that a new technique is available for the study of haemorrhagic diseases in the determination of coagulation time (Quick) with Russell-viper venom before and after the potentiating effect of ovolecithin, but we feel that work of a more specific nature is required before ascribing this effect to lecithin. Special precautions will, however, be necessary to avoid even a trace of haemolysis.

Summary

The effect of haemolysis in accelerating the coagulation time of plasma is recorded.

Experiments dealing with the influence on the coagulation time of the addition of venom and lecithin to haemolysed plasma are described.

The conclusions derived from the investigation are given.

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CYCLICAL MUCOSAL ULCERATION

BY

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Recurrent buccal and genital ulceration is a syndrome which has attracted but scant attention. Recurring ulceration of the mouth is a common condition, described in textbooks under varying titles—ulcerative stomatitis, dyspeptic ulcers, aphthous ulcers, periadenitis mucosa necrotica recurrens (Sutton and Sutton, 1935), and stomatitis neurotica chronica (Sibley, 1899 and 1914). Recurring ulceration of the vulva was first described by Lipschütz (1913). He called the condition "ulcus vulvae acutum," by which name it is usually known, and in a second paper, in 1923, he reported 51 cases, but only 1 of these also had buccal ulceration.

The coexistence in the same patient of both conditions—namely, non-venereal ulcerative lesions of the mouth and genitalia—was originally described by Neumann (1895); and Wien and Perlstein (1932) in a comprehensive review of the subject could find reports of such a combination in only 30 cases and themselves described a single case. Since then Ravell (1932), Gray (1932), Thompson (1932), Talalov (1934), Hunt (1934), Ziserman (1935), Deuell and Landon (1936), Behcet (1937), Michaëlis (1937), and Tagami (1937) have reported between them 19 cases. In only 9 of the total of 50 cases is there any mention of the effect of menstruation on the ulcers, and in only 6 of these had the ulcers a regular time relation to the menstrual cycle—three cases of McDonagh (1924) and those of Talalov (1934), Ziserman (1935), and Michaëlis (1937). In 5 of the 8 cases recorded below the ulcers bore a constant time relation to menstruation, and it is this association of the ulcers with menstruation that I particularly wish to emphasize.

In all the patients whom I have seen with this condition the stomal and the genital ulcers have always had the same general characteristics. They vary in size from a pin-head to about one centimetre in diameter, and their appearance is preceded by and associated with pain at the site of ulceration, often malaise and depression, and occasionally dyspeptic symptoms. They are superficial, often appear-

ing to start as small papules or vesicles; they are surrounded by an inflammatory halo, their bases covered with a yellow slough, and they heal without scars. I have seen them on the inside of the cheeks, lips, tongue, tonsillar region, and pharynx, and also the labia, vagina, and cervix uteri. The number of ulcers present at one time varies from one to about twelve. They are unassociated with an adenitis.

Of the 8 cases reported below the most interesting is a group of 6 patients, all of whom are near relatives. Mrs. A. died, aged 55, from cancer of the uterus. There is no history that she or her only sister had complained of either buccal or vulvar ulceration. But Mrs. A. had three daughters—Mrs. B., Mrs. C., and Mrs. D.—of whom the first and the last both suffer from recurrent ulceration, as do also three of Mrs. B.'s four daughters, one of Mrs. C.'s four daughters, and the only daughter of Mrs. D. All the male members are healthy.

The following diagram illustrates the position more clearly. Ages are given in brackets and the initials of those who have buccal and/or genital ulceration are printed in *italics*.

Case Records

Case 1.—Mrs. B., aged 53, has had buccal and vaginal ulcers for twenty years. The stomal ulcers occur on the inner aspect of the lower lip and at the side of the tongue. There is usually only one mouth ulcer present at a time. The vaginal ulcers always occur at the same time as the buccal and are accompanied by a great deal of soreness. All the ulcers appeared two to three days before the onset of menstruation and disappeared during actual menstruation, but they always reappeared for two or three days after the period had ceased. Her menstrual cycle was always regular 3/28 until the menopause, but the flow was scanty and she had severe premenstrual and intramenstrual dysmenorrhoea. Since the menopause the ulcers have still regularly recurred every four weeks. During her four pregnancies the ulceration was always very much worse, but it improved following delivery. The only investigation has been a blood Wassermann, and this was negative. She has had no treatment whatsoever for the condition. Mrs. B. has four daughters, and three of these have ulcers. The eldest, Mrs. E. F., has genital and mouth ulcers, but further details about her are not available.

Case 2.—Miss B. B., aged 17, the third daughter of Mrs. B., has had mouth ulcers for eighteen months but no genital ulcers. The ulcers have occurred regularly every four weeks, and last for one or two days. Although she is nearly 18 she has never yet menstruated, and secondary sexual characteristics have not appeared. Her general nutrition is poor and she is pale. Apart from these facts there are no other positive findings, and no investigations have been undertaken. She has not had any special treatment.

Case 3.—Miss C. B., aged 10, the fourth daughter of Mrs. B., has been troubled with ulcers on the side of her tongue at irregular intervals for the last eighteen months. Recently they have been very large and painful, previously having been only small and causing little inconvenience. She is a well-built, healthy-looking child, and there is no evidence of infection of her teeth, tonsils, or sinuses. No investigations or special treatment have been undertaken.

Case 4.—Mrs. D., sister of Case 1, is aged 36, and has had ulceration of the mouth and vulva since the age of 12—two

years before the onset of menstruation. The buccal and genital ulcers occur simultaneously two or three days before the onset of menstruation. They invariably disappear as soon as menstruation starts, but reappear for the two or three days following the cessation of the period. The menstrual cycle is regular 3/28, and there is no dysmenorrhoea. She is an exceptionally healthy-looking woman, and apart from the ulcers there are no positive physical signs. She has never had any treatment for the condition, and no investigations have been done. She has one son and one daughter, the latter also suffering from ulcers. During the two pregnancies the ulcers were very much worse.

Case 5.—Miss E. D., aged 12, the daughter of Case 4, has had ulceration of her tongue and cheeks frequently, but at irregular intervals, during the last twelve months. She has not yet started to menstruate and appears to be a healthy child, no abnormalities having been observed on clinical examination.

Case 6.—Mrs. G., aged 24, niece of Cases 1 and 4, has had recurrent buccal ulceration since childhood. The ulcers occur at irregular intervals and last one or two days. They have no relation to her menstrual cycle, which is regular. There is no history of genital ulceration. She has two daughters and one son, all of whom are healthy and free from ulcers. Her mother and three sisters are also not affected. She is the only daughter of Mrs. C. who bears a strong resemblance both in appearance and in temperament to Mrs. B. (Case 1).

Case 7.—Mrs. J. was 21 when I first saw her. She then had an acute bronchitis, and remarked casually that an ulcer in her mouth was a little troublesome. On questioning I discovered that she had had ulcers of the mouth regularly every month, one week before the onset of menstruation, for two and a half years. The ulcers lasted until the period began. There is no history of genital ulceration. The menstrual cycle is regular 3/28, and there is no dysmenorrhoea. Apart from bronchitic signs nothing abnormal was discovered on clinical examination. She refused further investigation. For the last two years I have been in frequent communication with her. During this period she has been entirely free from ulcers, although she has had no treatment.

Case 8.—Miss L., aged 45, was first seen by me when she had typical angioneurotic oedema of her face and arms. On routine examination ulcers were found in the mouth. Questioning elicited the fact that she had suffered from these for over three years. They always began one week before menstruation and lasted until the period started. There is no history of genital ulceration. Until twelve months ago her menstrual cycle was regular 5/28. Her general condition is good and, apart from the ulcers and recurring angioneurotic oedema, which bear no time relation to one another, clinical examination was negative. A blood Wassermann was negative and a blood count showed 4,232,000 red cells and 7,600 leucocytes per c.mm. with a normal differential count and 85% of haemoglobin.

One c.cm. of antuitrin S was given daily for one week before the expected onset of the ulcers. After the second course no ulcers occurred that month for the first time for over two years, and the following month she had only one small ulcer. The next month the ulcers were as bad as ever and, in view of the fact that the injections appeared to cause severe constitutional upset, 100 units of pregnyl and 20,000 units of oestrogen were substituted. During the following three months she had only two small ulcers and the associated pain was much less; but she developed a severe epimenorrhagia, and so the pregnyl was discontinued and the oestrogen given alone. The following period was normal, but the ulcers were very severe. The next month, after a further course of oestrogen, she had amenorrhoea and was free from ulcers. Since then she has had 100 units of pregnyl on each of the seven days preceding the expected onset of the ulcers, with varying success. Although the condition has somewhat improved it cannot be regarded as cured.

Aetiology

In discussing the various opinions as to the aetiology the main difficulty is to attempt to elucidate whether or not the authors were describing the same condition as is

reviewed in this paper. The exact relation of this syndrome of cyclical mucosal ulceration to similar conditions reported by other writers is hard to assess.

Lipschütz (1923) regarded *Bacillus crassus* as the causal organism of *ulcus vulvae acutum* and considered the finding of this bacillus as essential for the diagnosis. *B. crassus* is closely related morphologically to, if not identical with, Döderlein's vaginal bacillus. Several authors believe that recurrent buccal and genital ulceration occurring in the same patient is also due to *B. crassus*. But this organism is often in vaginal swabs of patients who have no ulceration: repeated attempts at auto-inoculation have all proved negative, and in only 4 cases has *B. crassus* been found in mouth ulcers.

Talalov (1934) described a patient in whom ulceration of the mouth and vulva was associated with a pustular eruption of the face and trunk which later ulcerated in parts. *B. crassus* was seen in a section taken through one of these ulcers and was isolated from the vulva but not the mouth. That author expressed the opinion that the patient had a generalized *B. crassus* infection, and quoted the case of Samek and Fischer (1929) of a girl of 19 who had ulceration of the vulva and a lesion of the legs resembling erythema nodosum. *B. crassus* was recovered from the genital ulcers, the skin nodes, and a blood culture.

Planner and Remenovskiy (1922), Schnabl (1927), Samek and Fischer (1929), Kumer (1930), Jaffe (1930), Matras (1932), Whitwell (1934), Talalov (1934), and Hunt (1934) have each recorded a single case of recurrent ulceration of the mouth and/or of the vulva in association with skin lesions which either resemble erythema nodosum or are papular and may ulcerate. The skin lesions have been regarded by some as tuberculides, but others consider the whole condition to be a type of erythema multiforme. Talalov suggested that the skin eruption is an allergic manifestation of a *B. crassus* infection.

Cantrell (1934) and Grant (1934) have each reported a case of combined vaginal and buccal ulceration due to the diphtheria bacillus, but it is highly improbable that any of the cases above recorded were due to this organism. Kumer (1932) considered, on experimental grounds, that recurrent stomal ulceration is an atypical herpes infection, but this view has had very little support and no confirmation.

An endocrinous theory of origin appears more entertaining than an infective one, but is even more difficult to prove. Ziserman considered that because his case cleared up with anterior pituitary lobe extracts and stimulating x-ray doses to the pituitary he had established the endocrinous nature of the condition. Four of my cases appear to support an endocrine basis strongly, but the evidence is far from conclusive. Perhaps it is of some importance to note that amenorrhoea, physiological or otherwise, was associated with amelioration of symptoms in some cases and with aggravation in others. The syndrome of recidivating buccal and genital ulceration seems to be peculiar to women. If this really be so, what is the significance?

McDonagh (1924) reported a case in which the ulcers of the vulva occurred immediately after the cessation of the menstrual period, and he mentioned that he had seen two similar cases. *B. crassus* was found in all three, and McDonagh stated: "Menstruation does lower a woman's resistance, and doubtless in these three cases it sufficed to render a saprophytic organism pathogenic." Opposed to such a viewpoint is the fact that in 4 of my cases the ulcers started before the onset of the period, the possible exhausting effects of which cannot therefore be considered a contributory factor.

Parkes Weber (1932), in a discussion on the subject, suggested that the primary factor was not a local infection but rather some condition of the mucous membranes analogous to epidermolysis bullosa, which is not necessarily hereditary. The familial incidence of the condition in 6 of my cases favours such an interesting idea.

In view of the occurrence of mucosal ulceration in agranulocytosis the possibility of such a condition in these patients has to be remembered. No investigated case has had a neutropenia. Embleton (1937) described the interesting case of a girl who had ulceration of the mouth regularly every seventeen to nineteen days, the attacks always being coincident with a marked neutropenia, the leucocyte count being normal between the paroxysms. Embleton states: "There is no relationship between the swing of the rhythm and the menstrual periods." But unless the menstrual cycle was extremely irregular it is difficult to understand how this could have been the case.

I suspect that cyclical mucosal ulceration, at any rate as a partial syndrome, is far commoner than is generally believed. Possibly many girls who have genital ulceration do not seek medical advice because of false modesty, especially if they are single. In cases of stomal ulceration the relation to menstruation may not be volunteered by the patient even if present or be asked about by the doctor, who is probably unaware of such an association. Almost all previously published cases have been severe, but some of mine were mild and lead me to suppose that frequently the condition does not trouble the patients enough to make them consult a doctor, and Case 7 of my series indicates that spontaneous cure does apparently occur.

I wish to emphasize that none of the 8 cases described above has ever been an in-patient of any hospital.

Summary

Eight cases of cyclical mucosal ulceration are described, six of the patients being near relatives. The ulceration affected the mouth in all cases, and in two the genital tract was also involved.

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SOME RECENT AIR-RAID CASUALTIES

BY

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The treatment of air-raid casualties at this hospital during the past few weeks is here recorded because a few points have arisen which may be of value in the conduct of further cases.

First Series of Cases

Twenty-three casualties were brought to hospital; the injuries were due mostly to the direct action of the explosive, the distribution of the fragments being such that nearly all the lesions were in the lower limbs. Of the 23 patients 6 were dead or died within a few minutes of admission. Of the remainder, 8 died within twelve hours and 9 survived. These 17 patients were admitted to the receiving ward within thirty minutes of the time of injury, and resuscitative treatment was started immediately. They were all between the ages of 19 and 30; their lesions were lacerations or compound fractures of one or both lower limbs, with shock and local injury roughly in proportion. It was found that they could be put into one of two groups with reference to severity of the shock and treatment (and, one might add, prognosis also, as was unfortunately confirmed by the poor results of resuscitative treatment). One group, containing 9 cases, were all suffering from severe shock and had comminuted compound fractures of one or both lower limbs. The other group, consisting of 8 cases, only slightly shocked, had multiple lacerations, some also with compound fracture of one limb.

The former group were from the start too ill to allow of immediate operation; they were all in the clinically recognizable state of severe shock and had to be resuscitated before operation could be considered. They were given morphine and blood or plasma transfusions. In not one case was there bleeding from a large artery. The results of resuscitation treatment were extremely disappointing. Of these 9 patients 8 progressively became worse, and they died in $\frac{1}{2}$, $3\frac{1}{4}$, 4, $6\frac{1}{2}$, $6\frac{1}{2}$, $6\frac{1}{2}$, 8, and 11 hours. The other patient improved sufficiently for operation to be performed after six hours, and after much anxiety he survived. The second group never really gave rise to any doubt about their treatment and immediate prognosis. All 8 were operated on within six hours, mostly by excision and plaster, and have done extremely well.

It is not proposed to describe the general organization or the routine treatment, which was on generally accepted lines, as frequently described in recent articles (Cohen and Schulenburg, 1940; Hodgson and McKee, 1940). The operative technique was that described by Cohen and Schulenburg in their excellent paper, except that in their cases "no attempt at excision or trimming of muscle was made," whereas in our cases excision of damaged muscle was regarded as an important step in the procedure. A few cases only will be detailed, as they were of uniform type in the two groups. Of the 9 patients with severe shock the following case was typical:

A man aged 22. Compound comminuted fracture of upper end of left tibia and fibula with much destruction of tissue and the limb almost completely severed; a tourniquet had been applied just above the knee. This patient was suffer-