it should not be used, as otherwise severe gastro-intestinal irritation may be set up. It has happened more than once that a horse when being bled for the purpose of supplying serum has been sufficiently refractory to necessitate the administration of ether. Serum from such an animal retains the smell and taste of ether for many months, and has been known to produce violent vomiting. The serum should be administered for at least a month in all ulcer cases, except the mildest, and then gradually discontinued. If given in the way directed, immediate symptoms of serum disease are of very rare occurrence. Personally I have never seen them. It has, however, happened in 5 cases that I have knowledge of that signs of hypersensitization have appeared, in 4 of which they were ephemeral and of little consequence. The symptoms were those of mild purpura and of eczema. Serum of the sheep gives as good results as horse serum. Human serum can also be used with proper precautions, but its chief use is in serious cases of hæmorrhage. Antilytic serum, which was prepared for me by Messrs. Allen and Hanbury two years ago, can be used in the same way, by oral administration, or as normal horse serum; and, in virtue of its increased antitryptic strength, is of great value. It is, of course, normal serum artificially treated. Unfortunately, it has not proved possible to increase materially the antiferment values of the serum of the horse by injection of the appropriate ferment.

GROUP II.

Chronic cases exhibiting acute exacerbations, or acute cases with initial severe hæmorrhage.

The treatment of this group of cases is primarily that of severe hæmorrhage.

Immediate and absolute rest is, of course, essential. If the bleeding still continues, or recurs to an alarming extent, good results are sometimes obtained by promoting cerebral anaemia by raising the head. This failing to arrest the bleeding in really urgent cases, the rapid but careful passing of a well-oiled tube just past the cardiac orifice with a funnel attached to the distal end, followed by the injection of a few ounces of iced water, is said to be sometimes followed by gratifying results. In all cases showing great disquiet a preliminary hypodermic injection of morphine and atropine is useful. Atropine alone in full hypodermic dose I have more than once found successful when everything else had failed. Ergot by mouth or skin, or adrenalin solution is of no value; calcium salts of less. Amyl nitrite inhalations are sometimes of slight service. Ice-bags on the epigastrium give occupation to the patient's friends, but they do not help the patient, may even greatly increase the pain, and certainly aggravate stasis of the gastric contents. Injections of gelatine may be followed by cessation of bleeding, but are subsequently painful and are not free from risk. Food by the mouth is as a rule out of the question so long as hæmorrhage is severe; food by the bowel except for a day or two gives a feeling of false security, and is synonymous with starvation, even if given in large quantities. The injection, repeated if necessary two or three times, at intervals of three hours into a vein, or under the skin of the flank or axilla, of normal horse serum, guaranteed as fit for injection, is of the utmost value. Sometimes it fails. Injections may have to be repeated once or twice for a day or two after the initial day of hæmorrhage. As soon as twenty-four hours have elapsed after the bleeding has ceased to be alarming, food by the mouth should be carefully begun. As quickly as possible the way should be then very cautiously felt till the case has been transferred into Group I, when the full treatment suitable thereto is adopted and maintained. Cases that have begun in Group I and have been successfully transferred to Group II naturally require very careful watching, but it is surprising how quickly the severest hæmorrhagic cases respond to generous feeding on the lines laid down. The diet suitable for cases whilst still in Group I, when the worst hæmorrhage is over, may roughly be outlined as follows, special care being taken to avoid milk and soups:

First Twenty-four Hours.—Every three hours during the day 2 or 3 drachms of freshly made chicken jelly alternating with half the yolk of a lightly boiled egg can be given. Occasionally the jelly increases the pain, in which case half an ounce of fresh raw beef-juice, double the ordinary strength, can be given. Cold water in 1-oz. doses may be given to allay thirst.

Second Twenty-four Hours.—Three or four drachms of pounded chicken may be given after boiling and rubbing through a hair

sieve, alternating with raw beef-juice and the whole yolk of a lightly boiled egg, intervals of two and a half hours separating the meals. During the night the interval may be increased to four hours.

Third Twenty-four Hours.—Pounded chicken, pounded meat, and the yolks of eggs can now be given every three hours in rotation, in rather larger quantities. Hot water is now useful in 5 oz. doses if slowly sipped, and if not given within an hour of a meal.

The subsequent dietary must be graduated according to the presence or absence of indications of recurrence of hæmorrhage. If this has quite ceased, rapid progress can be made. If it still continues, a day or two longer should be spent in very careful dieting, repeating once, or more often if necessary, injections into the stomach of iced water. During the days or hours in which at any time hæmorrhage is a cause of anxiety, free purgation with suitable salts is often necessary and always useful.

Such in sketchiest outline are the views that guide my own practice in the treatment of gastric and duodenal ulcer. If I have taken advantage of the opportunity offered by this lecture of presenting a somewhat unorthodox way of looking at these distressing complaints, I have done so in the hope that you will test for yourselves the truth of the principles involved. In conclusion, let me repeat that this serum and dry protein treatment lays no claim to being more than a stepping-stone to the final attainment of a truly specific treatment of the dyscrasia of which ulceration and hæmorrhage are but the local signals. In the meanwhile it is sufficient to accentuate the urgent necessity of fresh efforts to determine the essential meaning of the dyscrasia itself, about which we at present know absolutely nothing, and to remember that it is only in prevention of recurrence that the real merit of any form of treatment of these conditions lies.

AN UNUSUAL CASE OF TOXIC DERMATITIS; WITH REMARKS ON SYMMETRICAL ERUPTIONS.

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THE following details of an unusual case observed by the late Dr. Radcliffe Crocker and myself are worth placing on record:

The patient, a woman aged 54, was first seen by the late Dr. Radcliffe Crocker in January, 1908. The notes he made at that time were as follows (Q. 232): Duration one month. Commenced with redness and swelling of the back of the neck, which soon became worse and extended to other parts of the body. Large patches over shoulders, elbows, back, buttocks, back of thighs, and to some extent on lower limbs. The appearances were as if the epidermis had been raised up by an effusion of fluid, which had subsequently been absorbed, leaving black or otherwise discoloured epidermis still adherent. There was also swelling of left arm. The patches appeared at successive outbreaks, and not all at once, accompanied by much itching and burning. The temperature had been a little over 99° at times. Bowels kept open by aperients. Tongue was very furred.

There was a history of having partaken of a rabbit, which was so bad that the patient did not eat much of it. This was about two weeks before the skin became affected. Under treatment the condition subsided.

Early in June of the same year the patient was admitted to hospital, when she gave the following account of herself: In November a rash of beetroot-red colour made its appearance on the face and neck, which gave rise to great irritation. After a few weeks the rash got better somewhat, but did not entirely disappear, and the superficial layers of the skin began to peel off. The armpits were next attacked by the rash, but after some weeks they got better. Then the knees were involved. In all the parts affected there had been much irritation, and in the later stages shedding of the superficial layer of the skin as well. The upper part of the chest had also been attacked in a similar manner. As the rash disappeared there was a tendency for the parts affected to become brown. About a fortnight before the rash appeared the patient had some rabbit, which was bad. There were no intestinal symptoms after partaking of the rabbit.

Personal History.—Influenza (?) as a child. Very temperate. Menopause ten years previously. No leucorrhoea. Patient has had three children; healthy.

Family History.—Mother died of phthisis. Father also dead, cause unknown. Brothers, four, died young (?). Sisters, two, quite healthy.

Present Condition.—A well-built woman of 54. Pulse 102, regular. Heart apex beat normal. Heart not enlarged. Heart

sounds normal. Pulmonary system: emphysema. Some crepitations at left base. Alimentary: bowels regular, tongue furred. Teeth: most of upper and some lower gone. Abdomen distended, and a large smooth mass felt rising from the pelvis as far as the umbilicus, really due to distended bladder. Pus in urine.

Nervous System.—The patient of hysterical disposition; weeps with small provocation. The cranial nerves are all normal except the sixth; there is nystagmus, right eye only on looking to the left. The upper limbs have good power, and sensation and co-ordination are normal. The trunk is normal in power; the abdominal reflexes are present. The lower limbs are normal. Flexor response. Knee-jerks present; no ankle-clonus. These are the notes made by the clinical clerk.

As to the skin. The following details are mine: Distributed about the body are a number of red vascular areas, which become pale on pressure. The red vascular areas are most marked on the face and neck. A butterfly-shaped area occupies the centre of the face, covering the nose and cheeks and ending sharply on the upper lip, giving rise to a distinct circumoral pallor; elsewhere the area has a diffuse edge. There are symmetrical patches over the eyebrows, about a half-crown in size. The reddened area occupies the front of the neck, and extends over clavicles and on to the upper part of the chest, symmetrically. At the back of the neck, a palm-sized patch. The other symmetrical patches are on the backs of the shoulders, elbows, knees, and popliteal spaces. There is also a patch about the epigastrium.

A glance at the diagrams will show the symmetrical distribution better than a description (see Diagrams A, A a). I would

Diagram A.—Toxic dermatitis. Note the circumoral pallor.

Diagram A a (see also A).—Toxic dermatitis.

call attention to the distribution about the face and neck, which recalls that observed in some cases of lupus erythematosus. What I also desire particularly to emphasize, in addition to the symmetry, is the fact that the vascular areas were distinctly made up of numerous dilated vessels (telangiectases). They were not inflammatory. Before the case was transferred on account of possible malignant disease (abdominal) the following notes were made by the clinical clerk:

July 20th: There is a large amount of pus in the urine and the patient is of a very hysterical temperament.

July 26th: The pus in the urine has to a great extent disappeared as a result of boric lotion wash-outs, etc. The hysterical condition has greatly improved under bromide, valerian, and electric treatment.

No definite diagnosis having been made, the patient went home. She died not long after. No necropsy was allowed.

Commentary.—The original symmetrical rash, which manifested itself in successive outbreaks and which followed the ingestion of bad rabbit, appeared to have been due to an intoxication, the more so as no intestinal symptoms (elimination) followed. But taking the case as a whole, there were no doubt other factors (malignant disease, pus in the urine); and the patient was very probably already in a toxic condition when she ate some of the bad rabbit.

There is no record of the condition of the urine when the patient was first seen; and, as no necropsy was allowed, no firm diagnosis could be made as to abdominal conditions. During life nothing definite was made out by those who examined the patient from purely medical (apart from dermatology) and gynaecological points of view. That the intoxication was a severe one is sufficiently borne out by the condition of the skin when seen by the late Dr. Radcliffe Crocker a month after the first skin lesions had appeared. This is further emphasized, in my opinion, by the vascular, telangiectatic state of the affected areas which followed, showing that the vessels had been smartly attacked in the first place. Perhaps the general toxic condition of the patient added to the damage already experienced by the vessels in the affected areas prevented their recovery. In a small way, a close examination with a lens of some of the elements of a squamous syphilide recently observed by me, which had been present some time and untreated by mercury, revealed a telangiectatic condition (H. 278), may be mentioned here from a comparative point of view. The telangiectatic form again of lupus erythematosus should be alluded to in the present connexion. At the present moment I have under my care an obstinate case of chronic lupus erythematosus of a vascular type distributed about the eyebrows, temples, and cheeks (G. 313). This case had previously been under the care of the late Dr. Radcliffe Crocker, and was seen by him originally after the disease had been present for two years.

The symmetrical distribution in the toxic case I have described was very marked. With regard to symmetry in diseases of the skin, various theories have been brought forward to explain them. Testut's monograph, 1877, on the subject is a classic now¹; and other writers have followed on the same subject since that time. I do not propose to enter into details on this score as the matter is well known to those who have made a study of dermatology. I would merely in this place compare the distribution I have described with what obtains in some other more or less acute conditions.

First and foremost, as a typical symmetrical affection of the skin, I would again refer to lupus erythematosus. The bat's wing or butterfly patterns observed in that disease are familiar to you all, but what is perhaps less so, on account of its rarity, is the distribution observed in acute lupus erythematosus d'emblée, a case of which I had under my care and which I have dealt with at large elsewhere.² In the patient I observed the distribution will be readily made out by a reference to Diagram B.

Diagram B.—Acute lupus erythematosus d'emblée.

There is also the early butterfly swelling observed in leprosy, as in Diagram C (for which I am indebted to Dr. Ashburton-Thompson of Sydney).

Diagram C.

Diagram D.—Erythema haemorrhagicum faciei.

A more interesting symmetrical condition, however, is that exhibited in Diagram D (*Dermatology*, Book IV, E.). The patient was a female aged 23, and the condition—that is, erythema haemorrhagicum faciei—had been present fourteen days. The rash began on the face, the

forearms being subsequently affected. These are the notes made at the time by me: Purpuric punctiform and patchy symmetrical eruption of the face and nose. The patch does not disappear on pressure. Extensor surface of forearms: Slight mottling, leaving pale yellowish stain on pressure. Nothing on ears or fingers. The patient had been under a doctor for six years for asthma, she says. No history of rheumatic fever, scarlet fever, etc. No joint troubles. No hæmorrhage from mucous membranes. Is not prone to excessive bleeding. Catamenia scanty. Bowels regular. Tongue furred. Father, *felo de se*. Mother phthisical. As to origin, the only thing that could be made out was that the patient had been a good deal in the sun. When seen not long after first visit little remained of the rash.

Diagram E.—Pellagra (note pale areas about orbits and mouth.)

There is another condition—namely, pellagra—in which symmetry may also be fairly marked, as can be seen in Diagram E (from cast of a pellagrous “mask” in possession of Professor Ludwig Merk of Innsbruck). Here, again, we have pale areas about the mouth and orbits.

This short contribution to the subject of acute toxic and symmetrical rashes of the skin may be of some interest. As to theories, I feel somewhat in the position of the man who did not believe in ghosts because he had seen so many.

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VARIATION AMONG BACTERIA.*

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THAT the medium in which a bacillus is growing may alter the morphology of the micro-organism has been shown to be true by a number of observers. Thus the *B. typhosus* has been found to grow out into threads when acted on by various dyes (Ainley Walker¹), salts (Péju and Rajat²), urea (Wilson³), and by sewage (Almquist⁴). Similarly, Adami⁵ has shown that by the action of a high temperature and the presence of peritoneal fluid the *B. coli communis* assumed a diplococcoid form, and in this case the fermentative characters of the bacillus were also profoundly modified. In most of these cases the organisms soon regained their normal characters when the active agents were removed; in other words, they were examples of fluctuating variations. Torrey,⁶ Klotz,⁷ and Twort⁸ have shown that bacilli belonging to typhoid-coli and dysentery groups can be made to ferment sugars, on which at first they had no action, by growing them for some time in contact with these sugars.

I have on several occasions isolated from the intestine bacilli which required seven to twenty-one days to produce an acid reaction in lactose litmus broth, and two or three days more to produce gas. Where the reaction is so long delayed it is difficult to say whether one is to regard the organism as a slow fermenter of lactose or as a non-lactose fermenter which by contact with the lactose has acquired a new property. That there is this difficulty can be readily shown by the facts regarding the *B. typhosus*. It is invariably stated that this bacillus does not ferment dulcife, yet, like Penfold,⁹ I find that when this bacillus is grown in peptone water containing this substance acidity is produced at the end of ten days. In the case of the several varieties of dysentery and pseudo-dysentery bacilli there is great irregularity in the time required to bring about fermentation of maltose and saccharose.

The explanation of the delayed reaction may be that variations occur among the bacilli growing in the medium and that those bacilli which are able to make use of a sugar which the others are unable to touch crowd out the latter. When a loopful of a culture which after a long delay has fermented lactose

is planted out on the Endo or on the Conradi-Drigalski medium, the colonies formed become slowly reddish, a few being deeper in tint than the others.

When fermentation has occurred in a lactose tube and a second tube is inoculated from the first, in the second tube acid and gas are produced, as a rule, in twenty-four to forty-eight hours, although in the first tube it required several weeks to produce the same result. A third transfer to lactose broth results in acid and gas being produced in a single night. For the development of the lactose splitting enzyme it is necessary to have lactose present in the medium. By growing a bacillus which slowly ferments lactose in glucose broth the fermentative action on lactose is unaltered. The action on lactose results from adaptation. “The simple forms of life are able to adapt themselves to their surroundings, and the adaptation cannot be ascribed to chance, for with a given environment one particular alteration in properties surely results” (Adami¹⁰).

I recently isolated a bacillus from the urine of a patient, which is interesting from the fact that it possesses characters intermediate between those possessed by the *B. typhosus* and the *B. coli communis*. The patient was probably an “effective” typhoid carrier. Four years ago an epidemic of typhoid fever occurred in a fashionable district of Belfast, and the cases were centred round a certain milk supply. On investigation, it was found that one of the milkers had recently suffered from “influenza,” complicated with jaundice, and her blood gave a well-marked positive Widal reaction in a 1 in 50 dilution. When the supply of milk from this dairy was stopped, the epidemic came to an end. There were 30 cases notified, several of whom died. I had no opportunity of examining the urine and stools of this woman, but I have no doubt that at that time they contained the *B. typhosus*. This woman developed Bright's disease, from which a few months ago she died. Through the kindness of the doctor in attendance, I obtained a specimen of her urine a week before she died, and it was from it that I isolated this peculiar bacillus. Its characters were as follows:

The growth on all the ordinary media was very similar to that of the *B. typhosus*, and gelatine was not liquefied. At 37° C. the bacillus grew well, but the growth was slightly more profuse at 22° C. It was Gram-negative and showed marked oscillatory characters, but no true movement of transposition. In peptone water a trace of indol was produced. The character which made the bacillus remarkable was its behaviour in media containing lactose. I noticed that the colonies on a Conradi-Drigalski plate remained blue as long as the bacillus was kept at 37° C., but that at room temperature they became red. Lactose-litmus-agar inoculated with this bacillus and kept at 22° C. became red in two days, whilst at 37° C. no change of reaction occurred even at the end of a month's incubation. The lactose in litmus broth tubes was but slowly acted on even at 22° C., but when the same medium was poured out into a Petri dish fermentation occurred in three days. The explanation of this phenomenon might be found either in supposing (1) that at 37° C. the lactose-splitting enzyme was not developed, or (2) that at this temperature products of proteid decomposition neutralized the acid resulting from the fermentation of the lactose. The following experiment showed that the first hypothesis was the correct one: Ten c.cm. of lactose peptone water were added to a series of sterile Petri dishes, some of which were inoculated with the bacillus, the remainder serving as controls. Half of these dishes were put into the incubator at 37° C., and half at 22° C. At the end of a week the amount of fluid in each dish was made up to 25 c.cm., and the number of cubic centimetres required to reduce 5 c.cm. of boiling Fehling solution was determined. It was found that all the sugar had disappeared from the plates which had been inoculated and kept at 22° C., whereas the amount of lactose present in the plates at 37° C. was the same as that in the control uninoculated plates.

We have here an example of the development of an enzyme being dependent on the temperature at which the bacillus is cultivated. This may be compared with the behaviour of the *B. prodigiosus*, which produces little or no pigment at 37° C. Coplans Myer¹¹ has met with bacilli which possess a similar peculiarity in reference to dulcife.

It was of interest to discover whether the agglutinogens of the bacillus were in any way associated with the lactose-splitting enzyme. The following experiment showed that there was no connexion between the two characters:

A guinea-pig was inoculated on several occasions with a growth of the bacillus on litmus-lactose-agar at 37° C., and a second guinea-pig with a similar amount of a culture grown at 22° C. The serum of these guinea-pigs was then found to have the same action on the two growths, and an absorption experiment proved that both strains could exhaust the agglutinins from both serums.

* A paper read before the Bacteriological Section at the Annual Meeting of the British Medical Association, London, July 29th, 1910.