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SOME ASPECTS OF THE BIOLOGY OF THE EPIDERMIS*

BY

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The study of the skin in relation to its microbic environment is of special interest to the dermatologist, who in the everyday practice of his art has to cope with skin conditions in which the surface is abraded, eroded, excoriated, fissured, vesiculated, or blistered as well as with those in which the surface remains intact. The themes I wish to discuss are the natural defensive mechanisms against infection, the sources and reservoirs of cutaneous infections, and the role of certain organisms of doubtful pathogenicity.

Clinical experience shows that the sites particularly susceptible to infection are the deep infoldings of the pilosebaceous and apocrine gland units, but only in exceptional circumstances the eccrine sweat-gland units. Thus we commonly see nasal vestibulitis, aural meatitis, blepharitis, folliculitis, and boils. Other vulnerable sites are the nail-folds, the axillary, submammary, genito-crural, and natal folds, also folds at the toe-webs and flexures, and the folds that develop in obesity at the navel and beneath pendulous rolls of abdominal fat. In these situations, where sweat retention, maceration, and infection so often occur, the clinical picture of flexural and intertriginous dermatitis develops, sometimes erroneously still called "seborrhoeic dermatitis." Evidence has accumulated that the two major sources of infection from which other sites are infected or reinfected are the nasal vestibule and the perianal region, particularly the natal cleft, where midline fissuring is so often seen.

Flora

In dealing with this problem it is essential briefly to consider the microbic flora of the healthy intact skin. Malcolm Morris (1903, p. 20) quoted Galloway as stating that a description of all the species of bacteria of the skin would probably involve notes of all the species of bacteria at that time identified by bacteriologists. Since that time bacteriologists have gradually made out a clearer picture.

Price (1938) made the important distinction between transient organisms and resident organisms, the transient flora consisting of those organisms collected fortuitously from extraneous sources—for example, handkerchiefs, dust, bath water, or other contaminated material.

Colebrook (1941) found the flora of exposed parts to be greater than that of covered parts, excepting only the perineum, on which the flora was particularly varied. The commonest organisms were staphylococci, sarcinae, non-haemolytic streptococci, diphtheroids, and aerobic spore-bearing types.

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Evans, Smith, Johnston, and Giblett (1950) found that *Propionibacterium acnes* is the commonest organism in the scapular and deltoid region and that the site of greatest growth of bacteria is the sebaceous glands, hence the flora is predominantly anaerobic. Other organisms often found are *Micrococcus epidermidis*, *Staphylococcus albus*, *M. candidus*. *Staph. aureus* is rarely found, but *Staph. albus* is sometimes haemolytic.

Pillsbury and Kligman (1954) state that on unspecialized glabrous skin the following are often found: staphylococci, lipophilic corynebacteria, lipophilic fungi (*Pityrosporum ovale* and *P. orbiculare*) and the anaerobic *Propionibacterium acnes* and *M. saccharolyticus*.

Schermann, Knox, Sher, and Rothman (1960) state that some bacterial species on the surface of the skin produce substances which keep other bacterial and fungal species in check, and also that surface bacteria probably participate in the formation of free fatty acids on the surface.

Evans *et al.* (1950) found no significant increase in the bacterial population of skin of the scapular or deltoid regions which had not been washed for a week, and Christie (1958) described two Arctic explorers who went for 100 days with "almost no contact with externally applied soap and water" without deleterious effects and only qualitative changes in the population of skin bacteria. Washing is clearly important to avoid giving offence to the nose and eye, and also for the removal of transient organisms, which are inevitably deposited on the surface of the skin from extraneous or intrinsic sources. At the other extreme is the fact that in civilized communities to-day dermatoses due to excessive exposure of the skin to harsh or medicated soaps and detergents are commoner than those attributed to extraneous dirt (as opposed to bacterial self-contamination). Itching may even be caused or aggravated in dry skin, particularly of the elderly, by too many baths.

Pillsbury and Kligman (1954) emphasize that organisms from the respiratory, gastro-intestinal, and genito-urinary tracts are constantly being deposited on the skin. Exercise and sweating may cause minor increases of skin bacteria, and under conditions of high humidity and heat *Escherichia coli* may become part of the resident flora (Pillsbury and Kligman, 1954).

It has to be remembered that no hard-and-fast line can be drawn between resident and transient organisms (Colebrook, 1941). So far as staphylococci are concerned the coagulase test (Cruickshank, 1937) is the criterion of pathogenicity. Achromic variants of *Staph. aureus* are common and are no less pathogenic than

the yellow variety (Stuart-Harris, 1948). The term "Staphylococcus albus" is therefore largely meaningless, including as it does pathogenic and non-pathogenic strains.

Transient Organisms

Concerning transient organisms, it is clear that exposed sites collect more than covered sites, apart from the perianal region, where the flora is both rich and varied.

Coagulase-positive staphylococci are often found on the skin. *Pseudomonas pyocyanea*, *Proteus vulgaris*, *E. coli*, *Streptococcus faecalis*, and *Candida albicans* are not uncommon, whereas *Str. haemolyticus* is less often found. This organism tends to disappear spontaneously from the surface of the skin, apparently from the destructive action of the fatty-acid film, made up from sweat-emulsified sebum and desquamated horn cells. *Str. haemolyticus* flourishes in serous exudates—for example, in fissures in the skin. The alkaline serum makes an excellent nutrient medium and also counteracts the protective effect of the "acid mantle."

The Gram-negative bacilli cannot survive desiccation but can thrive and multiply in humid body folds and in apocrine glands or in their secretions on the surface.

Staph. pyogenes may persist on the skin for a long time. It survives for at least a month in handkerchiefs and clothes (Elek, 1959). It resists the acidity of the skin surface and can survive desiccation and exposure to the sun.

Colebrook (1941) pointed out that washing, conscientiously carried out, is enough to remove transient organisms from the skin. The application of antiseptics to the unbroken skin surface is quite unnecessary. Medical opinion is well aware of this, but antiseptics are still advertised to the public as a necessity for the maintenance of health. Dermatological experience is that the use of antiseptics on the skin may result in eczematous sensitization, exudation, impaired resistance, and (paradoxically) infection.

Blank and Coolidge (1950) state that bacteria normally carry a negative charge, as also does the surface of the skin. As a result the skin tends to rid itself of bacteria. Soap, by its alkalinity, raises the pH of the keratin above the isoelectric point and in so doing increases its negative charge and so facilitates the removal of bacteria from the surface. On the other hand, quaternary ammonium compounds convert the surface charge to positive, causing attraction between bacteria and the surface of the skin. The result is an illusory reduction of the surface bacterial population when swabbing is performed.

Different workers have described skin carrier rates for *Staph. pyogenes* of 5 to 30% when single samples are taken, but Williams (1946) recovered the organism from 70% of normal skins when 11 different sites were sampled. Storck (1948) recovered them from 92% of eczematous lesions. MacKee, Lewis, Pinkerton, and Hopper (1939) noted that the scalp and the covered areas of the trunk, when free from septic spots, rarely carried coagulase-positive staphylococci, the predominant carriage being on the face and hands. Gillespie, Devenish, and Cowan (1939) found in students 43.4% carriage in the nose, 19.5% on the skin, and 12.6% at both sites.

Sites of Infection

Hobbs, Carruthers, and Gough (1947) and Valentine and Hall-Smith (1952) found that the organisms on the

skin were usually of the same serological type as those recovered from the nose, and Tulloch (1954) found identical strains in nose and skin lesions in 88.2%.

Mercier, Pillet, and Le Mer (1948) described the nose as the main reservoir of pyogenic staphylococci. Whence come the remainder? Are they extraneous or do they come from other sites of carriage? Elek (1959) states that, apart from animal infections and the rare cases where staphylococci multiply in some article of food, the only reservoir is man. Spread by clothing dust is more important than air infection by droplet nuclei. The conjunctivae often harbour staphylococci, as also does the nasopharynx. *Staph. pyogenes* is a normal constituent of the human faecal flora, the survival of staphylococci in stools being profoundly affected by the coliform bacilli present: the greater the number of coliforms the more the staphylococci are inhibited. Other sources mentioned by Elek include wounds, crockery and feeding utensils, swimming-pools, syringes, carcasses, flies, bed bugs, bank notes, telephones, and nasopharyngeal dog carriers. Clinical experience points to the anal region as a second vitally important source of cutaneous infection, possibly even as important as the nasal vestibule itself.

Pillsbury and Kligman (1954) write: "After an injury to the skin, the only source of pathogens which need be seriously considered are bacteria which have been introduced from without, or from some focus within the body, such as the nasopharynx or the gastrointestinal tract. There is no indication that infection occurs from airborne contaminants with any regularity." Gleeson-White (1960) has emphasized that although the human nose is by far the greatest single source of pathogenic staphylococci the importance of contamination from the faeces of nasal carriers of staphylococci is often overlooked, and Brodie, Kerr, and Sommerville (1956) wrote that it seemed reasonable to suppose that the "weight" of organisms released to the environment by the faecal carrier greatly exceeds that of the organisms released by the nasal carrier. Ridley (1959) concluded from a study of 50 male adults that 22% had sufficient contamination of the skin of the perineum with staphylococci to classify them as perineal carriers; 12% were heavy nasal carriers as well. Ridley points out that one reason for heavy carriage in this site may be the presence of apocrine glands, which are also found in the nasal vestibule and in the aural meatus.

Russell (1956) found from taking swabs from multiple sites (nasal vestibule, palpebral fissure, aural meatus, paronychia fold, and other skin folds) of 100 patients with extensive infected dermatoses that approximately 67% were pyogenic staphylococci, 12% haemolytic streptococci, and 21% Gram-negative bacilli or faecal streptococci. From individual patients *Staph. pyogenes* and/or *Str. haemolyticus* were recovered in 62, mixed infections with pathogenic cocci and Gram-negative organisms or faecal streptococci occurred in 37, while *C. albicans* alone was recovered from all sites in one case. It was pointed out that the infection was conveyed from one site to another by the fingers, particularly when hygienic standards were poor or when paronychia infection was present. Livingood and Mullins (1952) gave the following figures for 710 patients with various types of cutaneous pyogenic infections: *Staph. aureus*, 67%; *Str. haemolyticus*, 36%; *Staph. aureus* and *Str. haemolyticus*, 26%; coliforms, 12%; *Proteus*, 10%; *Pseudomonas*, 7%; *Alcaligenes faecalis*, 3%.

Keogh and Russell (1956), in a study of 100 patients with otitis externa, emphasized that there is a predisposition to otitis externa in individuals with itchy or infective dermatoses elsewhere on the body. Organisms of intestinal origin but not including staphylococci were recovered from 56 of their 100 patients, from which it may be inferred that if a proportion of the staphylococcal infections were also of intestinal origin a preponderance of all cases of otitis externa can be attributed to this source.

In a recent survey of the sites on the surface of the body from which Gram-negative bacilli or faecal streptococci were recovered in 250 cases the findings were: aural meatus, 50; ulcer cruris, 49; nasal vestibule, 44; pubis, groin, vulva, perineum, 31; finger (paronychia fold), 23; axilla, arm, forearm, hand, 18; scalp, face, neck, 16; thigh, foot, toe webs, 8; trunk, 7; conjunctival sac, 4.

It is a significant pointer to the means of transmission that just over a half (126 cases) were either orificial or digital infections. Presumably the heavy infection of leg ulcers occurs either by digital transference or from underwear, bedwear, bedding, or gravitationally. The tendency of the nose to be infected from the anal region is significant as showing that infections may come to the nose as well as be transmitted from it by the fingers. Many of the nasal swabs were taken from the nasal vestibule in the absence of physical signs of local infection, purely to exclude nasal carriage of pathogenic organisms.

Recognition of Different Strains

The susceptibility of organisms to a variety of antibiotics can be used to indicate with some degree of precision the identity or difference of strains of infecting organisms. Edmunds, Elias-Jones, Forfar, and Balf (1955), commenting on this procedure, state: "While this method of labelling lacks the precision of serological and phage-typing methods, it does enable recognition of different strains to be achieved with a high degree of probability, although two strains giving the same pattern may not necessarily be identical."

Even if it cannot always be accepted that the particular organisms recovered are responsible for the observed clinical condition it can at least be said that antibiograms act as pointers to the source of infection. Russell found, in 124 cultures from the nose and from skin lesions, that 63 were similar (*Staph. pyogenes* 62, *Proteus vulgaris* 1), and 61 were dissimilar.

Of these, 16 had nasal carriage of staphylococci giving a different antibiogram from that of the staphylococci recovered from the skin lesion; five had nasal carriage of Gram-negative bacilli but not of staphylococci; and from 40 no pathogenic organisms were recovered from the nose.

An example of the value of the antibiogram is shown below. The patient had an infective dermatitis of the scalp, ears, axillae, submammary folds, umbilicus, genitocrural folds, and natal cleft, where there was a midline fissure.

		Chloram- phenicol	Neo- mycin	Tetra- cycline	Baci- tracin
Nose	Pr : <i>Staph. pyogenes</i>	+	+	+	+
Ear	Pr : <i>Str. haemolyticus</i>	+	—	+	+
Submammary fold	Sc : "	+	—	+	+
Natal cleft	Pr : <i>Staph. pyogenes</i>	+	+	—	+
	Pr : <i>Str. haemolyticus</i>	+	—	+	+

Pr = Profuse. Sc = Scanty.

It is reasonable to conclude that this infection did not originate from the nose but probably came from the fissure in the natal cleft.

An extreme example of mixed infection was recently seen in which swabs revealed four different organisms in different sites. The patient had a widespread infective dermatitis: nose, *Staph. pyogenes*; ear, *Pr. vulgaris*, *C. albicans*; wrist, *Staph. pyogenes*, *Pr. vulgaris*; axilla and genitocrural fold, *Ps. pyocyanea*.

Mixed infections in which two or three different organisms are present in one skin lesion are relatively common. Sometimes two strains of staphylococci occur in the same lesion.

Seborrhoeic Dermatitis

This evidence suggests that "seborrhoeic dermatitis" is in fact an infective dermatitis of body flexures, pilosebaceous and apocrine units, originating from the nose or the perineum, the organisms responsible usually being staphylococci alone, sometimes with Gram-negative bacilli in addition. The chief predisposing factor is any cause of widespread pruritus, particularly if the anogenital region becomes involved. Emotional disturbances and contact sensitizers are more important in this respect than drugs or organisms which cause toxic eruptions.

Malcolm Morris (1903, p. 508) evidently thought on somewhat similar lines when he wrote of seborrhoea: "It is not unlikely that more than one micro-organism may take a part in the production of the affection, or further invasion may take place after the process has been started. This would help to explain the differences in the appearance and severity of the disease."

The adjective "seborrhoeic" is clearly inappropriate when it is tagged on to dermatitis to describe a clinical condition which is often seen in individuals without seborrhoea and sometimes even in those with xeroderma. Hyperidrosis may be an important factor but not seborrhoea, and in the truly seborrhoeic disease acne vulgaris staphylococcal infection does not seem to be a major feature.

Another interesting fact is the relative rarity of secondary infection in Besnier's prurigo, a condition in which the face, neck, cubital and popliteal fossae, wrists, and ankles are often affected with gross excoriation and lichenification but not the anogenital region.

Paronychia

Studies of chronic paronychia have also supported the view that the anogenital region is an important source of self-infection. In this condition the predominant organism is *C. albicans*, although Gram-negative bacilli are also often recovered in both abundance and variety. *C. albicans* is also often recovered from the skin in angular cheilitis. Fox and Ainsworth (1958) found it in 70% of cases. *Candida* is also found in some cases of balanitis, vulvitis, and pruritus ani, and in interdigital infections on the hands or feet, also occasionally in the nose, ear, and flexures.

Frain-Bell (1957) found *C. albicans* in 70% of 590 patients with chronic paronychia. This organism can be recovered from the gut in most normal persons. Marten (1959) recovered *C. albicans* from 97% of the paronychia folds of his patients with chronic paronychia and in 50% of the rectal swabs and 75% of the mouth swabs taken from them. In 10 out of 12 cases where it was possible to type the *Pr. vulgaris* recovered from

the gut and from the paronychia folds the strains were identical.

Whittle, Moffat, and Davis (1959) showed that the right middle finger is most often affected and pointed out that in cleaning the perineal skin after defaecation this was the finger most likely to be contaminated in right-handed persons. In Frain-Bell's series the digits most affected were the right middle, right index, and left middle finger, in that order.

The incidence of candida infections has been increased since the introduction of antibiotics (Murray, 1954).

Ps. pyocyanea

The increased danger of infections with *Ps. pyocyanea* has also recently become apparent, confirming Miles's (1944) forecast of the danger of the emergence of infections with coliform organisms. Stuart-Harris (1948) pointed out that the pyogenic properties of coliforms, proteus, and pyocyanea bacteria render them important antagonists of healing of deeper lesions of the skin, and their resistance to some antibacterial agents which are effective against staphylococci and streptococci increases their importance. Livingood and Mullins (1952) expressed the view that proteus and pyocyanea infections were increasing.

Yow (1952) called attention to a relative increase in the incidence of infections due to pseudomonas. Howe (1951) described invasive infections due to this organism, which in the past had usually been regarded as a benign contaminant.

Barber (1961) thought it the greatest menace of the Gram-negative bacilli, beginning to rival *Staph. pyogenes* as the hospital scourge. Curtin, Petersdorf, and Bennett (1961) reported 88 cases of *Ps. pyocyanea* bacteraemia in some of which it was thought that the portal of entry was the skin or the ear. Finland, Jones, and Barnes (1959) report a sixfold increase of Gram-negative septicaemias since the introduction of antibiotics. The organism may prove resistant to antiseptics, antibiotics, and physical agents. Previous treatment with corticosteroids may also play a part (Williams, Williams, and Hyams, 1960).

The relation of eczema to infection is another fascinating subject. Storck (1948) found a raised level of Gram-negative rods in erythematous-squamous foci, acutely infiltrated erythematous foci, psoriasiform foci, vesiculo-crustose discharging foci (highest), and lichenified foci, but virtually nil in normal skin or in erythematous-papular foci. He pointed out that the tendency to massive contamination, even in primarily germ-poor oozing foci of eczema, is undeniable. Patch tests to slightly abraded surfaces of skin with cultures and filtrates of bacteria from eczematous foci gave positive reactions to *Staph. aureus* in 68%, *Str. haemolyticus* in 24%, *E. coli* in 11%, *Staph. albus* in 6%, and enterococci in 4%. Controls with healthy skins also sometimes gave strong reactions to cultures and filtrates, and Storck regarded these individuals as potential candidates for bacterial eczema.

It is certainly impressive to observe clinically how well eczematous lesions often respond to antibiotics or to antibacterial agents such as chlorhydroxyquinoline.

Lipophilic Organisms

I wish now briefly to discuss the possible relationship of the lipophilic organisms to seborrhoeic dermatitis and acne vulgaris. Barber (1948) considered that the

Pityrosporum ovale of Malassez, multiplying in the stratum corneum, is the cause of simple pityriasis, its growth being stimulated by circulating androgens and inhibited by oestrogens. Martin-Scott (1952) concluded that this organism is a non-pathogenic saprophyte, being recoverable from normal adults as often as from seborrhoeic subjects. He could not reproduce lesions by application of the patient's own strain of organisms to the skin.

Similar views have been expressed about the acne bacillus, but recently the role of this organism in acne has come up for review. Malcolm Morris (1903, p. 387) expressed the view that it was not improbable that a specific micro-organism would be discovered as the cause of acne. Unna, Sabouraud, and Whitfield thought that the comedo was a cystic reaction of horn cells to the presence of acne bacilli multiplying in the infundibulum of a pilosebaceous follicle. Fleming (1909) produced pustules by rubbing into the forearm of a patient with acne a broth culture of the organism but failed to do so in one who was free from acne. Many authors have stressed the efficacy of antibiotics in the treatment of acne, although it has often been claimed that the pustules of acne are sterile on culture; but Evans *et al.* (1950) have pointed out that anaerobes outnumber aerobes by 10 to 1 on the skin of the back, mostly living in the sebaceous glands and ducts. Smith and Waterworth (1961) observed Gram-positive rods, morphologically acne bacilli, in 59 of 67 patients and were able to grow *Corynebacterium acnes* in 57. The bacilli are sensitive to several antibiotics. Clinically the best results have usually been obtained with wide-spectrum antibiotics, such as tetracycline. However, Smith and Waterworth (1961) found little alteration in the bacterial flora from acne lesions after courses of chemotherapy of up to three months and no increased resistance to the antibiotic prescribed. It has been suggested that the efficiency of antibiotics is due to their effect on the intestinal flora, but Baer and Brodie (1960) gave nystatin and neomycin to acne patients without benefit. It still remains a possibility that antibiotics relieve acne, when they do, by some drug action other than the antibiotic one, as suggested by Cronk, Naumann, and Garrison (1956). Acne is undoubtedly a disease with multifactorial causes, and Grant (1957) has called attention to the importance of hairs as follicular "wicks" in maintaining the health of follicles. In acne he found the number of hair follicles in which both mature hair and succeeding hair are visible was reduced, and demonstrated retained coiled-up hairs beneath comedones.

It may be that acne results from a chain of factors, something as follows. On the background of an inherited tendency to seborrhoea, androgenic stimuli at puberty cause hyperkeratosis and increased seborrhoea, and this encourages the growth of *P. ovale* and *Propionibacterium acnes*. The latter uses up oleic acid in the sebum and ferments glucose, with the production of propionic acid, which, in the view of Pochi and Strauss (1961), may itself play an important part in the genesis of acne. As a result, the physical properties of the sebum within the pilosebaceous units may be modified, as, for example, by increased viscosity with resultant retardation of flow to the surface and impaired lubrication of the hair shafts. (The contents of follicles in acne are semisolid and cheesy, in contrast to the glairy mucoid contents of the follicles in rosacea.) At sites where there are small hairs and large sebaceous

glands, if there is any delay in sequential hair growth, horn cells are enabled to grow over the follicular orifice and thus prevent the hair from extruding itself. The unextruded hairs then act as foreign bodies, at first disrupting the pilosebaceous units, with the formation of papules, pustules, and cysts, and later bursting through the walls of the follicles into the dermis, causing fibrosis, scarring, and keloid formation.

It is true that Boughton, MacKenna, Wheatley, and Wormald (1959) did not find any abnormality in the composition of sebum in acne vulgaris, before and after treatment, as shown by a study of the surface skin lipid fatty acids. However, the key to the mechanism of acne formation is probably to be found in the physical, chemical, and bacterial study of the sebum actually within obstructed follicles.

Rosacea

Finally, I want to say a few words about rosacea, in which a heavy infestation with the *Demodex folliculorum* is the rule. This organism has been regarded by many as a harmless parasite because it can so often be found in the follicles of individuals without skin disease. Malcolm Morris (1903, p. 387) described this parasite as occurring in comedones but that it appeared to have no aetiological importance. He portrayed it in his textbook in a plate showing skin parasites, a veritable sheep among wolves. Nevertheless, in rosacea the infestation is sometimes enormous, as shown in the picture reproduced in the article by Ayres and Ayres (1961). Mr. Syms, of St. John's Hospital, tells me he has recovered as many as 60 demodices from material removed from the orifices of six follicles in one patient. St. John's Hospital findings (J. Oliver, 1961, personal communication) show an incidence of infestation of approximately 7/8 in rosacea, 1/4 in normal controls, and 1/9 in acne vulgaris. In dogs the species *D. canis* causes loss of coat and its presence is usually accompanied by staphylococcal infection, the two together giving the typical follicular mange (Hughes, 1959).

Spickett (1961), from a study of *D. folliculorum*, concludes that the male is found only in the follicular openings. The gravid female passes to the sebaceous gland for ovideposition (explaining the absence of ova in follicular orificial scrapings which so often reveal *Demodex* parasites in abundance). The larva gradually moves towards the surface. Half of the parasites within the follicular orifice are dead, and dead mites tend to block up the follicular orifices and to discourage fresh infestations.

Ayres and Ayres (1961) describe two conditions which they regard as being causally related to *Demodex* infestation—namely, pityriasis folliculorum and the "external" type of rosacea. They believe that the use of facial cleansing creams instead of soap for washing the face may be partly responsible. It is certainly true that many patients with rosacea get relief from the topical application of sarcopticides. Sulphur is the traditional remedy, and benzyl benzoate or crotamiton is sometimes effective. This problem demands solution by well-controlled trial, because rosacea also has a tendency to spontaneous remission. Not all patients improve with sarcopticides, possibly because the clinical picture called rosacea is of complex aetiology. Emotional disturbances and faulty eating and drinking habits are clearly often important, and

perhaps it is only in the follicular papular variety of rosacea that *Demodex* plays a part. Basically there is persistent flushing of the face in all cases, and Sequeira defined rosacea as vasolability in a seborrhoeic individual.

It seems unlikely that rosacea is a condition of allergic hypersensitivity to the *Demodex* or to its products. In states of allergy to bacterial infections the organisms present in the skin lesions are few in number and difficult to find. In rosacea the parasites are numerous and it seems likely that in this disease the *Demodex* can breed freely because of particularly favourable living conditions resulting from vascular dilatation and seborrhoea. The resultant over-population of the follicles causes inflammatory changes and the physical signs of rosacea, which histologically often show evidence of a foreign-body reaction.

Attempts to reproduce rosaceous lesions by the application to the skin of material removed from rosaceous papules fail, in my experience, possibly because, as Spickett has suggested, most of the parasites within the ostia of the follicles are dead. It may also be that the population of any one follicle has to reach a critical level before clinical rosacea is produced, and that the papular lesions of rosacea are in the nature of whitened sepulchres.

Summary

In coccal, Gram-negative, and candida infections of the skin an intrinsic source of infection is usual. The nasal vestibules and the ano-genital region are the main sources of infection, often with secondary reservoir sites in the external auditory canals, paronychia folds, and body flexures. While extraneous sources may replenish the nasal vestibule, the ano-genital, aural, paronychia, and flexural infections are essentially intrinsic.

The logical conclusion is that the shower-bath and the bidet are more effective pieces of bathroom equipment than the bath.

In acne vulgaris and rosacea it is probable that the acne bacillus and *Demodex folliculorum* respectively have important contributing roles in two conditions of complex aetiology.

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ANTICOAGULANTS IN ACUTE MYOCARDIAL INFARCTION

A CLINICOPATHOLOGICAL STUDY

BY

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Recently the controversy about the place of anticoagulant therapy in the management of myocardial infarction has centred on the problem of the long-term administration of anticoagulants to those patients who have survived the acute stage of the illness. It would be wrong to assume from this that the value of anticoagulant drugs in the treatment of acute myocardial infarction has been firmly established. It is true that the majority of clinical reports have demonstrated that anticoagulant therapy lowers the mortality rate and prevents a significant number of clinically detectable thrombo-embolic complications in the first four to six weeks after cardiac infarction. Most clinicians, impressed by these results, now use anticoagulants routinely unless there is some obvious contraindication. Others remain unconvinced and use these drugs occasionally or not at all.

One of the disturbing features to the protagonist of anticoagulant therapy is the conflicting nature of the available pathological information. When clinicians prescribe anticoagulants for patients with myocardial infarction they hope to prevent further thrombo-embolic episodes such as coronary thrombosis, intracardiac mural thrombus formation and systemic arterial embolism, and venous thrombosis and pulmonary embolism. We should therefore expect that pathologists would find a decreased incidence of these thrombo-embolic manifestations in patients dying of myocardial infarction who have been treated with anticoagulants. The evidence that this is so is far from convincing. On the other hand, the suggestion has been made that anticoagulant therapy may increase the incidence of haemopericardium both with and without cardiac rupture as a cause of death in myocardial infarction.

Literature

In the study conducted by the American Heart Association (Wright *et al.*, 1954) the pathological material showed a significant reduction of both mural thrombi in the heart and extracardiac thrombo-embolic

complications in the anticoagulant-treated cases. In this country, however, Gilchrist and Tulloch (1956) reported that their necropsy experience failed to show any significant reduction in the incidence of mural thrombi or peripheral infarcts in cases where anticoagulants had been used, but they did find a marked fall in the number of pulmonary infarcts. From the published results of others who have studied this problem from the pathological evidence a somewhat confusing picture emerges. For example, Lee and O'Neal (1956), in a survey of 500 necropsies, found that the incidence of thrombi within the heart, pulmonary embolism, and systemic arterial embolism was the same in necropsy cases examined before and after the introduction of anticoagulant therapy. In a more recent study (comparing 50 treated and 50 non-treated cases) Capeci and Levy (1959) reported similar findings.

On the other hand, Howell and Kyser (1954) found a significant reduction in the incidence of mural thrombi within the heart in cases where anticoagulants had been given, and Glueck *et al.* (1956) noted that anticoagulant therapy not only reduced the frequency of embolic episodes but also reduced the number of individual emboli in each case. Conrad and Rothermich (1959) in a good clinicopathological study compared the mortality rate and the incidence of thrombo-embolic complications in 623 cases. These were divided into three groups: those who did not receive anticoagulants, those who were adequately treated with anticoagulants, and those who were inadequately treated with anticoagulants. They found that anticoagulant therapy, whether adequate or inadequate, lowered the mortality, but at necropsy only the adequately treated cases showed an appreciable reduction in thrombo-embolic complications; the incidence of thrombosis and embolism was approximately the same in the untreated and inadequately treated groups. Hilden *et al.* (1961) were unable to demonstrate that anticoagulant therapy caused a definite reduction in the mortality from acute