptions excited by bromine and iodine and their respective salts, produce a distinctive form of eruption; all the rest belong to recognised types, and the diagnosis can in these only be made by a knowledge of the circumstances under which the rash appeared.

The forms of eruption produced by drugs are for the most part erythematous, urticarial, vesicular, bullous, or pustular; less common are purpuric, gangrenous, and pigment lesions, and there are a few other rare or doubtful eruptions which I will not confuse the subject by enumerating. Of all these, some sort of erythema is by far the most common. Thus, out of twenty-eight rash-producing drugs, twenty-three excite some form of erythema; and of the other five, two produce urticaria and three vesicular or bullous eruptions. The most usual kinds of erythema are scarlatiniform, morbilliform, and diffuse or patchy redness, but other varieties may be seen. The mode in which these exanthematous rashes are produced is open to discussion, but the probabilities are in favour of a vasomotor neurosis, the drug acting directly, for example, on the vasomotor centre, as in atropine, or indirectly by reflex irritation of the gastro-intestinal mucous membrane, as in nearly all the rest, for with the exception of belladonna, iodoform, and mercury, these eruptions are only produced when the drug is given by the mouth. The bromide and iodide eruptions are due to a more special and direct action probably on the vascular walls, and to these drugs we will give our chief attention.

BROMIDE ERUPTIONS.

These may be erythematous, urticarial, squamous, bullous, or pustular. The first three have nothing distinctive about them, and are pathogenetically on the same footing as similar eruptions produced by other drugs. The conglomerate bullous and pustular eruptions are the only characteristic lesions, and are readily distinguishable as a rule from all other forms of dermatitis except the almost identical eruptions produced by iodine and its salts. The bullous form of eruption is very rare from bromide of potassium, and I shall therefore reserve it until we are discussing eruptions from iodides, in which it is more often seen.

Among pustular lesions from bromides only the conglomerate form is distinctive. Isolated pustules are quite common

in those taking bromides, and are usually referred to as a form of acne—bromide acne as it is called. Individually, the pustules look like acne vulgaris, but usually the lesions are softer and larger than most acne pustules, have no antecedent comedones, and no special distribution. They are generally of rapid and almost painless evolution, occur chiefly in epileptics, have no necessary connection with the age of the patient, and, from all these circumstances, the causation may generally be inferred. The conglomerate or confluent form is much less common, much more important, and often produces a very formidable eruption.

Let us briefly consider some cases, taking first one, which although well developed, is not a very extreme instance.

The drawing (Figs. 1 and 2) was taken from a child, A.F., 1½ year old, admitted into the East London Hospital for Children under my friend and former colleague, Dr. Coutts, who kindly allowed me to have this drawing made. Five weeks before admission the child was treated for bronchitis. Two days later an eruption appeared over the lower part of the legs, "like small blisters, which soon got larger and ran together" and a weak large swelling had developed. The child was soon after taken to another doctor but the rash continued to be evolved and a third was called in, but the rash still increased. What the medicines were could not be ascertained. Vomiting after food was the only symptom. Besides the lesions depicted, there was abundant eruption on the front of the legs, but elsewhere there were only a few other lesions on the abdomen, face, scalp, and right arm. There was no pain or itching. No medicine was given for a week and no fresh lesions appeared, but there was a little more ulceration. Liq. arsenicalis was given, first in 1-minim doses and subsequently 4-minim doses three times a day, and in a week there was marked improvement in the rash, but the child was unwell, with a rise of temperature, and soon meningitis developed and death occurred in ten days. Most of the eruption by this time was almost well. Although the administration of bromide of potassium could not be proved from the history, there was not the least doubt about the diagnosis and the ready response to arsenic was confirmatory evidence.

The next drawing I show you is that of a boy aged 7 months. It is an extreme instance, owing to the drug having been continued for three months. The first appearance of the rash was interesting, as the doctor in attendance thought it was chicken-pox, and the lesions became purulent next day. The lesion near the ankle is to be specially noticed, as it is so like a papillomatous growth. The rest of the lesions individually correspond with the previous description, but the whole is so closely aggregated that, on the scalp, it forms a crusted, closely-fitting cap, while the number of lesions on the face is only moderate.

[Drawings and plates of other cases, which all presented similar characters, and only varied in extent and degree of development, were also exhibited. All were from infants and very young children.]

Though the eruption may occasionally be seen in adults, it is much rarer in them than in children.

Let us take a single typical lesion and examine it, and we shall find that it is a raised bright-red vascular plateau, soft to the touch, on which there is a close aggregation of pin's-head sized pustular points; the whole lesion varies from a threepenny piece to a shilling in area, but is sometimes larger from aggregation. This description perhaps suggests a carbuncle, but there is little or no pain during or after involution; the colour is a bright, not a livid red; the base is soft instead of brawny to the touch; there is no induration beyond the sharply-defined border; no central slough or oozing of pus, but the latter dries up into an irregular sulcated scab of a yellowish-brown or greenish-black colour. The number and aggregation of the lesions and the absence of constitutional disturbance are important criteria. Another peculiarity is the selective affinity for scar tissue. This of itself shows that the glands of the skin are not the seat of the lesion, and when, as I have witnessed more than once, the vaccination scars are the site of the eruption, it may in a young child lead to the erroneous idea that it is due to faulty vaccination. I have also seen it on the site of the scar of a burn, and in that of a strumous ulcer of the leg.

Formidable as these lesions appear, they seldom leave

TO ILLUSTRATE DR. RADCLIFFE CROCKER'S CLINICAL LECTURE ON ERUPTIONS FROM
BROMIDES AND IODIDES.

Fig. 1.—Bromide eruption; case of A. F.

Fig. 2.—Bromide eruption; case of A. F.

Fig. 3.—Bullous iodide eruption in a man with albuminuria.

scars, being situated almost entirely in the papillary layer, and beyond transitory staining involution is usually thorough and complete. In the most highly developed lesions a pseudo-papillary formation occurs, and one of the first cases of bromide rash on record is reported by Beigel as a case of papilloma of the skin.

IODIDE ERUPTIONS.

The first case to which I will call attention is a fine illustration of what is generally called the bullous iodide eruption, but this is not quite correct, as I shall presently show. The patient was a man aged 30, a painter, under my colleague Dr. Frederick Roberts, and I was asked to see him for the diagnosis of the eruption which had appeared on the face and neck three days previously, and had developed into the condition well depicted in the drawing (see Fig. 3). Recognising that the eruption was due to iodide of potassium, I inquired for kidney or heart disease, which might interfere with elimination, and I was informed that the man had albuminuria, probably from the large white kidney, and that he had taken 5 grains of iodide of potassium three times a day for four days, and that the eruption had begun to appear a few hours after the first dose. As usual, in spite of their bullous appearance, on pricking one of the lesions only a small drop of clear fluid exuded, the pseudo-bullæ being, in fact, solid. The discrete bullæ were distinctly raised about one-eighth of an inch, were flatly convex, of pearly translucent appearance, with a narrow red areola. Many were confluent into large plateaux of several square inches in area, but the component elements of the patch were still discernible. The man good-naturedly allowed me to remove a medium and a small vesicle which were close together; and I am therefore able to show a section under the microscope in which the solid nature of the lesion is evident. It is due to a copious cell exudation pushing up the epidermis as a whole. It has been a disputed point as to whether lesions were seated at a hair follicle or not. This specimen shows clearly enough that it may be round a hair follicle, but that they are not essential to the process is proved by their occurrence in scar tissue, where there are no hair follicles or glands, just as we have seen that bromides have a special predilection for cicatrices.

[Drawings of other iodide eruptions were shown. In one there was very extensive scarring and fungation of the sores in a man with mitral regurgitation. The drug had been given perseveringly on the supposition that the lesions were syphilitic. The photograph of another case was shown in which the lesions were solid nodules of the same colour as the surrounding skin.]

In this case (Dr. Crocker continued) I made the diagnosis from the description and the photograph, as I never saw the patient, and in the face of apparent proof that he had had no iodide of potassium. On cross-examination, at my suggestion, it was clearly brought out that the eruption appeared after taking a quack medicine called "Clarke's Blood Mixture." The man was a chronic drinker, had jaundice and other symptoms of hepatic disease, but there was no albuminuria. He was also very sensitive to arsenic, showing symptoms of arsenical intoxication after a few 2-minim doses—all being evidence of his defective power of elimination.

DIFFERENTIAL DIAGNOSIS.

On comparing bromide and iodide eruptions we find great resemblances, but also a few differences which enable us often, but not always, to distinguish the one from the other. The compound bromide eruptions are, as a rule, more pustular than those from iodides. The latter are, as a rule, bullous or pseudo-bullous, which is a rare form of eruption from bromide of potassium. On the other hand, I have never seen in iodide eruptions the aggregation of small pustules on a raised inflammatory base which is typical of bromide rashes.

Bromide eruptions are most common in children, those from iodides in adults, but this is probably largely because children seldom have iodide of potassium given them, and except to epileptics, bromide is not often given for any long period to adults, while iodides are very frequently given to adults for many conditions. Nevertheless, there is over

and above this a special susceptibility in infants to bromine in all forms, and even such small quantities as could be derived from the mother's milk when she was taking the drug have produced the eruption in the suckling infant. There is no doubt, however, that iodide eruptions are the most serious in persons with defective elimination, as several fatal cases testify.

TREATMENT.

Treatment of these cases, both from bromides and iodides, is simple. Of course the drug must be stopped; but the eruption, it must be borne in mind, may continue to come out for some eight or ten days after the cessation of the exciting cause. If the patient is old enough, copious diluent drinks should be given to promote diuresis. Liquor arsenicalis in 3 to 5 minim doses three times a day should be given internally, and simple antiseptics, such as boric acid ointment, may be applied externally if there is any denuded surface requiring protection. Under this kind of treatment the lesions dry up, shrink, and involute, so that when the scab falls off nothing but a reddened surface marks the site of the lesion. Occasionally a few hypertrophied papillæ require to be snipped off. Much, however, may be done in the prophylaxis of these eruptions.

Do not give iodides to people with chronic renal or heart disease. Where, as in epileptics, bromides have to be taken for long periods, it is often possible to omit the bromides for one, or even two, days a week without losing control over the fits. Arsenic, too, has a prophylactic as well as curative effect for both bromide and iodide eruptions, and 2 or 3 minims of Fowler's solution may be combined with the bromides, but this, too, should not be given for long periods continuously, or arsenical pigmentation and keratosis may be produced in a high degree.

Another plan is said by M. Féré to be prophylactically successful—namely, to produce intestinal antisepsis by means of naphthalin internally, or, as I prefer, by salol gr. v three times a day. This method requires further trial, but I commend it to the attention of those who have to treat chronic epileptics.

THOMAS'S OPERATION FOR BENIGN TUMOURS OF THE FEMALE BREAST.

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IN the BRITISH MEDICAL JOURNAL for 1888 (vol. i, p. 1216) I published a case of this operation, illustrated by a woodcut from a photograph, which showed that a tumour as large as a Tangerine orange may be removed from the shapely breast of a young woman without a trace of mutilation and with hardly a trace of interference. Such a result is so desirable from the cosmetic point of view, while the risk of breast tumours, benign at their origin, assuming disorderly action and becoming malignant or semi-malignant is so great, that it is a matter of surprise to me that the procedure with which, in 1882, Gaillard Thomas enriched surgery has not received more attention than has actually been accorded to it.

Mr. Bryant¹ alludes to it without comment; Dr. Hayward,² of Liverpool, reports a successful case. I have referred to four cases and published one in full, and now offer another. I have not found any other reference to the operation in European or American professional literature, though of course I do not pretend that my search has been exhaustive. This paucity of published instances is no doubt largely due to the comparative rarity of the cases to which the operation is suitable. But that the method is of great value is undeniable, inasmuch as it induces patients to consent to operation at a period when their disease is manageable, and thus saves them from the worse than doubtful chances of their future. In none of my cases could I have obtained consent to operation, once the growth was declared non-malignant, had I not been able to promise recovery without deformity. Accordingly I venture to make a second claim on the already

¹ *The Diseases of the Breast*, p. 107.

² BRITISH MEDICAL JOURNAL, 1889, vol. i, p. 410.