



# Pachyonychia Congenita Project

15 March 2005

## Use of Articles in the Pachyonychia Congenita Bibliography

The articles in the PC Bibliography may be restricted by copyright laws. These have been made available to you by PC Project for the exclusive use in teaching, scholarship or research regarding Pachyonychia Congenita.

To the best of our understanding, in supplying this material to you we have followed the guidelines of Sec 107 regarding fair use of copyright materials. That section reads as follows:

Sec. 107. - Limitations on exclusive rights: Fair use

Notwithstanding the provisions of sections 106 and 106A, the fair use of a copyrighted work, including such use by reproduction in copies or phonorecords or by any other means specified by that section, for purposes such as criticism, comment, news reporting, **teaching (including multiple copies for classroom use), scholarship, or research**, is not an infringement of copyright. In determining whether the use made of a work in any particular case is a fair use the factors to be considered shall include - (1) the purpose and character of the use, including whether such use is of a commercial nature or is for nonprofit educational purposes; (2) the nature of the copyrighted work; (3) the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and (4) the effect of the use upon the potential market for or value of the copyrighted work. The fact that a work is unpublished shall not itself bar a finding of fair use if such finding is made upon consideration of all the above factors.

We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.

## **Pachyonychia congenita with candidiasis**

HELEN MAWHINNEY, SANDRA CRESWELL AND J. MARTIN BEARE  
*Royal Belfast Hospital for Sick Children, and Royal Victoria Hospital, Belfast, Northern Ireland*

*Accepted for publication 14 February 1980*

### **Summary**

Pachyonychia congenita in a mother and two siblings, with associated oral candidiasis, is reported. In the propositus lymphocyte stimulation by candida and delayed hypersensitivity skin reactions to candida were absent. All other parameters tested were within normal limits. Pachyonychia congenita is a dominantly inherited condition, first described by Jadassohn & Lewandowski in 1906, in which the most constant feature is gross thickening and discolouration of finger and toe nails. Other abnormalities may include palmar and plantar hyperkeratosis, leukoplakia of the tongue and buccal mucous membranes, hyperhidrosis, blistering of the feet and candidiasis. This latter association is described in a mother and two siblings.

### **Case reports**

The propositus (III, 2; see Fig. 1), an 18-month-old boy was first noted to have abnormal nails at the age of 5 months. His mother had first noticed oral candidiasis when he was several weeks old. On referral, all finger and toe nails were found to be abnormal with an appearance typical of pachyonychia congenita. Oral candidiasis was present but there were no other skin or mucous membrane lesions. *Candida albicans* was cultured from the mouth but not from nail clippings. At 18 months of age hyperkeratosis of the plantar aspects of the great toes developed.

The mother (II, 1; see Fig. 1), a 36-year-old female: has had abnormal nails since early childhood and developed insulin-dependent juvenile-onset diabetes mellitus at the age of 10 years. She had had recurrent oral candidiasis in childhood and has had persistent oral candidiasis and angular stomatitis for the past 3 years. She had required total dental clearance for dental caries at the age of 31 years. On referral she was noted to have changes typical of pachyonychia congenita in two finger nails with less marked changes in the remaining finger and toe nails. Oral candidiasis, angular stomatitis and acne rosacea were also present. *Candida*

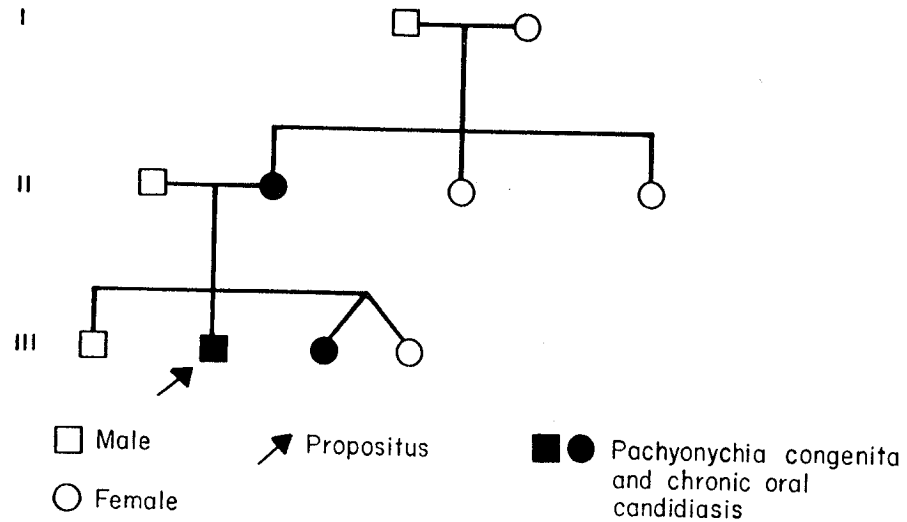


Figure 1. Pedigree of family with pachyonychia congenita and chronic oral candidiasis.

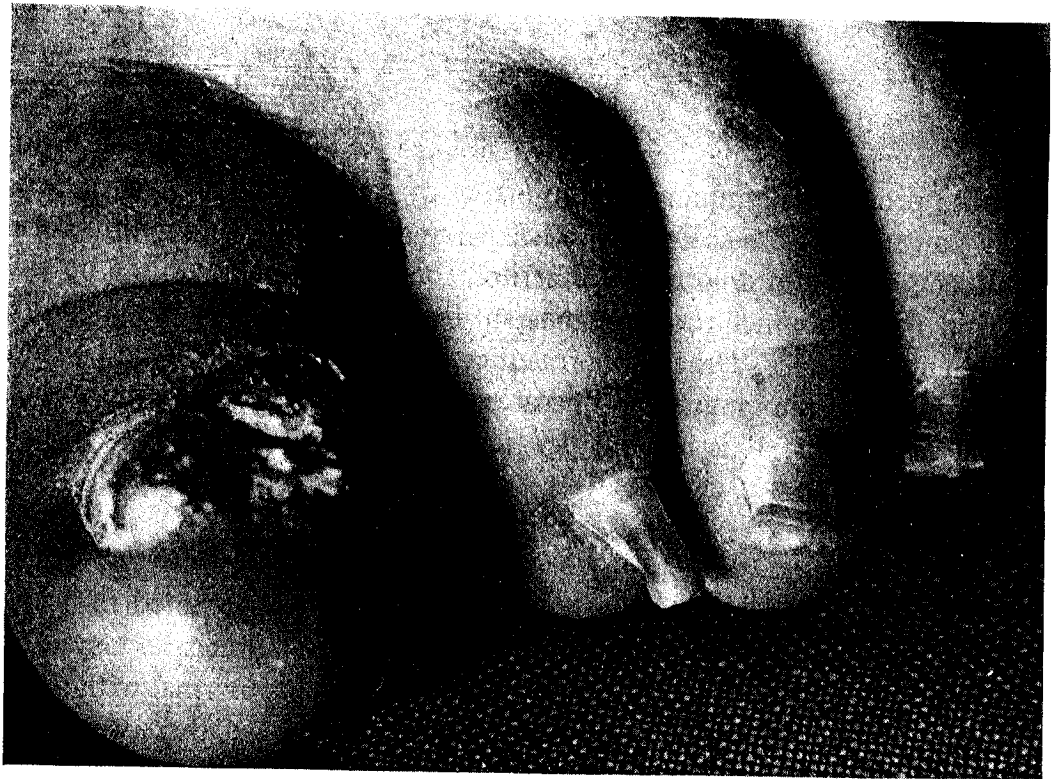


Figure 2. Nail defects in III,2.

*albicans*, *Candida tropicalis* and *Torulopsis glabrata* were grown from the mouth but not from nail clippings.

The sister of the propositus (III, 3; see Fig. 1) one of dizygotic twin girls, had normal nails and no evidence of oral candidiasis at the age of 1 week. When reviewed at the age of 6 weeks, the changes of pachyonychia congenita were obvious in all nails and there was candidiasis of the tongue.

The other two siblings (III, 1 and III, 4; see Fig. 1), the two maternal aunts and the



**Figure 3.** Nail defects in II,2.

maternal grandmother are healthy. There is no family history of diabetes mellitus or other endocrine disease.

### **Materials and methods**

Delayed hypersensitivity skin testing was carried out using 0.1 ml 0.33% *Candida* antigen (Bencard), 0.1 ml 0.5% trichophyton (Bencard) and 5 units tuberculin (Evans). Peripheral blood mononuclear cell preparations obtained by centrifugation on Ficoll-Triosil (Böyum, 1968), were examined for E-rosette-forming cells (Pang, Baguley & Wilson, 1974) and lymphocyte responses to phytohaemagglutinin (PHA) (PHA-P, Difco) and *Candida* antigen (kindly provided by Professor D. Mackenzie, London School of Hygiene and Tropical Medicine) by a method based on that of Penhale *et al.* (1974). Mononuclear cells were incubated for 72 h with PHA at dilutions ranging from 1/500 to 1/8000 and for 6 days with *Candida* antigen at 1 µg/ml, 10 µg/ml and 100 µg/ml. Leukocyte candidicidal activity was determined by a methylene blue exclusion technique (Lehrer & Cline, 1969).

Serum immunoglobulin and complement levels, surface membrane immunoglobulin (SmIg)-bearing cells, C<sub>3</sub>-receptor-bearing cells, leukocyte bactericidal activity and neutrophil chemotaxis were determined by methods previously described for this laboratory (McCrea *et al.*, 1979; Mawhinney, Gleadhill & McCrea, 1979).

The following battery of tests was performed to assess cell mediated immunity: peripheral blood lymphocyte count, percentage of rosette-forming cells, lymphocyte stimulation tests with PHA and *Candida*, antigen and delayed hypersensitivity skin tests to *Candida*, trichophyton and tuberculin.

Humoral immunity was assessed by measurement of serum immunoglobulins (IgA, E, M and G) with percentages of SmIg-bearing cells and C<sub>3</sub>-receptor bearing cells.

Peripheral blood neutrophil counts, leukocyte bactericidal activity, leukocyte candidicidal activity and neutrophil chemotaxis were measured to monitor neutrophil function. Serum complement (C<sub>3</sub>, C<sub>4</sub> and total haemolytic activity) levels were also carried out.

## Results

The results obtained on immunological assessment of the three affected family members were as follows.

In the propositus (III, 2) despite a normal peripheral blood T lymphocyte count and a positive lymphocyte response to PHA, lymphocyte stimulation by *Candida* antigen and a delayed hypersensitivity skin reaction to *Candida* were absent when tested both at 6 months and 13 months of age. In contrast, the mother (II, 1) showed normal cellular immune responses to *Candida* with positive lymphocyte stimulation and delayed hypersensitivity skin reactions. No inhibitor of the response to *Candida* antigen by the lymphocytes of a normal sensitized donor could be demonstrated in the serum of the propositus. No definite abnormalities of humoral immunity, neutrophil function or complement were found. Although both the propositus and mother had low SmIg-bearing mononuclear cell counts, the normal numbers of C<sub>3</sub>-receptor-bearing cells excluded a deficiency of B lymphocytes in the peripheral blood. No autoantibodies to endocrine tissue including pancreatic islet cells and parathyroid were present in the serum of the propositus or mother. All tests carried out in III, 3 were within normal limits apart from raised IgM (1.29 g/l) (normal value 0.2–0.9 g/l), the significance of which was not clear.

Serum calcium levels were normal in the propositus and mother. Serum iron levels were also normal but a low serum ferritin was recorded in the mother during pregnancy.

## Discussion

Since pachyonychia congenita is thought to be a state of abnormal keratinization of oral epithelium, nails and skin (Samman, 1978), it has been suggested that the abnormal oral mucosa may predispose to the development of chronic oral candidiasis. It is therefore of considerable interest that in this family the mother who has only had chronic oral candidiasis for 3 years has an intact cellular immune response to *Candida albicans*, while the propositus who has had chronic oral candidiasis since early infancy has no evidence of such a response.

The immunological findings in the propositus are very comparable to those in patients with chronic mucocutaneous candidiasis, whether familial or sporadic, in whom the most characteristic defect is absence of a delayed hypersensitivity skin reaction to *Candida albicans* (Valdimarsson *et al.*, 1973; Kirkpatrick, Rich & Bennett, 1975). This child therefore provides further evidence in favour of the argument that chronic mucocutaneous candidiasis may be an acquired disorder. The inherited abnormality of the oral mucosa may predispose to infection with *Candida albicans* in early infancy, and hence the absence of a normal cellular response to *Candida*. The dichotomy between the immunological finding in the propositus and his mother is unusual since the same immunological defect has generally been found in the affected relatives of each pedigree with chronic mucocutaneous candidiasis (Wells *et al.*, 1972) but may reflect the greater severity of pachyonychia congenita in the propositus.

The cases reported in this paper would fit in with the clinical features of Type II pachyonychia congenita described by Samman (1978).

## References

- BÖYUM, A. (1968) Separation of leucocytes from blood and bone marrow. *Scandinavian Journal of Clinical and Laboratory Investigation*, **21**, Suppl. **97**, 9-109.
- FORUM, L. & WELLS, R.S. (1975) Pachyonychia congenita with chronic candidiasis of the mouth in a father and two children. *Proceedings of the Royal Society of Medicine*, **68**, 762.
- HIGGS, J.M. (1973) Chronic mucocutaneous candidiasis: iron deficiency and the effects of iron therapy. *Proceedings of the Royal Society of Medicine*, **66**, 802-804.
- VON JADASSOHN, J. & LEWANOWSKI, F. (1906) Pachyonychia congenita. Keratosis disseminata circumscripta tylosa et keratosis linguae. In: *Ikonographia Dermatologica* (Ed. by A. Neissei and E. Jacobi), pp. 29-31. Urban and Schwarzenberg, Berlin.
- KIRKPATRICK, C.H., RICH, R.R. & BENNETT, J.E. (1971) Chronic mucocutaneous candidiasis: model-building in cellular immunity. *Annals of Internal Medicine*, **74**, 955-978.
- LEHRER, R.I. & CLINE, M.J. (1969) Interaction of *Candida albicans* with human leukocytes and serum. *Journal of Bacteriology*, **98**, 996-1004.
- MCCREA, S., KILLEN, M., THOMPSON, J., FLEMING, W.A., MCNEILL, T.A. & MILLAR, J.H.D. (1979) Tests on peripheral blood cells in multiple sclerosis. *Ulster Medical Journal*, **48**, 83-90.
- MAWHINNEY, H., GLEADHILL, V.F.D. & MCCREA, S. (1979) *In vitro* and *in vivo* responses to thymosin in severe combined immunodeficiency. *Clinical Immunology and Immunopathology*, **14**, 196-203.
- PANG, G.T.M., BAGULEY, D.M. & WILSON, J.D. (1974) Spontaneous rosettes as a T-lymphocyte marker: a modified method giving consistent results. SRBC rosettes. *Journal of Immunological Methods*, **4**, 41-46.
- PENHALE, W.J., FARMER, A., MACCUISH, A.C. & IRVINE, W.J. (1974) A rapid micro-method for the phytohaemagglutinin-induced human lymphocyte transformation test. *Clinical and Experimental Immunology*, **18**, 155-167.
- SAMMAN, P.D. (1978) *The Nails in Disease*, 3rd edn. pp. 162-166. Heinemann, London.
- VALDIMARSSON, H., HIGGS, J.M., WELLS, R.S., YAMAMURA, M., HOBBS, J.R. & HOLT, P.J.L. (1973) Immune abnormalities associated with chronic mucocutaneous candidiasis. *Cell Immunology*, **6**, 348-361.
- WELLS, R.S., HIGGS, J.M., MACDONALD, A., VALDIMARSSON, H. & HOLT, P.J.L. (1972) Familial chronic mucocutaneous candidiasis. *Journal of Medical Genetics*, **9**, 302-310.