seen recently an example, there being at first intense putrefactive fever, easily subdued, in a case which ended with characteristic *post mortem* evidence of pyæmia.

It is a neglect of the distinction I have just drawn, and of the peculiar anatomical conditions of lying-in women, that has led Fritsch* to the unnecessary ingenuity of appealing to a *status puerperalis* of the female constitution as the explanation of the special liability of lying-in women to septicæmia from putridity.

It is easily comprehended, then, that treatment in ordinary septicæmia is in a very different and greatly less satisfactory position than the treatment of septicæmia from putrefaction and the prophylaxis of septicæmia of all kinds. Local antiseptic treatment after ordinary septicæmia is begun is something like locking the door after the horse is stolen. Yet, even though late, locking the door may be of some use, preventing the admission of more injurious germs. I fear, however, that the theory of septic fermentation in the blood, as distinguished from the mere conveyance of putrid ichor into it from without, a theory universally adopted for this form of disease, does not allow us to attach paramount importance to the quantity of germs admitted. A little leaven soon leavens the whole lump.

We have no fine theoretical basis for antiseptic treatment of ordinary septicæmia, and we have no delightful facts or other testimony to appeal to in evidence of its utility; while there is a great amount of such evidence in favour of the treatment of septicæmia from putrefaction and in favour of the prophylaxis of all forms of the disease.

Yet there can scarcely be a doubt that hope for the future does meantime rest on the study of this matter; for, striking at the sepsis, we believe we are striking at the root of the disease. Many treatments of puerperal fever are directed against symptoms. Some attack the rate of the pulse, some its weakness, some the temperature, and so on; and of the utility of such treatments I desire here to say nothing. Antiseptics are directed against the essence of the malady. Just as benefit has been supposed to arise from improving the conditions or symptoms referred to, so benefit from local antiseptic treatment is alleged—Fritsch describing a lowering of the temperature as produced by antiseptic intra-uterine lotions; but the value of the observation is lost, from the author not having distinguished between the two forms of septicæmia that prevail.

It is natural, and I believe proper, to imitate surgeons in cleansing and dressing a wound even when septicæmia is present. Such care consists in the use of drainage and in antiseptic cleanliness; and I do not hesitate to secure the evacuation of the uterus when lochia are retained, and to use antiseptic cares if there be any discoverable occasion for them. In most cases of ordinary septicæmia, no such treatment is called for, the lochia being not retained, and the discharges being healthy.

There is one important department of antiseptic midwifery that must not be passed over, although it is second in importance to what we have been considering. It is the antiseptic management of the child, and for it the same prophylactic and therapeutical antiseptic cares are as valuable as for the mother. The subject is in all, except its practical aspects, one that has been long fully recognised, and in this place I shall do little more than mention it. The child is liable to infection through its umbilical ulceration and vessels. Here it may imbibe poison from a putrid cord, or it may receive ordinary septicæmic infection. The child is believed also to be liable to be infected through inspiration of foul or poisonous matter more or less deeply into the respiratory tract. It appears that the delicate organism of the infant is easier poisoned than its mother's, and the poison affects its system differently. Besides producing inflammation and other ordinary septicæmic and pyæmic changes, it may produce in the child inward fits, trismus, and nervous conditions that are not observed in the mother. The same prophylaxis and treatment that are useful for the mother are equally useful for the child, when varied so as to suit its peculiar circumstances.

There are in this paper many imperfections arising from its authorship, for which I can only plead, in palliation, the haste with which I have prepared it. Such imperfections are of little moment to any one but myself. The great imperfections arise from the incompleteness of our knowledge; and I shall be amply rewarded for the trouble I have taken if I have contributed to the diffusion of sound views or stimulated any of my professional brethren to further investigation.

* Volkmann's *Sammlung*, No. 107, s. 789.

LECTURE

ON

THE VARIOUS FORMS OF SKIN-IRRITATION DUE TO THE ADMINISTRATION OF DRUGS.

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(Concluded from page 224 of last number.)

PASSING now to the various eruptions produced by the internal administration of drugs, I shall first lay down, so far as I can, one or two headings of causation, and then run over each substance which has the property of causing any marked cutaneous manifestation. And first, we are naturally led up to the recollection, that a part of the poisonous action of several agents expends itself on the skin, and that, again, something of this nature may also be observed as a regular sequence of their minor physiological effects, when pushed up to a certain point.

Secondly, some rashes are due to irritation of certain structures, like the sebaceous glands, through which a particular drug is normally eliminated in part; and others are distinctly of the nature of nettle-rash, depending on stomach-irritation; or the blood-corpuscles may be disorganised or broken up, and we may have purpura. Defects of elimination may account for a good deal, and it is quite reasonable to hold that, if the principal means of exit for any particular drug are blocked up, we are liable to meet with unexpected excess or irregularity of physiological action. Thus, we find kidney-disease in many of the recorded cases of bromide-rash; and Brunton and Power (*vide* Brunton's *Goulstonian Lectures—BRITISH MEDICAL JOURNAL*, 1877) have experimentally shown that, if digitalis be given until the renal arteries are powerfully contracted, its elimination is checked, and poisonous symptoms may suddenly arise, or, on the contrary, elimination may be too swift to allow the drug time enough to act, and this specially occurs in the case of curare, which is thrown out of the blood so rapidly by the kidneys, that administration by the mouth produces none of those toxic effects which are so well marked when hypodermic infection is employed.

This question of the integrity of the eliminating organs in connection with therapeutics is of vast importance; and, although it has received the attention of Gubler and other eminent men, I recommend it to your attention as a good field for future investigation, counselling you, meanwhile, to consult an interesting paper by Duckworth "On the Passage of certain Substances into the Urine in Healthy and Diseased States of the Kidney", in the third volume of *St. Bartholomew's Hospital Reports*.

Finally, we have a class of cases which cannot be explained at all, and which we say are due to idiosyncrasy; and of this we have a good example when we find that a simple small dose of an usually harmless drug brings out the irritable rash. With these principles to guide us, then, let us approach the various substances in succession, beginning with arsenic, which, in poisonous doses, causes cutaneous irritation, with an eczematous eruption. Herpes has also been observed during its ordinary medicinal administration; and as it is partly eliminated by the skin, it stimulates that structure, and has a powerful influence over some of its more chronic affections, very injuriously irritating the more acute disorders of an inflammatory nature.

Phosphorus, also, is a cutaneous stimulant, and has been recommended for the purpose of encouraging the insufficiently developed, or prematurely faded, rash of the eruptive fevers; but the only skin affection for which it is primarily responsible seems to be purpura, which occasionally coincides with gastro-intestinal derangement and jaundice, in preceding the fatal issue of a poisonous dose.

We next come to iodide and bromide of potassium, which produce definite, but, luckily, comparatively rare, skin-eruptions, which have recently been much discussed. The limited time at my disposal will not allow me to do more than give a very terse *résumé* of the work of many industrious authors; but those who wish to pursue the subject further may profitably consult Wood and Ringer, but more especially Tilbury Fox, who, in his paper before the Clinical Society, gives very exhaustive references to the opinions of our best authorities on the iodide of potassium rash. This, in its most common form, appears as papules, quickly becoming pustular, and bearing a strong superficial resemblance to acne, which, indeed, it is usually held to be. Dr.

Duckworth lately showed an excellent example before the Clinical Society, in the person of a man with cardiac and renal disease, who, after taking thirty-six two-grain doses of the salt, was affected with an eruption, principally developed on the face, beginning as papules, which, running through a vesicular state, eventually became hard shotty pustules, strongly suggestive of variola. That these were not true acne was proved by the fact of their appearance on a patch of cicatricial tissue, where no sebaceous glands can, of course, exist.

Dr. Tilbury Fox points out how matters may go far beyond this; that the papules may develop into ecthyma, or into bullæ, which, occasionally bursting, may form fungoid masses, from the size of a pea to that of a shilling; and this he considers due to excessive stimulation of the sebaceous glands, looking upon this class of cases as essentially distinct from hydroa, that formidable eruption which Mr. Jonathan Hutchinson tells us is often, if not always, the result of the administration of iodide of potassium. But the most important contribution to this subject is undoubtedly that of Dr. Thin (Royal Medical and Chirurgical Society, November 1878), who examined the skin of a patient who chanced to die whilst covered with the bullous rash described by Fox and others. The sebaceous glands were found to be quite unaffected, the main pathological condition being the blocking of the vessels at certain points leading to rupture, and the formation in varying degree of the various local lesions. But whether true acne is really never produced by iodide of potassium must, I think, still be considered as *sub judice*.

Bumstead has described a pemphigus due to the drug; but these formidable results fortunately are not common, and the little rounded military petechial spots seen below the knee, and principally noticed by Ringer and Fournier, are also rare, although I have myself met with them on several occasions. Bromide of potassium, on the other hand, much more frequently causes skin-irritation, and the resulting acne is very commonly met with in epileptics who have taken the drug for long periods. Some persons, however, are very intolerant even of small doses, and I know one lady who cannot even take ten grains without the appearance on the forehead of dull reddish points, up to which dilated vessels are seen to run, and on which papular and pustular elevations are later observed, if the drug be not withdrawn. We are told that the simultaneous administration of arsenic will obviate all this, but I fear that idiosyncrasy will override all preventive means; and we must remember not only the frequent appearance of acne, but the fact that the comparatively trifling pustules have been known to develop into boils, followed by rupial ulcers.

Children over the age of one year bear bromide of potassium remarkably well; but below this they seem to be specially susceptible; and two cases in particular have been published, in which infants of eight or nine months were attacked, in both instances, with curious aggregations of acne pustules, causing much discomfort and disfigurement, and occurring, strange to say, several days after the drug had been entirely left off.

Defects of elimination, no doubt, must be held responsible for some part at least of these and other untoward results; and this view is borne out by the fact that, in many of the recorded cases of iodide and bromide rash, and more especially of the latter, albumen was detected in the urine. These drugs, as you know, are principally eliminated by the kidneys, and when their functions are partly suspended, the stress is naturally greater on other organs, such as the sebaceous glands, which also have a share, if only a small one, in casting these very diffusible substances out of the body. And I would suggest that this is also borne out by the common observation, that small doses of both, and notably of the iodide, are much more apt to produce iodism and bromism than large, the larger quantity, in all probability, exercising a more stimulating influence on the kidneys than the smaller; in other words, acting as a diuretic.

We next come to nitrate of silver, which, as you know, produces an indelible dull leaden colour, fortunately but seldom observed in these days, when we know that the therapeutical advantages of the drug in no degree balance its possible risks. The only case which I have myself had an opportunity of examining is that of an elderly man, who occasionally presents himself in the out-patient department of St. Mary's Hospital, seeking relief for a winter cough. Years ago, he was a martyr to gastralgia of so severe and intractable a kind that, although warned of the dangers of the nitrate of silver plan of treatment, he preferred to run the risk rather than go on in his misery. A three-months' course effectually and permanently removed his pain, and he is well pleased with the result, although his skin is most effectually discoloured, those parts exposed to the light suffering most, and the conjunctivæ, gums, and all visible mucous membranes, sharing in the general staining.

Mercury, when pushed up to poisonous limits, brings out an ecze-

matous eruption on the skin; but this is generally an advanced symptom, coinciding with the marasmus and tremors and general nervous prostration which a reckless use of the mineral rendered not unfamiliar to our forefathers, but which, I hope, will always remain a matter of history to you.

The hydrate of chloral is so useful a drug, that we are almost inclined to wonder how we got on without it, before the genius of Liebreich added this to our list of narcotics. The literature of the subject has now reached very formidable proportions, and the monotony of constant success is varied by the occurrence of numerous uncomfortable accidents, many of which are no doubt due to impure preparations of the drug (see Oscar Liebreich, *Lancet*, July 20th, 1878). We can only concern ourselves at present with the cutaneous manifestations of idiosyncrasy, most of our knowledge being contributed by Schüle, Crichton Browne, Cholmeley, and Ludwig Kirn, whose exhaustive paper, translated by the late Dr. Anstie for the tenth volume of the *Practitioner*, gives an admirable summary of most of the available evidence on the subject. Firstly, then, Schüle and Crichton Browne have independently described a chloral erythema, occurring at first in spots, but afterwards more diffusely; earliest manifested on the head, but generally spreading over the body, and following by preference the course of the greater nerve tracks. Crichton Browne seems to have been the first to point out a very curious intolerance to alcohol in persons under the influence of chloral, a single glass of beer being sufficient to cause intense congestion of the face and head, with excitement of the muscular system, and conjunctival injection, due, he believes, to temporary paralysis of local vaso-motor centres.

The same author records two very formidable cases of a kind of scurvy, beginning as purple-red spots, coalescing and extending over the body, eventually becoming petechial, attended by ulceration of the lips and gums, with great depression, and followed in one instance by a fatal result. In the first case, which recovered, the woman, aged sixty-nine, took twenty grains of chloral thrice daily for four days before the rash appeared, whilst in the second, nineteen days' treatment by fifteen-grain doses were necessary to initiate the symptoms, which ended in death.

Eruptions like scarlet fever have also been described, and a rash resembling slight variola, with hæmorrhagic purpura, caused death after four days' administration of chloral; but the most obstinate case of all is that recorded by Kirn himself, where the drug produced violent fever, followed by oedematous swellings, and a combination, or rather succession, of impetigo, eczema, and ichthyosis, followed by very free desquamation and pyæmic symptoms, from which the patient with difficulty recovered. These instances of chronic blood-poisoning fortunately are rare; and luckily so, because their frequent occurrence would rather induce us to persuade our patients to abandon chloral altogether, and "rather bear the ills they have than fly to others that they know not of". Practically, I think, however, that you are not likely to meet with any chloral rashes in the course of your future routine of work, beyond some scattered petechiæ, which will do good service as the shadows of the events which may be expected to come, if you continue under these circumstances the use of the drug.

Coming next to the medicinal substances of the vegetable kingdom, we find that the diaphoretic action of aconite is occasionally attended by an irritable vesicular eruption, and that the itching of skin not very uncommonly complained of after the use of morphia, may sometimes be shown to depend on a minute papular or vesicular rash.

Copaiba, in addition to its excessively nauseous taste, often produces a sort of urticaria, beginning usually on the hands, in the form of bright red discrete stains, gradually spreading over the body, causing much itching and tingling, sometimes rising to a suspicion of measles, from which, however, it really has many points of distinction, being more vivid in hue, less raised from the surface, and unaccompanied by lacrymative or bronchial catarrh.

Cubebs has been observed, but much more rarely, to cause the same symptoms.

Urticaria has also been shown by Dr. Sieveking to be occasionally produced by santalin.

Some attention having been recently directed to the eruptions following the administration of quinine, I have carefully looked up the literature of the subject, and find that, although this all-important drug has been in universal use since its discovery in 1820, our knowledge of the effects occasionally following its use dates from little more than eight years ago. The cases are not numerous, and have been so assiduously collected by one or two industrious authors, that we may give a confident opinion concerning their rarity. Dr. Walter G. Smith, in the *Dublin Medical Journal* for 1870, 1871, and 1877, quotes nine from all sources, and supplies one of his own in the *BRITISH MEDICAL JOURNAL*, July 9th, 1878. I have reported one to the Clinical Society; the

Lancet for November 30th, 1878, contains two; Dr. Lent, in the *Medical Record* mentions three in his own practice, and in that of Professor Koebner of Breslau. MM. Bergeron and Proust have also observed one or two; and in the discussion following the reading of my case, Dr. Nott of Ohio stated that he was quite familiar with these eruptions whilst practising in the malarious regions of Georgia.

This is but a small outcome of the fifty-eight years' administration of our most extensively employed drug; and it is fortunate that it is so, for these quinine eruptions are not only terrifying, but, from their suddenness, are so extremely irritating and uncomfortable, that their more frequent occurrence might seriously imperil the popularity of their exciting cause. They may be divided into two classes. The first are erythematous in character, attended by most distressing itching and tingling, and resembling scarlet fever, both in the appearance of the rash and in the free desquamation which follows. The second assumes a more measly aspect, being occasionally papular, but more generally suggestive of that form of urticaria which occurs not in wheals, but in discrete rose-red patches spreading universally over the skin, and occasionally attended with marked gastric disturbance. I show you a drawing of a case which, by the kindness of Dr. Cheadle, I was recently enabled to report to the Clinical Society, and which differs from others on record in the dose required to produce an abundant crop of thickly scattered pink stains. Here the patient, a lad aged twelve, had taken about ten-grain doses, but much more usually a small quantity is sufficient. Thus, in a case in the practice of Mr. Garraway, one grain produced a severe erythematous rash; Dr. Skinner twice produced a scarlatinoid eruption by one grain and a half; Lightfoot observed a similar accident half-an-hour after a grain and a half had been taken; Dr. W. Newman has even seen half-a-grain produce erysipelatous redness and oedema of the right side of the face, beginning half-an-hour after the dose had been swallowed and lasting twelve hours. It is curious to note that a large proportion of the victims of this idiosyncrasy have belonged to the female sex.

We do not hear so much about these effects in Germany, under the influence of the "massive" doses there prescribed to reduce the body-heat; and it may be that the drug, when thus taken wholesale, stimulates the emunctories, whereas the smaller quantity is longer retained, and has therefore more ample opportunity of producing its toxic effect. Quinine is well known to be very rapidly eliminated by the kidneys, so rapidly, indeed, that good continental authorities hold that, in order to produce its full antipyretic effect, we must get from forty to seventy grains into the system in divided doses, *coup sur coup*, within the first half-hour. It may be that the smaller dose is longer retained than the larger; but this is mere speculation, and the small number of cases at our disposal for analysis does not enable us to do more than summon the unsatisfactory explanation of idiosyncrasy once more to our aid.

Cinchona and the decoction of cinchona are also said occasionally to cause the same rash. Strychnia, in doses of twenty-four grains, has been stated by Skinner to have produced on one occasion a rash precisely similar to that which he has recorded in the case of quinine; and one marked result of the poisonous action of belladonna is a bright rash resembling scarlet fever. I may remind you that the professors of the now exploded faith of "*similia similibus*," used to lay great store by this apparent connection between the physiological action of the drug and the eruptive fever, using it as one of their favourite illustrations, until even the credulity of their followers perceived the total want of prophylactic or of curative influence of the drug over the disease. In smaller doses, and more especially in children, we not infrequently observe localised flushing about the head and face, whilst the same symptom has been noted during the administration of hyoscyamia.

Cod-liver oil occasionally causes acne, from the passage through the cutaneous glands of some of the acrid constituents which it contains. Salicylic acid, on at least one occasion, produced a peculiar bright punctate rash with erythematous patches eventually surmounted by vesicles, with sore-throat and constitutional disturbance strongly resembling scarlet fever.

I have thus placed before you, in as much completeness as my own information will permit, the various eruptions caused by, or at all events following, the administration of certain drugs. You will see that the range of variety is fairly great, and that papules, and pustules, and bullæ and vesicles, and rubeoloid, and erythematous blushes, and purpura are freely met with under a variety of conditions, which, unhappily, for the sake of our patients as well as for our own, we are as yet quite unable distinctly to formulate. But I think I am at least justified in saying this: that these local manifestations of idiosyncrasy are not mere accidents of stomach-derangement, but that they are sufficiently definite and consistent, within their own narrow limits, to be quite worth taking into account when we prescribe the medicines which seem to be their responsible cause. Perhaps some day, fuller

knowledge may enable us to lay down the laws on this subject which nature at present conceals from our dim vision; but, in the meantime, let us work on at the accumulation of facts, collecting materials for the master mind who will one day knit all the tangled threads into one harmonious whole. We, as practitioners, are bound to know all the irregular and abnormal effects of our remedial agents; and, whenever we find the sudden appearance of some skin-eruption which we cannot readily explain by the usual dermatological reasoning, or even when a more chronic affection is difficult to explain on other grounds, let us never forget carefully to inquire what medicines our patient has been taking. We may thus clear up many a difficult case; we may dispel doubt and apprehension; if we possibly suffer in credit at one time, we shall gain tenfold at others; and, above all, we will add to the general store of knowledge whilst largely supplementing our own.

REPORT ON THE ATTACK OF DIPHTHERIA IN THE GRAND DUCAL FAMILY OF HESSE-DARMSTADT.*

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V.—CONCLUSION.

THE fourth case made its appearance twenty-four hours after the beginning of the second.

Princess Irene, aged 12, fell ill in the night of the 12th and 13th of November. On the morning of the 13th, diphtheritic membranes, a *centimètre* in diameter, were already to be observed on both tonsils. The fever was then slight; but the temperature reached 103 deg. in the evening. On the 14th, at 8 A.M., the temperature was 99.9 deg.; at noon, it was 102.5 deg.; between 3 and 4 P.M., nearly 104 deg. A water-cushion filled with water at 59 deg. Fahr. was, therefore, employed. One hour later, the temperature had sunk to 102.2 deg. A further fall of the temperature was ascertained by measurements, which were repeated every three hours. On the morning of the 15th, at 8 A.M., 99.2 deg. were found, after which the employment of the water-cushion was discontinued. On this and on the next day, the temperature in the evening was 100.4 deg.

From the 17th, the normal height was not surpassed. The local process took a considerable extension in this patient. The diphtheritic membranes were not only propagated over the tonsils, but also continually extended downwards deeply behind the base of the tongue as well as towards the lateral walls of the pharynx; they covered both borders of the uvula and a great part of the soft palate. The deposits, which were at first of a greyish-white colour, soon became discoloured and ecchymotic, and regained their white colour only shortly before their expulsion. The uvula and the tonsils were very much swollen, and lymphatic tumours of considerable size were developed on both sides of the neck. On the 17th, the separation of the membranes began, and they were expelled partly in pieces two *centimètres* wide, partly in smaller threads. The process of separation was repeatedly retarded by the formation of new deposits, and lasted up to November 26th. Not rarely the separation of the membranes was accompanied by some hæmorrhage. There still remained for a considerable time ulcers, two or three *centimètres* in diameter, on the tonsils and on the palate, which healed but slowly.

The fifth case began on the same day as the fourth.

Prince Ernest, aged 13, fell ill on November 13th, at 5 P.M., with severe rigor and violent fever. Already, one hour later, *fator ex ore* was to be observed, and it became even stronger the next day. At 9 P.M., some very thin deposits, about four *millimètres* in diameter, were to be seen in different places on both tonsils, and there was some difficulty in deglutition. On the morning of the 14th, the temperature did not fall below 100.9 deg., and reached, at 2 P.M., 104 deg. Salicylate of soda and the water-cushion were, therefore, employed as antifebrile remedies. Nevertheless, the temperature had not gone down at 6.30 in the evening, and, one hour later, a decrease of only half a degree was to be observed.

As the temperature was still 102.2 deg. at 12.30 A.M., the water-cushion was again filled. After that, the measurements, which were repeated every second hour, showed a gradual decrease, until the temperature of the body had fallen to 100 deg. at 10 A.M. on the 15th, after which the cushion was removed. As, however, one hour later, there was a new rise to 100.7 deg. at noon, the cushion was again used. At 1 P.M., the temperature was 102.4 deg.; at 3.45, it was 102.1 deg.; at 5.45, it was 100.8 deg.; at 7.45, it was 100.6 deg. After this, the

* Concluded from page 188.