

Discussion

The typical coronary lesion that usually predisposes for the development of cardiac infarcts in man is an atheromatosis, primarily characterized by lipid deposition and intima proliferation with comparatively little calcification. In our experiments, on the other hand, the D.H.T. pretreatment caused mainly calcium deposition, with little intima proliferation and virtually no lipid deposition. However, in both cases the mechanical effect of the morbid lesions is essentially the same: some degree of constriction and considerable rigidity of the arterial wall. It will be recalled that our object in carrying out these experiments was to verify whether an artificially produced vascular change of this kind would predispose the cardiac muscle to the necrotizing action of subsequent treatment with Me-Cl-COL plus NaH_2PO_4 . The data presented here show that this was the case. It remains to be established whether interference with the coronary circulation, no matter how produced, would exert a similar sensitizing effect. However, the present experimental series justifies the conclusion that short-term treatment with D.H.T. can so stigmatize the heart that even after clinical recovery the animals remain sensitized to such metabolic derangements as are induced by the subsequent administration of Me-Cl-COL plus NaH_2PO_4 . In a sense, this stigmatization may perhaps be compared with the effects of ageing and the associated atheromatosis in the human coronary circulation.

Although we suspected that the coronary damage produced by D.H.T. could thus predispose the cardiac muscle to the necrotizing effect of Me-Cl-COL plus NaH_2PO_4 , it was not expected that the latter treatment would also aggravate the arteriosclerosis itself. It is noteworthy, however, that, under these circumstances, not only cardiac infarction but organic obstruction of the coronary vessels can regularly be produced by humoral means.

Further experiments will have to show whether there is any close relationship between this experimental disease and the spontaneous coronary infarcts of man. It also remains to be seen whether the magnesium and potassium salts that proved to be so eminently effective in the prophylaxis of the phosphate-steroid-cardiopathy will also prevent those types of cardiac necroses that are associated with vascular obstructions.

Summary

Based on the literature concerning the infarct-like cardiac necroses that are produced by combined treatment with phosphates and steroids (the "phosphate-steroid-cardiopathy"), experiments were designed to determine whether a pre-existent coronary lesion would sensitize the cardiac muscle to this type of damage.

Albino rats were pretreated during 10 days with dihydrotachysterol (D.H.T.), so as to produce mild narrowing and calcification of the coronary arteries. After this, no further treatment was given until all the animals had recovered, as judged by their growth and clinical appearance. Then, combined treatment with NaH_2PO_4 plus 2 α -methyl-9 α -chlorocortisol (Me-Cl-COL) was initiated at a dose level which in non-pretreated animals caused only occasional microscopical foci of myocardial necrosis, localized in certain areas of predilection. It was found that in the D.H.T.-pretreated rat this same NaH_2PO_4 plus Me-Cl-COL treatment produces extensive macroscopically visible patches of necrosis throughout the myocardium and, at the same time, evokes intense, proliferative, and eventually obstructive changes in all parts of the coronary tree.

The possible relationship between this type of experimental disease and the spontaneous coronary infarcts of man is discussed.

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TREATMENT OF APHTHOUS ULCERATION OF THE MOUTH

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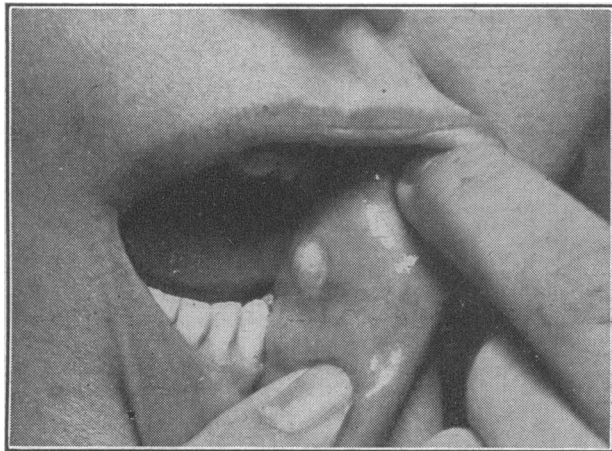
(From the Radcliffe Infirmary, Oxford)

Aphthous ulceration of the mouth is one of the commonest minor maladies. It is probable that within the British Isles more than a million persons are affected with the condition. In its common or *minor* form a single ulcer or a small crop of ulcers appears on the buccal mucous membrane several times a year. The ulcers occur most often on the inside of the cheeks (see illustration) opposite the molar teeth, inside the lips, and occasionally on the tongue, although any part of the mouth or pharynx may be affected. They are painful and interfere with speech and eating, but normally they run a short course and heal in about a week without scarring.

Some patients suffer from a *major* form of aphthous ulceration, which is a much more severe condition. The ulcers are multiple and the patient may be seldom, if ever, free from them over the course of years. When this is so, the disorder ceases to be merely a painful inconvenience and assumes the dimensions of incapacitating illness. Patients thus afflicted with the major form of the condition are fortunately a small minority of the total, but they are nevertheless numerous within the general population.

There is a *special* group of patients showing ulceration of the mouth which is, at any rate superficially,

closely similar to simple aphthous ulceration. This is a mixed group which can be divided into two main categories. The first is when the aphthous ulceration is only one feature of a disease in which several mucous membranes and the skin may be involved. Examples of these muco-membranous diseases are erythema multiforme major (Stevens-Johnson syndrome) and Behçet's syndrome. The second is when the ulceration of the mouth is a symptom of some underlying disease. For



Photograph showing aphthous ulcer inside the cheek.

example, in tropical sprue and idiopathic steatorrhoea, aphthous stomatitis is extremely common; indeed, the term *sprue* is derived from the Dutch word *spruw*, which means aphthous disease (Dubois and van den Berghe, 1948). In ulcerative colitis, aphthae occur fairly often during the stage of symptoms.

Aetiology

The aetiology of aphthous ulceration is essentially unknown, though many theories have been advanced, the most popular being that the ulcers are psychosomatic or allergic manifestations or that they are caused by a virus. Treatment is therefore empirical and has remained unsatisfactory. Simple mouth-washes and paints have little influence on the course of the ulcers. Various vitamins have been used, but without convincing evidence of success. The ulcers can be cauterized by touching them with a silver nitrate stick or with chromic acid solution, but such violent methods can only be deplored, because they enlarge the ulcers and are likely to give rise to residual scarring.

The situation has been summed up admirably by Erich (1955) in a celebrated textbook of medicine when he says: "There is no known cause for aphthous stomatitis and there is no treatment which is of any value." This discouraging comment is reinforced by the findings of Sircus *et al.* (1957) in a recent study of 120 patients suffering from the disorder. They carried out blind controlled trials of many of the most popular treatments, and found none that would reduce the chance of ulceration occurring. The agents thus found to be useless were: folic acid, nicotinamide, riboflavine, a vitamin-B mixture, small doses of cortisone by mouth, ethisterone for premenstrual aphthae, and local radiotherapy. Their one positive finding was that the local application of chlortetracycline appeared to speed up the healing of the ulcers although it did not prevent them from recurring.

Treatment

In view of the fact that cortisone and its analogues have been found useful in the treatment of inflammatory conditions when they are applied locally, it is natural to wonder whether these compounds have any useful place in the treatment of aphthous ulceration. Fisher (1955) treated eight

patients who suffered from recurrent aphthae with hydrocortisone ointment, but did not find it very helpful, as five obtained no relief whatever. Rivin and Barton (1955) made a "blind" controlled study of the effect of hydrocortisone ointment and found no effect on the time of healing, although a few patients experienced relief of pain. However, Hillman (1956) and Morton (1957) claimed good results from treating aphthous ulcers by the direct application of hydrocortisone ointment. It is evident that no agreement has yet been reached on whether hydrocortisone ointment is of any great value in the treatment of the condition.

The mouth is far from being a suitable place for the use of an ointment for local therapy. The whole surface is bathed in saliva, which must impede the action of a substance carried in an ointment. The movements of the tongue and cheeks make it improbable that an ointment will stay long in place on any localized lesion within the mouth. It occurred to us to make a virtue out of necessity by using a water-soluble compound of hydrocortisone which would dissolve in the saliva. Instead of being an inconvenient barrier, the saliva then becomes the actual solvent for the hydrocortisone and the medium by which it is transported to the lesion. At our request Glaxo Laboratories prepared a tablet especially for use in the mouth; it contained 2.5 mg. of hydrocortisone in the form of its hemisuccinate sodium salt, a compound freely soluble in water and one which has proved to be beneficial in the local treatment of ulcerative colitis (Truelove, 1957). The tablets have a lactose base and are designed so that they will dissolve slowly.

We have treated 52 patients suffering from aphthous ulceration with these tablets. The results have been highly favourable, and we now report them with brief illustrative case histories.

Minor Form of Aphthous Ulceration

In 23 patients with the minor form we have found it sufficient to wait for the appearance of an ulcer and to apply treatment by placing one tablet in the mouth in close proximity to the ulcer and leaving it to dissolve. This takes about three-quarters of an hour. It is usual for the pain of the ulcer to be relieved by the time the tablet has dissolved. This is repeated up to four times a day until the ulcer disappears. With this treatment a fully established ulcer will usually heal in 36 to 48 hours. When the treatment is used with an ulcer in the earliest phase of development—that is, when its diameter is only 1–2 mm.—the ulcer does not develop but remains small, and is commonly gone by the next day. Typical examples are given.

Case 1.—A schoolgirl aged 16 (the daughter of one of us) for several years had suffered from aphthous ulcers which occurred every few weeks. In June, 1957, she had an unusually severe ulcer which was very painful. When it was fully developed, a tablet was placed in the mouth in contact with it. The next morning, when asked how the ulcer was, she replied, "Oh, I had forgotten all about it." Examination then revealed the ulcer to be still present, but it appeared to be in a healing phase, and without further treatment had gone by the next day, being painless throughout. Since that episode she has had four aphthous ulcers, but each time the ulcer has been treated during its early stages while it was still very small. On no occasion did the ulcer develop into its usual full size. On three occasions it had disappeared by the next day, and on the fourth in 48 hours. A conspicuous feature has been the prompt relief of pain, so that after the use of a tablet the tongue can be rubbed vigorously over the ulcer without causing discomfort.

Case 2.—A schoolboy aged 13 (the son of one of us) had been subject to aphthous ulcers for several years, though they came at less frequent intervals than in Case 1. During the period of our study he has had three aphthous ulcers, and on each occasion, following treatment with one or two tablets, the ulcer has failed to develop and has gone by the next day. The relief of pain is rapid after the use of the first tablet.

Case 3.—A medical specialist aged 33 had suffered from recurrent aphthous ulceration since the age of 12 years. Ulcers came at irregular intervals, sometimes singly and sometimes in crops. They persisted with pain for 7 to 10 days. On September

18, 1957, he was conscious of soreness inside the right cheek, and by the next day a definite ulcer had appeared. That evening he applied two tablets at an interval of two hours. The next morning he was free of pain, but the ulcer was still present and there was some pain by the evening. A third tablet was then used and thereafter there was no pain and the ulcer disappeared. In his own words, "cure in 36 hours." A few weeks later another aphthous ulcer occurred. One tablet gave rapid and complete relief of pain, which was followed by healing within 48 hours without further treatment.

The other 20 cases of minor aphthous ulceration have, with one exception, responded similarly to the three described above. This was a general practitioner aged 31 who had suffered from aphthous ulcers for a number of years and was accustomed to treat them by the application of a silver nitrate stick. This would cause severe immediate pain; but the pain would soon go, although the ulcer would persist for a week or 10 days. In October, 1957, he developed a streptococcal sore throat with fever and malaise, and three days later three large aphthous ulcers occurred. He treated these by his usual method of cauterization, but on this occasion failed to obtain relief. At this stage he tried treatment with the hydrocortisone mouth tablets, but these were totally ineffective. We do not regard this as being a straightforward case of failure, because the lesions had already been transformed from aphthous ulcers into chemical burns. He has not yet had a recurrence, so that there has been no opportunity for treatment of a primary lesion.

Major Form of Aphthous Ulceration

In 22 cases of the major form we have found it best to begin treatment with one tablet four times a day and to continue at this level until ulceration has ceased. All patients have made a good initial response.

Thereafter we have continued a regular maintenance use of the hydrocortisone tablet in an attempt to prevent or abort further ulceration. In some patients two tablets a day have been sufficient for maintenance therapy, but others have been left on the full dose of four tablets a day. Five patients have remained completely free of ulceration for some months on this regime. Most of the others have continued to get sporadic sore spots in the mouth, but without ulceration, so that their actual disability has ceased. Some others, although greatly improved, have continued to develop occasional single ulcers while under treatment. One patient (Case IV) has shown evidence of temporary relapse during treatment. Illustrative examples follow.

Case I.—A senior Government official aged 46 had suffered from almost continuous aphthous ulceration since early childhood. He would have two or three ulcers at a time, and as one crop healed another developed. He was never free for more than a week or two. He had consulted many doctors and had received numerous treatments, none with any great effect. When first seen by us he had ulcers on the right cheek and soft palate, and extensive areas of intense erythema which were sore to contact. He became free of symptoms within two days of starting treatment with the tablets, and when examined two weeks later the mouth was normal. He then went on to maintenance treatment with two tablets a day and has remained normal during the succeeding six months. During this period of freedom from symptoms he was undergoing considerable mental strain through personal friction at his work, which is interesting because of a prevalent view that mental stress causes aphthous ulceration.

Case II.—A typist aged 22 had suffered from the minor variety of aphthous ulceration in childhood, but at the age of 14 the ulceration became more frequent and more severe. Since that time she has seldom been free from multiple ulcers for longer than a fortnight, and often suffers from them continuously for three or four months at a time. When first seen by us she had three large ulcers and several small ones. Three days after starting treatment she was improving, and after the first week only the healing residue of the largest ulcer was left. She continued on the full dose of four tablets a day for a further three weeks without ulceration, and was then put on to two tablets a day. On this dose occasional tiny tender spots developed in her mouth which did not ulcerate and which disappeared in two to three days. Pain was negligible, whereas previously she had found eating and speaking an ordeal.

Case III.—A housewife aged 33 had suffered from severe aphthous ulceration with every menstrual period since the age of 18. Six days before the beginning of menstruation numerous aphthous ulcers would develop, scattered all over the mouth. They grew and were very painful until the actual onset of menstruation, and then healed during the next six days. If the menstrual period came early the ulcers also came early, preserving the exact time relationship. We gave her intermittent treatment timed to precede the expected outbreaks. On each successive occasion numerous tiny ulcers developed; these never increased in size, although they persisted for several days. They were painful when she awoke in the morning, but the pain disappeared while she was using the first tablet of the day and was not felt again until the following morning. On one occasion when there were 25 of these tiny ulcers inside the upper lip she demonstrated to us that she could rub the tongue vigorously over them without pain.

Case IV.—A female factory hand aged 30 had suffered from severe aphthous ulceration since her earliest recollection. She had never been free of ulcers at any time and usually there were at least six. When first seen by us several ulcers were present. During the first week of treatment she improved, but tiny ulcers continued to appear, and during the next fortnight two ulcers developed which healed quickly. During the fourth week of treatment she was free of ulcers for the first time in her memory. In the second month of treatment she had one ulcer following influenza, but it remained small and healed in four days. In the third month there was recurrence of ulceration with a crop of ulcers in the mouth, of which one was still present when we saw her. With further treatment she has again become free of ulcers.

Aphthous Ulceration as Part of a Mucous Membranous Disease

In the few examples of this which we have had an opportunity to treat, the aphthous ulceration has shown the same response to treatment as simple aphthous ulceration.

Behçet's Syndrome

There were three probable cases of this syndrome, which in its complete form consists of recurrent oral and genital ulceration, with associated eye lesions, especially iritis (Phillips and Scott, 1955). It is often known as the triple symptom-complex of Behçet, who first described it as a distinctive syndrome (Behçet, 1937). It is a generalized disorder, and various systemic manifestations may occur in addition to the local changes already mentioned (France *et al.*, 1951). Neurological complications may occasionally arise because of widespread vascular lesions. The syndrome is often incomplete, with only two, or even one, of the mucous membranes affected.

Case A.—A housewife aged 64 had suffered from aphthous ulceration for 12 years. For the first 10 years she had attacks of ulceration every few months associated with epigastric pain and a retrosternal burning sensation, together with anorexia and a furred tongue. Each attack lasted about a month. Then, following the accidental death of her son, the aphthous ulceration became almost continuous and very severe, while the associated symptoms also continued. Ulcers were apt to affect the pharynx as well as all parts of the mouth. At the same time she developed severe pruritus ani and vulvae, which were treated with hydrocortisone ointment with benefit. When first seen by us she had two ulcers on the soft palate. There was also mild conjunctivitis. The E.S.R. was raised, being 31 mm. in one hour (Westergren) and it has remained at this level since. On two tablets a day for two months she was free of ulcers in the mouth proper, but continued to get ulcers about the fauces and in the pharynx. Judging that the mouth tablets were not a satisfactory means of getting a sufficient concentration of hydrocortisone to the pharynx, we then put her on a gargle of hydrocortisone (free alcohol) made up by diluting 50 ml. of the alcoholic solution (containing 250 mg. of hydrocortisone) with 500 ml. of normal saline. This was gargled several times a day for as long as was practicable on each occasion and then spat out. This treatment relieved the ulceration of the pharynx and fauces. We next instructed her to return to the use of the hemisuccinate tablets, but to hold saliva in the mouth until there was sufficient accumulated to permit it to be used as a gargle. This method has proved as effective as the use of a gargle prepared along more conventional lines.

Comment.—The occurrence of pruritus ani and vulvae, the mild conjunctivitis, the severe retrosternal burning sensation and epigastric pain, and the persistently raised E.S.R. make

us regard this patient as an example of Behçet's syndrome. Such patients benefit from cortisone and its analogues used systemically, but we have not so far made use of this form of treatment.

Erythema Multiforme Major (Stevens-Johnson Syndrome)

There was one case of this illness. In its complete form this syndrome manifests itself as erythema multiforme, ulceration of the mouth, urethritis, and conjunctivitis, but incomplete forms often occur. It is an acute disease, usually self-limited, and clearing up in six to eight weeks.

Case B.—Apart from one isolated crop of aphthous ulcers 14 years previously, a children's nurse aged 36 had had no mouth lesions until October, 1957, when she developed herpes labialis at the same time as the children under her care had influenza. A few days later a bullous eruption appeared on the backs of both hands and in front of both knees and lower legs. A day or two later severe ulceration of the mouth occurred, together with much malaise and a low-grade fever. Her family doctor described the mouth as "the worst I have ever seen, with large, deep, excoriated ulcers on the insides of her cheeks and the sides of her tongue, while the tip of the tongue was raw." This clinical picture persisted for a month, when the skin lesions died down and she became well in herself but repeated crops of aphthous ulcers continued. When we saw her at this stage there were two active ulcers inside the lower lip with hyperaemic and oedematous zones surrounding them and patches of hyperaemia and superficial scarring elsewhere in the mouth. Pigmented areas 1 to 2 cm. in diameter were present on the skin at the site of the original eruption. Treatment with mouth tablets relieved her of all pain and soreness in two days, and there has been no further ulceration.

Comment.—The disease being self-limited, the tablets were used only at the tail-end of the attack, and we have not had the opportunity of testing their action at the height of an attack.

Aphthous Ulceration in Association with Some Underlying Disease

Idiopathic Steatorrhoea (1 Case)

Both in tropical sprue and in idiopathic steatorrhoea, aphthous ulceration is very common. In idiopathic steatorrhoea Cooke *et al.* (1953) found that 90% of patients suffered from the ulceration.

Case C.—A housewife aged 24 had been diagnosed as suffering from coeliac disease as a child. Her development was slow, with the menarche at the age of 18. For some years her bowel habit had been normal, but she had been on a gluten-free diet for two or three years. For the whole of her life she had been subject to recurrent aphthous ulceration, which was of a "minor" character until two years previously, when she came to Oxford and abandoned the gluten-free diet. Since that time she had had increasingly severe ulceration, which was almost continuous during the six months previous to seeing us. She could not eat without pain and could not enjoy a cigarette. When we first saw her there were extensive areas of hyperaemia of the buccal mucosa with frank ulceration at six places. Use of the tablets in a full dose of four a day made the mouth normal. She then went on to a maintenance dose of two tablets a day. With this level of dosage there was no ulceration, but occasional small red tender areas appeared on the buccal mucosa and lasted for a few days.

Comment.—It has already been mentioned that this patient had no bowel symptoms. A radiological survey of the skeleton by Dr. F. H. Kemp revealed normal maturation and no evidence of osteomalacia. Her stature was that of a small normal woman. Her fertility was normal, as she conceived quickly after marriage and gave birth to a healthy baby. Blood examination revealed a persistent mild hypochromic anaemia with anisocytosis and polychromasia of the red cells. We have little doubt that the coeliac disease has persisted as idiopathic steatorrhoea, even though her domestic obligations have made it inconvenient for her to enter hospital for a study of the fat balance. It is now known that coeliac disease persists into adult life (Lindsay *et al.*, 1956), and that adult patients with idiopathic steatorrhoea have commonly suffered from symptoms in childhood. Both are due to sensitivity to gluten in wheat and rye, and a lifelong diet which excludes this appears to

be advisable (French *et al.*, 1957). We have now put this patient on to a gluten-free diet, but we regard the fact that the aphthous ulceration responded well to the mouth tablets in the absence of any dietary treatment as a matter of interest.

Ulcerative Colitis

In this disease, of which there were two cases, aphthous ulceration of the mouth not infrequently accompanies the stage of bowel symptoms. In both cases the mouth ulceration has responded swiftly to the use of the mouth tablets.

Discussion

The method of treatment which we have described is not only effective in the great majority of patients but is also simple and safe. A tablet is easily held in the mouth and will rest in the gingival sulcus, where aphthous ulcers most commonly occur. Its slow dissolution ensures that the ulcer is bathed in saliva charged with hydrocortisone for a rather long period. A certain amount of trouble must be taken to obtain contact between the tablet and the ulcer in patients with ulceration of the tongue or palate. So far as safety is concerned, our maximum dose has been four tablets a day, which represents 10 mg. of hydrocortisone, a dose unlikely to have any harmful systemic effect, however long continued.

When ulceration is present the tablets must be kept in close relationship to the ulcer if they are to be effective. When the tablets are being used as maintenance treatment to prevent ulceration, we have advised patients to shift them about the mouth every few minutes in order to carry the hydrocortisone to all parts of the buccal mucosa.

There has been a tendency to combine hydrocortisone with antibiotics for local application. We have not used antibiotics for treating aphthous ulcers, for two reasons—they are unnecessary and are potentially dangerous. Hydrocortisone has emerged as a satisfactory treatment when used alone by the method described. Antibiotics are known to carry the risks of sensitizing mucous membranes and of encouraging fungal growth; their use on mucous surfaces for indefinite periods therefore demands caution. In any event, there is no evidence that simple aphthous ulceration is an infective condition. Although it has often been thought to be herpes simplex affecting the buccal mucosa, this idea has been refuted by many studies, of which a particularly good one is that by Stark *et al.* (1954).

It is not our purpose here to deal generally with the aetiology of aphthous ulceration, but there is one aspect to which we should like to draw attention. It has commonly been supposed that mental stress is an important causative factor, a view advanced in the first British description, which bore the title of "Neurotic Ulcers of the Mouth" (Sibley, 1899). We ourselves have been more impressed by the mental disturbance created by the major form of aphthous ulceration and by the improvement in mental well-being when treatment is effective. For example, the father of our Case II, a superintendent of police, spontaneously told us of the great improvement in their home life since his daughter obtained relief from almost continuous oral pain. In another of our major cases (not one of those reported in detail) the patient described how he had become silent and morose because of the pain it gave him to talk, whereas after treatment he took delight in being normally sociable.

Summary

A method of treatment of aphthous ulceration of the mouth is described using a water-soluble compound of hydrocortisone incorporated in tablets which dissolve slowly in the mouth. The saliva then acts as the medium of transport to the mucosal surface.

Treatment has been given to 52 patients, of whom 23 were examples of the common or minor form of the condition, 22 were examples of the major form, and 7 were special cases of muco-membranous disease or of aphthous ulceration complicating another disease.

With one exception, the minor cases have obtained rapid relief of pain and healing of the ulcer has been accelerated.

The major cases have generally derived great benefit from the treatment. All showed initial improvement. With maintenance treatment some have been completely free of ulceration during several months of observations. Others have had minor ulceration but are greatly improved. Only one has shown a tendency to relapse during treatment.

The special cases have likewise shown a good response.

We are indebted to Glaxo Laboratories, who not only made the hydrocortisone hemisuccinate tablets specially for this study but also supplied them as a gift.

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SPREAD OF STAPHYLOCOCCI IN A SURGICAL WARD

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In the summer of 1956 a surgical unit at St. Bartholomew's Hospital suffered a severe outbreak of staphylococcal infection in which staphylococci of a single phage type caused 31 infections in two months. The staphylococcus appeared to be spread in part by a member of the surgical team who was a carrier, but there was also evidence of spread within the ward (Shooter, Griffiths, Cook, and Williams, 1957). The large number of staphylococci found in the air and on the bedclothes in the ward raised the question of the importance of air-borne transfer in the spread of infection within the ward, and of the value of measuring air and dust contamination with staphylococci in the prediction of outbreaks of infection.

The male ward of the unit was redecorated in September, 1956, and the opportunity was thus presented of observing the recolonization of a clean ward by

staphylococci, and possibly of tracing the source of staphylococci isolated from the air and from objects in the ward.

This study of the natural history of *Staphylococcus aureus* had not proceeded far when we observed the first example of the wide dissemination of a single phage type of staphylococcus, without, however, the occurrence of any wound sepsis. The study continued for eight months (until May 31, 1957), during which we observed nine waves of staphylococcal "broadcast," in each of which the numbers of staphylococci of one phage type reached an unusually high level (0.1 bacteria-carrying particle per cu. ft. (3.5 particles per cubic metre) of air) and, in most cases, comprised 60-80% of the staphylococci found in the air at the time. Of the nine staphylococcal broadcasts, only three were associated with clinical infection in more than one patient. These observations lend colour to the idea that some staphylococci are less virulent than others, and also that some patients shed staphylococci more freely than their neighbours.

In this paper we record, first, the extent to which patients acquired staphylococcal infection of wounds and other parts, and to which patients and nurses became nasal carriers during their stay in the ward. We also describe the extent of staphylococcal contamination of inanimate objects—particularly bedclothes and bed-curtains—and the air. Second, we describe the staphylococcal broadcasts and discuss their probable genesis and observed effect.

By means of phage-typing it is now possible to recognize many separate and distinct types of *Staph. aureus* that are ordinarily quite stable. With an organism as common as *Staph. aureus* some typing method of this sort is essential for a study of the epidemiology of infections. The usefulness of the method is emphasized by the fact that some 186 apparently distinct types of staphylococci were recognized during our eight months' study.

A possible source of confusion was introduced into our investigation of the spread of infection by the decision, prompted by experience in the summer outbreak, to isolate in a side-room any patients infected with staphylococci thought to be particularly virulent, which in the event proved to be those resistant to both penicillin and tetracycline.

The Investigation

The study was made in a male surgical ward. The work of the unit consisted of general surgery with a considerable proportion of abdominal and rectal operations. The ward had 22 beds, spaced about 6 ft. (1.8 m.) apart, with three more beds in two side-rooms. There were cotton curtains, suspended from rails 7 ft. (2.1 m.) high, that could be pulled out to surround each bed. Wound dressings were done in the ward by a no-touch technique. Patients infected with what were thought to be dangerous staphylococci were nursed in one of the two side-rooms. Special nurses were not employed, but a strict barrier-nursing routine, including the wearing of gowns, was followed.

A variety of minor steps were taken which it was hoped would help to check the spread of staphylococci. All the bedding from the patients who were nursed in isolation was disinfected with formaldehyde before being sent to the laundry. Curtains in the ward were changed once every four to five weeks. The floors were