Pachyonychia Congenita Project

15 March 2005

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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.

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earch projects. This leaves impedance the forefront; it is valuable and it sed.

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ling S, Terkildsen K & Thomsen K A
'aryng., *Stockh.* Suppl. 140, 116
3) *J. Speech. Dis.* Suppl. No. 11
1) *Acta otolaryng., Stockh.* Suppl. 164
nderson H (1960) *Acta otolaryng., Stockh.* 51, 184
rch. Otolaryng., Chicago 55, 536
Thomsen K A (1959) *J. Laryng.* 73, 409
955) *Acta otolaryng., Stockh.* 45, 544

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Section of Dermatology

President F R Bettley FRCP

Meeting February 17 1966

Cases

Anhydrotic Ectodermal Dysplasia

R S Wells MD
(*Institute of Dermatology, London*)

W S, male, aged 63
History: The patient has always been intolerant of heat and only sweats very slightly on the palms of the hands and axillæ. As far as he knows he has only had four teeth, which were sharp and pointed, and extracted when he was younger. His hair was fine and fair, and a picture taken as a young man shows that he was nearly bald at that time.
Family history: His son is not affected, but both his daughters had an abnormal dentition and three of their sons have anhydrotic ectodermal dysplasia.
On examination: He is bald, edentulous and has a rather snub nose. His height is 5 ft 5 in. and the skin on his trunk and limbs is smooth and shiny with hypotrichosis.
Investigations: In a biopsy from the forearm there were no sweat or sebaceous glands and no hair follicles.

Comment
The pedigree is compatible with a sex-linked hypothesis with some expression of the gene in carrier females. There is little doubt that there is an X-linked form fully expressed in males, but the evidence for an autosomal dominant type of anhydrotic ectodermal dysplasia is inconclusive. The deficiency of sweat glands is generally regarded as complete, but under experimental conditions slight sweating has occasionally been noted in the axillæ.

Female relatives who were either carriers or who had a 50% chance of being heterozygous for the gene have been reported to show some manifestations of the condition such as partial anodontia and smooth, non-sweating areas of skin. This patient's daughters have both been investigated by Dr C B Kerr and Dr K E Cooper and both had an abnormal sweating pattern in addition to abnormal dentition. Compared with the controls there was a relatively localized distribution of sweating, best demonstrated on the face, chest and back.

The results from sweat distribution tests on these heterozygous females were consistent with a quantitative defect of sweat glands and this is suggestive evidence of tissue mosaicism as predicted on the inactive X-chromosome theory (Lyon 1961). Confirmation of this assumption requires more precise quantification of active sweat glands.

Full details of this family will be published elsewhere (Kerr *et al.* 1966).

REFERENCES
Kerr C B, Wells R S & Cooper K E (1966) *J. med. Genet.* (in press)
Lyon M F (1961) *Nature, Lond.* **190**, 372

Pachyonychia Congenita

Alan B Shrank MRCP (for E J Moynahan FRCP)
(*Hospital for Sick Children, Great Ormond Street, London*)

N W, girl aged 4
Born with six 'gristly' teeth in the lower jaw, which were shed after a month. When she was 10 days old all her nails began to thicken (Fig 1). Her scalp hair became coarse and sparse. At the age of 3 follicular hyperkeratosis appeared on her elbows and knees, and occasional bullæ developed on her soles. In September 1965 her left knee became painful and swollen.

Several relatives (Fig 2) developed the same stigmata though the number of teeth present at birth varied from four to eight; in addition, at puberty many cysts appeared all over the body.

Fig 1 *Pachyonychia congenita: thumb nails*

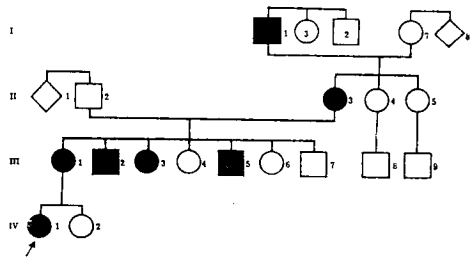


Fig 2 *Pachyonychia congenita: family tree*

On examination: All the nails were wedge-shaped with a nearly normal proximal part, a thick free edge and a smooth surface. There was sparse coarse scalp hair and follicular hyperkeratosis of the elbows and knees. The lower central incisors and molars were absent but the rest of the primary dentition appeared normal. The eyes were reported normal and sweating was normal. The left knee was stiff and the adjacent muscles wasted.

Her mother (III.1) and grandmother (II.3) exhibited the same lesions as well as a normal permanent dentition and many cysts of all areas, suggestive of sebaceous cysts.

Investigations: Hb 66%; ESR (Westergren) 39 mm in 1 hour; latex test positive; ANF test weakly positive. Chest radiograph normal. Biopsy of knee-joint showed rheumatoid changes.

Comment

This family was first reported by Jackson & Lawler (1951), and the propositus is the first affected member of the fourth generation. The syndrome manifested in this family differs from that first described by Jadassohn (1906) as leukokeratosis oris is lacking and in addition to the characteristic nail dystrophy, follicular hyperkeratosis and bullæ on the soles, there are other features such as erupted teeth at birth, a hair disorder and multiple cysts from puberty.

There appears to be some variation from family to family in the clinical pictures reported as pachyonychia congenita, while within each family there is little or no variation. The autosomal dominant mode of inheritance shown by this disorder is explicable on the basis of a single gene, but it is difficult to understand how a single aberrant gene could be responsible for such interfamilial differences. It may be that closely linked genes are responsible or that the gene is different in each family.

REFERENCES
Jackson A D M & Lawler S D (1951) *Ann. Eugen.* 16, 142
Jadassohn J (1906) *Verh. dtsch. derm. Ges.* 9, 381

Dr P R Montgomery: I saw a case like this at Guy's Hospital. She had follicular hyperkeratosis, thickened nails, blisters on the soles, and these cysts. The histology was that of sebocystomatosis with the sebaceous glands stretched out over the cyst wall. The cysts of Dr Shrank's case look clinically like those of sebocystomatosis.

Dr R S Wells: From the pedigree of Dr Shrank's case, and from others in the literature, I would think the condition is due to a single pleiotropic gene inherited as a mendelian dominant trait.

Bullous Ichthyosiform Erythrodermia

R S Wells MD (for C D Calnan FRCP)
(*Institute of Dermatology, London*)

Y C, girl, aged 4

History: It was reported that during delivery the skin was stripped off giving the appearance of a macerated stillbirth. She lost a great deal of fluid, was treated with tetracycline and cortisone, and recovered. Later she developed the appearance of a collodion baby, which was followed by widespread ichthyosis. She still has marked bulla formation from time to time. Sweating has been noted in the axillæ and groins.

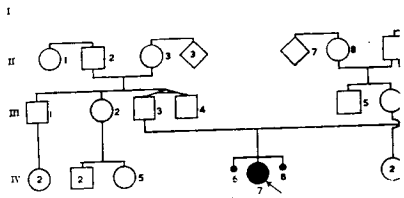
Family history: Several members of her family are affected and the pedigree is compatible with an autosomal dominant mode of inheritance (Fig 1).

On examination: There is extensive gross hyperkeratosis with some sparing of the lower arms and lower legs. The palms of the hands and soles of the feet show thickening and there is marked hyperkeratosis of the elbows and knees. The lower part of the face is more severely affected than the upper. The mother shows a very similar appearance and distribution of her lesions.

Histology: Histology from the mother is typical for bullous ichthyosiform erythrodermia (Dr E Wilson Jones).

Comment

When Brocq first described ichthyosiform erythrodermia he noted that a minority had bullæ. I have examined nine families with bullous ichthyosiform erythrodermia with more than one affected member and there is no doubt that this form is inherited as an autosomal dominant, whereas the non-bullous is an autosomal recessive trait. Even if the patients are only mildly affected, the histology of the bullous form is diagnostic, with vacuolation and cavitation in the upper layers of the epidermis. The non-bullous form shows changes similar to those seen in sex-linked ichthyosis, with an increase in thickness of the upper layers of the epidermis.



In addition to genetic and histolog ferences there are also clinical featu enable the two varieties to be distinguisl most obvious is the formation of bullæ w generally most severe between the ages o 15. These may be large, leaving raw areas, and control of secondary infecti an important part in treatment. The an fossæ and axillæ may look moist. Gros keratosis, often with an appearance si ichthyosis hystrix, may be seen particula elbows and knees. A background eryth is generally more marked in the bullous non-bullous form.

In the bullous type the lower face i more severely affected and ectropion is in the other form. Finally the scales that in the bullous patients are often hard, s shotty compared with the large flat scal non-bullous ichthyosiform erythrodermi

Generalized Hyperkeratosis – ? Ichthyosi Erythrodermia. Psoriasis

R S Wells MD (for F Ray Bettley FRCP)
(*St John's Hospital for Diseases of the Sk London*)

E J W, woman, aged 53

History: This patient was told that she all over' shortly after birth and was left lesions similar to those of her father. Sh no further blistering episodes, but he always been markedly ichthyotic wi keratosis of the flexures. For the last si has had psoriasis.

Family history: She is emphatic that h now dead, had dry, flaky skin all his lif his flexures were also the most severe areas. In addition he had gross hyperk the palms and soles. There are no oth members in the family and there is sanguinity.

On examination: Generalized mild ichth uniform hyperkeratosis of the palms and rather warty lesions on the backs o and dorsum of the feet. There is smooth hyperkeratosis of the wrists, antecu popliteal fossæ, axillæ and groins.