Seborrheic Dermatitis and Malignancy

An Investigation of the Skin Flora

D. C. CLIFT, H. J. DODD, J. D. T. KIRBY, G. MIDGLEY* and W. C. NOBLE*

Department of Dermatology, St. Bartholomew's Hospital, London, England

Clift DC, Dodd HJ, Kirby JDT, Midgley G, Noble WC. Seborrheic dermatitis and malignancy. An investigation of the skin flora. Acta Derm Venereol (Stockh) 1988; 68: 48–52.

The skin flora of patients with disseminated malignant disease and seborrheic dermatitis has been investigated and compared with controls as well as with otherwise healthy patients suffering from seborrheic dermatitis. Although significant differences were detected in both bacterial and yeast counts between different sites on the body, no significant qualitative or quantitative differences were found between the three groups of subjects. Whereas abnormalities of the skin flora have been described in seriously ill patients and in individuals subjected to occlusion, we were unable to demonstrate any changes in skin flora in patients with malignant disease and seborrheic dermatitis. Our results do not support the view that increased numbers of *Pityrosporum* yeasts are important in the pathogenesis of seborrheic dermatitis. (Received February 8, 1987.)

H. J. Dodd, Department of Dermatology, Royal Free Hospital, Hampstead, London NW3 2QG, England.

We have noted a large number of patients suffering from seborrheic dermatitis (SD) amongst patients referred to us from the Oncology Department. These patients have received or been about to receive various chemotherapeutic agents for disseminated malignancy. It has been suggested that yeasts of the *Pityrosporum* genus are important in the etiology of SD (1) and one report has appeared of SD being responsive to the antifungal drug ketoconazole (2).

As it seemed possible that immunosuppression might lead to uninhibited microbial growth in patients receiving cytotoxic drugs for malignancy, we decided to compare the skin flora in patients suffering from both malignant disease and SD with otherwise healthy subjects suffering from SD as well as with control individuals.

PATIENTS AND METHODS

Fourteen patients with seborrheic dermatitis referred from the Oncology Department were studied. All had disseminated malignant disease and a wide range of neoplasms was represented: Hodgkin's disease (2), carcinoma of the larynx (2) and the following contributed one patient each; acute lymphocytic leukaemia, non-Hodgkin's lymphoma, carcinoma of the breast, carcinoma of the tongue, thyroid carcinoma, polycythaemia rubra vera, ocular melanoma, lymphoplasmacytoid lymphoma, and bronchial carcinoma. In one patient the site of the primary tumour was unknown. Seventeen otherwise healthy patients with SD and 9 control subjects were also studied. The 9 controls were patients attending the Skin Department for treatment of warts or other benign skin tumours. Care was taken to exclude subjects as controls if they gave a history of infective or inflammatory skin disease. Subjects who had received any previous topical treatment for SD were asked to discontinue therapy for 5 days before the sampling, and those who had recently received any systemic antimicrobial therapy were excluded from the study.

* Skin Infection Unit, Institute of Dermatology, Lisle St, Leicester Square, London WC2H 7BJ, England.

Samples were taken from four sites: the forehead, the presternal skin, the posterior chest wall and the ventral aspect of the forearm using the Williamson scrub method with 10 ml of wash fluid (Triton X-100 in 0.075 M phosphate buffer pH 7.9) (3). These sites were chosen to include three sites commonly affected by SD and one site rarely involved. All samples were serially diluted in saline/Tween 80 (0.1%) to give dilutions of 1:10 and 1:100. Five aliquots each of 0.025 ml of the original sample and the two dilutions were inoculated in duplicate on CA agar (30 g tryptone Soya Broth (Oxoid), 5ml Tween 80, 10 g Yeast Extract (Oxoid), 10 g Agar No. 1 (Oxoid)). One plate was incubated aerobically for 48 h at 37°C followed by 24 h at bench temperature, and the other was incubated anaerobically using a gas-generating kit (Oxoid) and cold catalyst for 3 days at 37°C.

Colonies were recognized and identified by conventional tests based on those of Cowan (4). Samples were examined for Micrococcaceae including *Staphylococcus aureus*, Coryneforms, Gram-negative rods and anaerobes including *Propionibacterium acnes* and *Prop. granulosum*. The fluid from the original sample was used for the estimation of *Pityrosporum*. After centrifugation at 4000 r.p.m. for 15 min the supernatant was discarded and the deposit resuspended in the remaining 0.1 ml of fluid. This concentrated suspension was divided equally and placed dropwise onto a glass slide and onto a plate of bile salt medium (5). The deposit on the slide was allowed to dry at room temperature and then covered with a drop of Parker stain (equal parts 30% potassium hydroxide and Parker blue-black ink) and a coverslip. This was examined for *Pityrosporum* using a ×40 objective and the total number of yeasts in the specimen was estimated with the aid of an eyepiece graticule. The two forms *Pityrosporum ovale* and *Pityrosporum orbiculare* were distinguished by their morphology. The results for these yeasts are presented both individually and combined, as some workers have reported interchange of these forms in subculture and regard them as single species (6, 7). The plates were incubated at 32°C for 7 days and the *Pityrosporum* spp. recovered confirmed their presence in the sample. An attempt was made to estimate the numbers present in the sample from the culture results but as these were consistently lower than the results for direct counting they are not presented. Direct counts probably give a more realistic estimate by including non-viable yeasts and allowing the counting of clumped organisms which would only form one colony on culture.

RESULTS

Table I shows the results for aerobic and anaerobic bacteria for all sites in the three groups and the differences between sites with all subjects considered together. A small increment

Table I. *Results for aerobic and anaerobic bacteria for all sites in the three groups of subjects and the results for different sites, with all subjects considered together*

The analysis of variance technique was used to compare the results. There was no significant difference between subject groups for aerobic or anaerobic bacteria but there was a significant difference between sites for both aerobes and anaerobes ($p<0.001$) with greater numbers on the presternal skin and forehead. Results are expressed in colony forming units per cm^2

	Aerobic			Anaerobic		
	Log. mean	Standard error	Geometric mean	Log. mean	Standard error	Geometric mean
All sites						
Control	2.49	(0.45)	309	3.13	(0.69)	1 340
SD	3.13	(0.29)	1 334	3.19	(0.44)	1 567
SD + Neoplasm	2.45	(0.31)	282	2.43	(0.48)	267
All patient types						
Arm	2.12	(0.39)	131	−0.12	(0.40)	0.8
Presternal skin	3.56	(0.29)	3 597	4.51	(0.50)	32 659
Post. chest wall	1.53	(0.35)	34	2.37	(0.51)	234
Face	3.79	(0.42)	6 237	4.92	(0.60)	83 753

of 0.001 was added to all data values so that a log (base 10) transformation could be performed on all the data. The data were normally distributed under this transformation. The analysis of variance technique was used to compare the results for different sites and the three groups of subjects. There were no significant differences between the three groups for aerobic or anaerobic bacteria. There was a significant difference between the different sites studied ($p<0.001$) with greater numbers on the presternal skin and forehead.

Results for both the yeasts (Table II) were also treated by the analysis of variance technique. There was again no significant difference between the three groups, but there were significant differences between sites for *Pityrosporum ovale* ($p<0.01$), *Pityrosporum orbiculare* ($p<0.001$) and total yeasts ($p<0.001$).

DISCUSSION

Seborrheic dermatitis is a common disorder and yet the cause has not been established. The sites affected in adult patients are those which have the highest surface lipids (8). In addition the affected side is more oily in unilateral SD and sebum levels are increased in Parkinson's disease which is associated with SD (9). An improvement of the SD (10) and a reduction in sebum levels (11) have both been documented following treatment with L dopa (12). Whilst some authors have claimed abnormalities of skin lipids in SD (13), others have failed to find any quantitative or qualitative abnormality of sebum production (14, 15).

Although Sabouraud in 1904 (16) suggested that *Pityrosporum* yeasts might be responsible for SD, proof for this theory has been lacking. *Pityrosporum* yeasts are abundant in the normal scalp and no area of skin is free from this organism (17, 18). They are markedly increased in scalps affected by dandruff and in SD (1). However, many consider these increased numbers of organisms to be a secondary colonization of the rash (19, 20). Recently the response of SD to oral ketoconazole has been reported (2), although no

Table II. *Results for Pityrosporum ovale, Pityrosporum orbiculare and total yeasts*

Using the analysis of variance technique, no significant differences were demonstrated between the three groups of subjects. There were however significant differences between sites for *Pityrosporum ovale* ($p<0.01$), *Pityrosporum orbiculare* ($p<0.001$) and total yeasts ($p<0.001$). Results are expressed in counts per cm^2

	P. ovale			*P. orbiculare*		
	Log. mean	Standard error	Geometric mean	Log. mean	Standard error	Geometric mean
All sites						
Control	2.11	(0.18)	128	2.48	(0.24)	301
SD	2.35	(0.13)	222	2.13	(0.12)	134
SD + Neoplasm	2.64	(0.19)	438	2.51	(0.18)	321
All patient types						
Arm	1.70	(0.12)	50	1.37	(0.12)	24
Presternal skin	2.57	(0.21)	371	2.83	(0.19)	675
Post. chest wall	2.60	(0.14)	400	2.74	(0.14)	547
Face	2.65	(0.22)	450	2.27	(0.20)	185

measurements of *Pityrosporum* were made in this study. Some studies have provided support for the role of *Pityrosporum* by showing that treatment which suppresses their numbers is accompanied by a reduction in scaling. Agents shown to decrease dandruff and numbers of yeasts include selenium sulphide (19, 21), zinc pyrithione (22), and undecylinic acid derivative (23), and econazole (24). All these have anti-fungal activity in common but despite this there remains some controversy as to whether seborrhea, *Pityrosporum* infection or increased cell turnover is the primary abnormality in SD.

Our study was conducted to determine whether any abnormality of skin flora was present in patients with malignant disease who develop SD. Previous studies have shown major changes in skin flora in individuals subjected to occlusion (25) and in severely ill patients (26). One study of patients on immunosuppressive medication for renal transplantation and dialysis patients showed no increase in skin organisms (27) although it has been noted in another centre that such patients have a high incidence of skin infections, including pityriasis versicolor, itself a manifestation of *Pityrosporum* infection (28). Seborrheic dermatitis has been noted as a feature of the acquired immune deficiency syndrome (AIDS) (29, 30) and it has been suggested that this may be due to uninhibited fungal growth as a result of the immunodeficiency (30). Our patients with malignant disease and SD may have been immunocompromized and yet we found no evidence of bacterial or fungal overgrowth in this group. Nor did we find significant differences in the numbers of bacteria or yeasts between the patients with a wide range of malignant disease and SD, controls, and otherwise healthy individuals with SD. Our results therefore provide no evidence for the view that increased numbers of *Pityrosporum* yeasts or any other micro-organism play a primary role in the etiology of seborrheic dermatitis.

ACKNOWLEDGEMENTS

We are grateful to Dr P. F. M. Wrigley and Dr T. A. Lister of St. Bartholomew's Hospital for allowing us to investigate their patients. The Cancer Research Committee, St. Bartholomew's Hospital, provided funds for this work.

REFERENCES

1. McGinley KJ, Leyden JJ, Marples RR, Kligman AM. Quantitative microbiology of the scalp in non-dandruff, dandruff and seborrhoeic dermatitis. J Invest Dermatol 1975; 64: 401–06.
2. Ford GP, Farr PM, Ive FA, Shuster S. The response of seborrhoeic dermatitis to ketoconazole. Br J Dermatol 1984; 111: 603–07.
3. Williamson P, Kigman AM. A new method for the quantitative investigation of cutaneous bacteria. J Invest Dermatol 1965; 45: 498–503.
4. Cowan ST. Manual for the identification of medical bacteria, 2nd edition. London: Cambridge University Press.
5. Van Abbé NJ. The investigation of dandruff. Journal of the Society of Cosmetic Chemists 1964; 15: 609–30.
6. Randjandiche M. Polymorphism de *Pityrosporum ovale* (Bizzozero) Castellani & Chalmers *in vitro* et *in vivo*. Bull Soc Fr Mycol Med 1976; 5: 79–84.
7. Salkin IF, Gordon MA. Polymorphism of *Malassezia furfur*. Can J Microbiol 1977; 23; 471–5.
8. Hodgson-Jones I, Mackenna RMB, Wheatley VR. The surface fat in seborrhoeic dermatitis. Br J Dermatol 1953; 65: 246–51.
9. Krestin D. The seborrhoeic facies as a manifestation of post-encephalitic parkinsonism and allied disorders. Q J Med 1927; 21: 177–86.
10. Parish LC. L-dopa for seborrhoeic dermatitis. N Engl J Med 1970; 283: 879.
11. Burton J. Effect on L dopa on the seborrhoea of parkinsonism. Br J Dermatol 1973; 88: 475–9.
12. Kohn SR, Pochi PE, Strauss JS, Sax DS, Feldman RG, Timberlak WS. Sebaceous gland secretion in Parkinson's disease during L-dopa treatment. J Invest Dermatol 1973; 60: 134–6.
13. Gloor M, Wiegand I, Friederich HC. Über Menge und Zusammensetzung der Hautoberflächenlipide beim sogennanten seborrhoischen Ekzem. Dermatol Monatsschr 1972; 158: 759–64.

14. Pye RJ, Meyrick G, Burton JL. Skin surface lipids in seborrhoeic dermatitis. Br J Dermatol 1977; Suppl 15: 12–13.
15. Burton JL, Pye RJ. Seborrhoea is not a feature of seborrhoeic dermatitis. Br Med J 1983; 286: 1169–70.
16. Sabouraud R. Pityriasis et alopécies péliculaires: Les maladies desquamative, 1st edition. Paris: Masson et Cie, 1904.
17. Martin-Scott I. The pityrosporum ovale. Br J Dermatol 1952; 64: 257–73.
18. Spoor HJ, Traub EF, Bell M. Pityrosporum ovale types cultured from normal and seborrhoeic subjects. Arch Dermatol 1954; 69: 323–30.
19. Leyden JJ, McGinley KJ, Kligman AM. The role of micro-organisms in dandruff. Arch Dermatol 1976; 112: 333–38.
20. Kligman AM, Leyden JJ. Seborrhoeic dermatitis. Semin Dermatol 1983; 2: 57.
21. Leyden JJ, Kligman AM. Dandruff—cause and treatment. Cosmetics and Toiletries 1979; 94: 23.
22. Imokawa G, Shimuzu H, Okamoto K. Antidandruff mechanism of zinc pyrithione. Washington D.C.: Procedings of the meeting of the Society of Cosmetic Chemists, 1981.
23. Alexander S. Do shampoos affect dandruff? Br J Dermatol 1967; 79: 92–95.
24. Aron-Brunetière R, Dompmartin-Pernot D, Drouhet E. Treatment of pityriasis capitis (dandruff) with econazole nitrate. Acta Derm Venereol (Stockh) 1977; 57: 77–80.
25. Marples RR. The effect of hydration on the bacterial flora of the skin. In: Maibach HI, Hildick-Smith G eds. Skin bacteria and their role in infection. New York: McGraw-Hill, 1965; 33.
26. Stratford B, Gallus AS, Mathiesson AM, Dixson S. Alteration of superficial bacterial flora in severely ill patients. Lancet 1968; i: 68.
27. Noble WC, Rebel MH, Smith I. An investigation of the skin flora of dialysis and transplant patients. Br J Dermatol 1974; 91: 201–07.
28. Koranda FC, Dehmel EM, Kahn G, Penn I. Cutaneous complications in immunosuppressed renal homograft recipients. JAMA 1974; 229: 419–24.
29. Eisenstat BA, Wormser GP. Seborrhoeic dermatitis and butterfly rash in AIDS. N Engl J Med 1984; 311: 189.
30. Farthing C, Staughton RCD, Rowland-Payne CME. Skin disease in homosexual patients with Acquired Immune Deficiency Syndrome (AIDS) and lesser forms of human T cell leukaemia virus (HTLV III) disease. Clin Exp Dermatol 1985; 10: 3–12.