OCCASIONAL REVIEW

SKIN MICROBIOLOGY: COMING OF AGE

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In 1965, Mary J. Marples' seminal book *The Ecology of Human Skin* was published, as also was Maibach and Hildick-Smith's *Skin Microbiology: Its Relation to Clinical Infection*. Skin microbiology as a subject with its own intrinsic interest and also one that contributes to other disciplines may, therefore, be said to be fast approaching maturity. It is interesting to examine the changes that have occurred in this time, but it is essential to understand that, in the early years, appreciation of the intrinsic interest of skin microbiology was limited; skin was simply another surface that needed disinfection before surgery. It is convenient to discuss the evolution of the subject in three principal parts: (i) a more precise definition of the skin microflora, (ii) interactions between members of that flora (coactions), and (iii) interaction between the flora and the host. Finally, some lacunae in our present knowledge will be explored.

The resident skin flora

Before the work of Marples (1965) it was thought possible to dismiss the normal skin flora as comprising micrococci and diphtheroids with a few yeasts. Now we expect a normal healthy adult to carry several representatives of the genera *Staphylococcus*, *Micrococcus*, *Propionibacterium*, *Corynebacterium*, *Brevibacterium* and *Acinetobacter* as well as *Pityrosporum* as resident members of the normal skin flora. There will also be a variable number of transients or contaminants.

The cocci. The greatest changes in our knowledge of taxonomy and ecology have occurred amongst the gram-positive cocci. At the time of Baird-Parker's initial attempts to define the cocci (Baird-Parker, 1965), the genera *Staphylococcus* and *Micrococcus* (*Sarcina*) were regarded as closely related; taxonomically, they must now be regarded as very distinct. Baird-Parker's (1965) schemes have now largely been superseded but they were instrumental in opening the way to a rational study of the cocci. There is still no full agreement on the classification of the cocci but the major historical trends are shown in table I. The major error in laboratory studies with the cocci, as later with the coryneforms, was overconfidence in simple 'biochemical' tests, so that *Micrococcus* spp. were classified amongst the staphylococci. Later work

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TABLE I

Some steps in the evolution of the classification of the Micrococcaceae

Baird-Parker (1963)	Baird-Parker (1974)	Kloos and Schleifer (1975 <i>et seq.</i>)*
<i>S. aureus</i>	<i>S. aureus</i>	<i>S. aureus</i>
<i>S. species</i> (5 biotypes)	<i>S. epidermidis</i> (4 biotypes)	<i>S. capitis</i> <i>S. cohnii</i> <i>S. epidermidis</i>
<i>M. species</i> (5 biotypes)	<i>S. saprophyticus</i> (4 biotypes)	<i>S. haemolyticus</i> <i>S. hominis</i> <i>S. saprophyticus</i>
	<i>M. species</i> (? 4 biotypes)	<i>S. simulans</i> <i>S. warneri</i> <i>S. xylosum</i> <i>*S. auricularis</i> <i>*S. carnosus</i> <i>*S. hyicus</i> <i>*S. intermedius</i> <i>*S. saccharolyticus</i> <i>*S. sciuri</i> <i>M. krystinae</i> <i>M. luteus</i> <i>M. lylae</i> <i>M. nishinomiyaensis</i> <i>M. roseus</i> <i>M. sedentarius</i> <i>M. varians</i>

M. = *Micrococcus*, S. = *Staphylococcus** More recent species of *Staphylococcus* have been described by several authors, usually including either K. H. Schleifer or W. E. Kloos.

showed that, whereas *Staphylococcus* spp. possess low G+C ratios (30–40%), *Micrococcus* spp. possess high G+C ratios (66–75%) and, therefore, cannot be considered to be closely related. Indeed, according to Stackebrandt and Woese (1979) *Micrococcus* spp. may be more closely related to *Arthrobacter* than to *Staphylococcus*. The collaboration in the mid 1970's of a geneticist and a cell wall chemist caused a fundamental swing in coccal taxonomy with the definition of 11 species of *Staphylococcus* and seven species of *Micrococcus* (Kloos and Schleifer, 1975), to which others are still being added. There are those who dissent from this "splitters" view of taxonomy and maintain that the original scheme, with some modifications, is more satisfactory; thus Marples (1981) would expand the classification scheme of Baird-Parker (1974). The merits and demerits of these schemes may be lost in an uncritical acceptance of the API method of classification which is convenient and available commercially in kit form; the API STAPH method is based, generally, on the Kloos and Schleifer system.

The various schemes have made it clear that a wide variety of staphylococci and micrococci inhabit human skin and that some have currently unexplained preferences for different habitats. *S. epidermidis* and *S. hominis* are the species recovered most frequently, but *S. epidermidis* colonises the upper part of the body preferentially; this may be related to the greater production of sebum. Relatively few surveys of the skin flora have been performed since the general promulgation of the Kloos and Schleifer scheme, but enough has been done to show that there are differences between age

groups and between populations in the carriage of the cocci (Noble, 1981). Much more will need to be done before we have a clear knowledge of the coccal flora of human skin.

Baird-Parker (1965) defined the two opportunist pathogens amongst the cocci; *S. epidermidis* (SII) is a wound invader, especially where a foreign body such as a catheter or prosthesis is involved, and the M3 complex are urinary tract pathogens in young women outside hospital. The ecologically unsatisfactory situation in which M3 strains could be found in other, completely disparate habitats such as the scalp, was more or less resolved by the Kloos and Schleifer scheme that divided the M3 complex into *S. saprophyticus* that colonises and invades the urinary tract, and *S. cohnii* and *S. warneri* that are found elsewhere (Namavar, de Graaff and MacLaren, 1978). The current problems in understanding the source and behaviour of multiresistant "*S. epidermidis*" isolates that cause catheter-associated sepsis or necessitate revision of implanted prostheses, may be resolved by an ecological approach. Such problems are a legacy of the view that the coagulase-negative cocci are unimportant.

The rods. The coryneforms remain in a worse taxonomic state than the cocci, but this is resolving slowly. The initial problems stemmed from an assumption that only one genus of coryneform was resident on human skin. In theory, it should then have been possible to devise schemes for the identification of species based upon classical biochemical tests. Three tests dominated the minds of skin microbiologists in relation to the coryneforms—lipophilia, lipolysis and porphyrin production (UV fluorescence); to some extent this was a product of a clinical and ecological approach. To many workers it seemed obvious that because many skin coryneforms lived in the lipid-rich environment of the face and upper thorax, the ability to hydrolyse lipid and the apparent need for lipid to permit growth on agar would prove to be of prime importance in classification. Porphyrin production was seen as a clinical marker for the "species" that "caused" the mild skin infection erythrasma, in which the scaly skin lesions fluoresce coral pink if exposed to UV light. Somerville (1973) had pursued classification of the skin coryneforms most avidly and her scheme promised some ecological success; for example, most nasal strains reduced nitrate and seemed fairly recognisable on agar media. Others produced similar schemes. However, the recognition that these schemes were less than wholly successful led Pitcher (1977) to perform cell wall analyses of cutaneous coryneforms. He found that the classical *Corynebacterium* spp. that possess *meso*-diaminopimelic acid (*meso*-DAP), arabinogalactan and mycolic acids in the cell wall formed only *c.* 60% of cutaneous coryneforms (table II). Another 20% of strains lacked arabinose and mycolic acids and were species of *Brevibacterium*; a small percentage represented a new genus that contained LL-DAP and arabinose and the remainder were probably environmental contaminants that contained ornithine or lysine. The composition of the flora was very dependent upon the source of the samples. Identification of the species of coryneforms has proceeded at a very slow rate however. There are two basic reasons for this. One is the technical problem that modern descriptions of new species demand that DNA homology studies be performed and the coryneforms have proved singularly reluctant to yield sufficient DNA for this to be done. The second reflects a past deficiency in that new taxa are found that have no representatives in the various national culture collections. This is seen clearly in a recent study by Jackman (1982*a*) in which two new taxa are seen in a dendrogram of axillary coryneforms; the named collection strains cluster elsewhere.

TABLE II
Current taxonomic status of cutaneous coryneforms

Genus	Cell wall composition	G + C ratio	Comments	Percentage of aerobic skin coryneforms
<i>Corynebacterium</i>	meso-DAP arabinogalactan mycolic acids	a) 51–61% b) 67–70%	Poorly speciated except for <i>C. diphtheriae</i> complex Some probably overlap with <i>Rhodococcus</i>	60
<i>Brevibacterium</i>	meso-DAP galactose	62–67%	One, perhaps two, species inhabit skin	20
" <i>P. aerobicum</i> "	LL-DAP arabinose	...	? aerobic <i>Propionibacterium</i>	5
...	lysine/ornithine various sugars	...	Probably contaminants but may contain true inhabitants	15
<i>Propionibacterium</i>	LL-DAP	57–63%	Three species inhabit skin All adults colonised by <i>P. acnes</i>	...

Based on Noble (1981); Pitcher (1983).

Anaerobic coryneforms, now acknowledged as *Propionibacterium* spp. had been recognised and separated from the aerobes at an early stage, but skin microbiologists were reluctant to acknowledge this. Studies by Johnson and Cummins (1972) showed that *Propionibacterium* was a distinct genus and it was later agreed that three species commonly inhabit human skin. *P. acnes* and *P. granulosum* are found on skin with a high sebum content; *P. acnes* is, numerically, the most dominant and is found essentially in all post-pubertal individuals whereas *P. granulosum* is found regularly in 10–20% of individuals and then in numbers about 100–1000 fold fewer than *P. acnes*. The third species, *P. avidum*, is found in the axilla and seems to need conditions with a high availability of water rather than the presence of abundant lipid.

Our inability to give names to coryneforms found on skin is reflected in the uncertainty with which clinical microbiologists regard coryneforms isolated from blood-culture specimens. The ability to distinguish those coryneforms unlikely to be of skin origin would surely be of value in deciding the "significance" of their isolation from blood.

Gram-negative bacilli. Amongst the gram-negative bacilli resident on the skin, the greatest change has been the lumping together of *Mima polymorpha* and *Herellea vaginicola* as varieties of a single species, *Acinetobacter calcoaceticus*. Here too, recent views are tending to modify the picture. It seems possible that skin strains, "pathogens" and environmental strains may be distinct. Again, this has been brought about by an increasing awareness of *Acinetobacter* spp. in infections. Although these are frequently of the very old, the very young or the debilitated, studies from Center for Disease Control, Atlanta (Retalliau *et al.*, 1979), show a summer peak of infection, especially in young men, a trend which is the reverse of that for most other pathogens. It seems likely that this is a reflection of the greater rate of sweat production in males, particularly in hot weather, which leads to greater colonisation of the skin (Kloos and Musselwhite, 1975) with consequent scope for colonisation and infection of surgical wounds.

Fungi. Formerly, the skin fungi were thought to comprise the two yeasts of the genus *Pityrosporum*, *Pi. orbiculare* and *Pi. ovale*, that were separated principally by cell

shape, *Malassezia furfur* (a filamentous fungus found in pityriasis versicolor), the dermatophytes, and a variable collection of yeasts inhabiting the various body cavities and specialised sites such as the toe webs but not the general skin surface. It is now accepted generally that *Pi. orbiculare* can exist as a yeast (*Pi. orbiculare*) or in a mycelial form, formerly known as *Malassezia furfur*; there is also a strong suspicion that *Pi. ovale* and *Pi. orbiculare* may represent only one species (Faergemann, 1979). Modern taxonomic techniques have not been applied to these organisms. Chemotaxonomy has been applied to the dermatophytes but has not yet modified the general view on the way these organisms are inter-related, but some reservations may now be necessary about the validity of the various species. It may be inappropriate to apply prokaryote standards to eukaryotes, but the findings of Davison, Mackenzie and Owen (1980) that the G + C ratio of 34 species belonging to three genera of dermatophytes fell within the range 48.7–50.3% could be interpreted as meaning that only a single species of dermatophyte exists. Davison's study of DNA-DNA hybridisation amongst the dermatophytes offers a more valuable, if more cumbersome, method of analysing the relationship between strains (Davison, 1983). Studies of isoenzymes (Jones and Noble, 1982) and of dermatophyte sterols (Jones and Mallet, 1983) also seem to offer more rational ways of classifying this group but, generally, come to the same classificatory conclusions as the original, more botanic studies.

Coactions between cutaneous inhabitants

Antibiotic production. Studies of coactions have centred on antibiotic production as an inhibitory factor between skin microorganisms. Although Selwyn's group has reported probiotic production (Selwyn and Ellis, 1972) this has not generally been taken up.

Amongst the bacteria, most attention has been paid to the peptides, probably cyclic, of mol. wt *c.* 1000, produced by the staphylococci and, to a lesser extent, by coryneforms (Selwyn, Marsh and Sethna, 1976; Noble and Willie, 1980*a*; Al-Admawy and Noble, 1981). There is disagreement about the prevalence of antibiotic production amongst skin bacteria but it seems improbable that more than *c.* 5% of the staphylococcal flora of the skin produce cyclic peptides. Other substances are undoubtedly produced as demonstrated by the work of Holland, Cunliffe and Eady (1979) who found that cocci inhibit *c.* 3% of other cocci but *c.* 20% of *P. acnes* strains. However, these workers emphasised that care is needed in interpreting inhibition phenomena on agar media unless a specific chemical agent can be extracted and identified.

Production of antibiotic *in vivo* has been shown experimentally by Selwyn *et al.* (1976) in pigs and by Noble and Willie (1980*b*) in mice. Noble, Lloyd and Appiah (1980) used antibiotic-producing staphylococci, including a strain of *S. aureus* that produced a bacteriocin, not a peptide, to suppress skin infection by the actinomycete *Dermatophilus congolensis* in a mouse model. Antibiotic is, therefore, clearly produced *in vivo*. Selwyn (1975) reported that patients who possessed an antibiotic-producing skin inhabitant were colonised by *S. aureus* significantly less often but Noble and Willie (1980*a*) were not able to substantiate this. Changes in patient populations and in the method of demonstrating antibiosis may prevent agreement. At St John's Hospital, therapy of three patients infected with *S. aureus* has been attempted

with a staphylococcal strain that was a good inhibitor in in-vivo experiments. In each case, other forms of therapy had proved wholly inadequate. The results were not clear cut. In one instance, the *S. aureus* infection was too deeply seated to be eradicated by a "non-pathogenic" *S. epidermidis*, which may be related to the findings of Noble and Willie (1980b) that inhibition did not occur regularly in a subcutaneous model of infection in mice in contrast with surface models. One patient with chronic granulomatous disease developed a folliculitis caused by the implanted strain, although the *S. aureus* that was causing deeper lesions was eliminated. The third patient, a 10-month-old with severe staphylococcal superinfection of a congenital blistering disease, was probably relieved of the *S. aureus* by the measures taken before the application of the antibiotic producer. This lack of success contrasts with the results reported for the use of *S. aureus* strain 502A in therapy. Aly, Shinefield and Maibach (1982) have reviewed experience with this organism and confirm its usefulness in the suppression of chronic furunculosis. The mechanism of coaction does not seem to be known; strain 502A is certainly not an antibiotic producer. Nevertheless, the potential for the therapeutic or preventive use of inhibitor producers warrants further attention, especially in animal infections such as that described by Noble *et al.* (1980).

Amongst the dermatophytes there is increasing knowledge of antibiotic production; representatives of dermatophytes may produce penicillins, 6 amino-penicillanic acid, fusidic acid and several uncharacterised substances that include antibacterial, antifungal and anticancer compounds. The characterisation of these compounds has lagged sadly behind the recognition of their existence. In man, penicillin production has been shown to suppress the bacterial flora in fungal lesions but also to select a penicillin-resistant flora (Youssef *et al.*, 1978, 1979). In-vitro and in-vivo models of dermatophyte infection with superimposed staphylococcal colonisation have shown that penicillin-resistant cocci can be selected in controlled conditions (table III) (Ryall, Holt and Noble, 1981; Noble, unpublished results). There is additional evidence from experimental dermatophyte infections of man that the proportion of penicillin-resis-

TABLE III

Survival and growth of S. aureus strain 8325 with and without penicillinase plasmid pI 258 in the presence of a penicillin-producing and a non-producing Trichophyton mentagrophytes in vitro

Period of incubation (h)	Viable counts* of resistant (R) and sensitive (S) strains of <i>S. aureus</i> in							
	single culture (R or S) with				mixed culture (R + S) with			
	non-producing <i>Trichophyton</i>		penicillin-producing <i>Trichophyton</i>		non-producing <i>Trichophyton</i>		penicillin-producing <i>Trichophyton</i>	
	R	S	R	S	R	S	R	S
0	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
24	4.66	4.80	4.19	<0.01	4.39	4.91	4.07	<0.01
48	5.49	5.86	5.70	<0.01	4.61	5.57	6.25	2.08
72	5.95	5.63	5.82	<0.01	5.13	6.05	6.29	2.42

Based on Ryall, Holt and Noble (1981).

* Data expressed as log percent count with 0h = 100% (2.00).

tant cocci increases during infection and then falls to base level at the end of the experiment (Bibel and LeBrun, 1975).

This natural production of clinically-relevant antibiotic is of interest in suggesting a way in which resistance may be maintained in the absence of therapeutic antibiotic and, perhaps, in suggesting an original stimulus for selection or development of resistance genes. Equally, we are becoming aware of mechanisms that maintain penicillin resistance in staphylococci without the presence of exogenous penicillin. Naidoo (1981) has demonstrated *in vitro* that possession of a penicillinase plasmid may protect staphylococci against the inhibitory effect of skin fatty acid and Noble (1983*b*) has reported the existence of an unknown mechanism that selects penicillin-resistant cocci on the skin of mice. The use of the term penicillinase plasmid, whilst indicating which genes may be of prime interest medically, ignores the fact that a considerable number of other genes, only some of which are characterised, are present on the plasmid. It is doubtless a gene other than the penicillinase genes that mediates persistence of the plasmid-bearing strains.

Gene exchange. A well established area of research that has developed principally during the last decade is the exchange of genetic information between organisms on skin. Lacey (1971) found that neomycin-resistant *S. aureus* strains were able to transfer resistance to other *S. aureus* strains if donor and recipient were placed together on human skin for a period of about 6 h. Naidoo and Noble (1978) demonstrated the same phenomenon with gentamicin resistance markers and extended the observations to include transfer from coagulase-negative to coagulase-positive species (Naidoo and Noble, 1981). Others have reported similar findings (Jaffe *et al.*, 1980). J. Naidoo (personal communication) has found that about one third of gentamicin-resistant coagulase-negative cocci can donate resistance to *S. aureus* strains. It is now clear that coagulase-negative and coagulase-positive skin cocci share plasmid-borne genes (Cohen, Wong and Falkow, 1982), and that transfer is accomplished, at least in some cases, by a conjugative type of mechanism. The presence of the gentamicin resistance plasmid apparently mobilises plasmids mediating resistance to penicillin, tetracycline, erythromycin and chloramphenicol (table IV) (Forbes and Schaberg, 1983; McDon-

TABLE IV
Co-transfer of R plasmids from a S. epidermidis strain to S. aureus strain M1

Plasmids from <i>S. epidermidis</i> contained in donor <i>S. aureus</i> 8325	Frequency of transfer determined on selective media containing		
	gentamicin	tetracycline	erythromycin
Gm	3×10^{-5}	...	...
Gm Pc	5×10^{-5}	...	...
Tc	...	1×10^{-10}	...
Tc Pc	...	0	...
Tc Pc Gm	4×10^{-6}	2×10^{-6}	...
Em	...	...	1×10^{-8}
Em Gm	2×10^{-5}	...	3×10^{-5}
Em Pc Gm	5×10^{-6}	...	2×10^{-7}

Gm = gentamicin, Pc = penicillin, Tc = tetracycline, Em = erythromycin.

All resistances were determined by separate plasmids and all originated in *S. epidermidis* strain 100724. Plasmids were initially transferred to *S. aureus* strain 8325 rif^R and from this strain to *S. aureus* strain M1 strep^R. The table shows that the presence of the gentamicin plasmid results in an increased rate of transfer of the other plasmids. (J. Naidoo, unpublished data.)

nell, Sweeney and Cohen, 1983). It is not clear whether this is a new mechanism in staphylococci or has simply come to prominence with the more extensive use of topical antibiotics. There are similarities between the descriptions of outbreaks of infection with gentamicin-resistant staphylococci and the earlier outbreaks with neomycin-resistant strains that suggest that the phenomenon is not wholly new.

The genetics of the coryneforms have scarcely been investigated, but the existence of erythromycin resistance plasmids (Schiller, Groman and Coyle, 1980) and of a gentamicin resistance plasmid have been established (Kerry Williams, Naidoo and Noble, 1983; Kono, Sasatsu and Aoki, 1983). At present, perhaps the most interesting strains of coryneforms in the clinical context are the co-called JK organisms that bear some resemblance to *Rhodococcus* spp. (Athalye *et al.*, in press) and that are most often recovered from deep infection in immunosuppressed patients. These coryneforms are often resistant to most antibiotics except vancomycin, yet appear not to possess plasmids. Their origin is not known.

If a general picture of cutaneous gene transfer can be envisaged, it is that transfer between strains of staphylococci, and, presumably, between various coryneforms, occurs all the time at a low level even in the absence of an antibiotic. Isolates that have only recently received a plasmid appear unstable and clones bearing the resistance markers are only maintained at a very low level in the absence of antibiotic pressure. That pressure can arise from antibiotic production by other members of the skin flora, or from clinical therapy, or may be fortuitous because of the action of other genes on the plasmid.

Interaction between host and microbe

Some notable advances have occurred in our understanding of the pathogenesis of some skin diseases, whilst others remain sadly underinvestigated. Two contrasting diseases that are now partially understood will be described to illustrate the nature of the problems encountered.

Acne. There has been a gradual weaning of investigators from dependence on the "lipase" theory of acne. This theory, dominant in the early years of skin microbiology, held that the lipolytic action of *P. acnes* produced short chain, irritant fatty acids by hydrolysis of sebaceous triglyceride. Once it was fully appreciated that lipase inhibitors were not effective in the therapy of acne, and that completely unphysiological amounts of fatty acid were needed to produce inflammation, a search was initiated for a more logical sequence of events. That search cannot be regarded as completed, but the following concepts have emerged. Prepubertal children are not colonised by *P. acnes* but colonisation commences during puberty and proceeds rapidly until about 16–17 years of age after which the colonisation density increases slowly until about age 40 (Leyden *et al.*, 1975) in parallel with secretion of sebum, and may depend upon changes in triglyceride components (Nordstrom, 1983). Follicles become blocked by excess keratin production; the mechanism for this is not known, but may be sebum related. Sebum continues to be produced and organisms continue to grow in blocked follicles leading to the formation of closed comedones which are, however, not inflamed. If appropriate pH, pO₂ or other specific physiological parameters are reached—and there are very sharp optima *in vitro* (Greenman, Holland and Cunliffe, 1983)—the intra-follicular *P. acnes* produce protease, hyaluronidase or other enzymes that can cause the follicle wall to become "leaky" to the body defence

mechanism. Because the cell wall of *P. acnes* alone will initiate complement lysis, leukocytes invade and inflammation follows. This proposal explains many of the phenomena in acne, such as the apparent paradox that although acne is clearly associated with circulating hormones, only a few of the thousands of sebaceous glands develop into comedones and fewer still become inflamed. We are slowly beginning to appreciate the complex immunology of acne; for example, severe scarring acne develops in those with impaired immunity, it is not simply part of a spectrum of disease (Gowland *et al.*, 1979).

Scalded Skin Syndrome. In contrast, the staphylococcal scalded skin syndrome (SSSS) is a rare manifestation of the rather more common disease bullous impetigo (Melish, 1982). Staphylococcal impetigo may present as bullae from which the skin splits easily at the granular cell layer and is associated with infection at the site of bullae, so that the fluid may be cloudy with organisms and white cells. In SSSS, the infected lesion may be at a site remote from the most obvious bullous lesions, from which the skin easily rubs off (the Nikolsky sign) leaving a glistening, painful surface. The mechanism of splitting is not known but the site of action is extracellular and desmosomes are the apparent target. There is considerable specificity, for not only is the granular layer apparently the only tissue affected, but whereas man, monkey, mouse and hamster are susceptible, rat, rabbit, guinea pig, dog, frog and chicken are not. Two very similar, but not identical, toxins cause the splitting; in minor forms of the disease the toxin may be specified by chromosomal genes but in the severe form, in which abundant toxin is produced, the genes are plasmid-borne. Both toxins produce the same effect but to different degrees (Wiley and Rogolsky, 1977). Several variants of the epidermolytic toxin plasmid are known and some plasmid evolution has occurred (O'Reilly *et al.*, 1981).

Lacunae

With so much apparently known, what remains to be discovered? Our knowledge of skin chemistry, in the sense of comprehensive lists of substances found at the skin surface has improved greatly during the last 20 years, but we still have a very imprecise idea of how this is related to the microbial flora. Although fatty acids may keep some organisms, such as streptococci, in check, they may be essential for some coryneforms, but precisely which fatty acids we do not know. The factor of greatest importance however, is water. Occluding skin increases the water content and enables skin bacteria to grow at much faster rates, but it also increases pCO₂, pH and temperature and the role of these is difficult to assess. We do not know why some organisms such as *S. epidermidis* can colonise skin whereas the closely related *S. aureus* cannot; nor do we know why *S. aureus* colonises patients with atopic dermatitis but much more rarely colonises the lesions of psoriasis or some other dermatoses. This may be related to adherence; there is increasing evidence that skin strains of some recognised pathogens, such as *Streptococcus pyogenes* and *C. diphtheriae*, colonise cornified epithelial cells much better than buccal epithelial cells, whereas the reverse is true for throat strains of these species. The role of the host is unknown, although Kinsman *et al.* (1983) have proposed that HLA DR antigens may govern the ability of nasal carriers to be colonised by *S. aureus*. A serious study of adherence phenomena might enable us to prevent adherence, which would be especially valuable in relation to colonisation and

infection of skin around catheters and the prevention of catheter-associated sepsis. Our knowledge of the epidemiology of skin disease is rudimentary (Noble, 1983a).

The role of the skin flora in relatively trivial skin disease has not been well studied. Feet smell cheesy because the *Brevibacterium* spp. present liberate CH_3SH from methionine after the release of amino acids during keratolysis by the brevibacteria (Jackman, 1982b). The brevibacteria may achieve dominance because they are selected by antibiotic-producing dermatophytes that initiate the lesions. Axillary odour is a far more complex matter; microbial modification of sterols secreted from the apocrine glands is believed to be responsible for the odour. Any pheromone effect is conjectural at present.

No mention has yet been made of skin virology. This is partly because there does not appear to be a normal virological flora of the skin but is also because the most spectacular advances have not been made by those primarily interested in skin. It is salutary to recognise that, whilst warts have generally been the least interesting disease to dermatologists, papilloma viruses are now amongst the most interesting viruses in relation to oncology.

Poorly though the microflora of the skin has been studied, it is the role of the host that is least understood. What accounts for the excess of patients with a history of atopy amongst those with fungal infection? What surface component is suppressed in the immune deficient or immunosuppressed patient to increase the prevalence of pityriasis versicolor? Clearly much remains to be done in the field of skin microbiology. The problems remain as interesting as they ever were and skin microbiologists can only applaud the gradual recruitment of research workers to the study of this fascinating habitat.

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