SOME CONSIDERATIONS CONNECTED WITH THE CLASSIFICATION AND EXPLANATION OF NAEVI AND NAEVOID CONDITIONS*

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The word "naevus" is the Latin for a "mole" or "birth-mark," but should, I think, now be used to signify a usually more or less localized congenital or developmental abnormality of tissue as evidenced by its form, bulk, texture, colour, and functional and metabolic activity—including urtication, pruritus, lipid or amyloid or calcareous deposits, etc. This is the extended definition of "naevus" as I use the term.

Dermatologists are naturally more interested in superficial naevi, but it is obvious that internal parts may be analogously affected. In support of this one need only mention the Sturge-Kalischer-Weber disease, a developmental condition in which a vascular naevus, especially of the trigeminal region of the face, is associated with an ipsilateral vascular abnormality of the underlying leptomeninges, evidently of similar naevoid nature. Patches of peritoneal pigmentation and certain connective-tissue thickenings and minute fibrous (sometimes calcifying) nodules and adenomatous "tumours" in various viscera may also be mentioned here. I would include as naevoid the rare developmental disease known as "osteochondromatosis" of articular synovial membranes (cf. Lauber and Parkes Weber, 1950). But with few exceptions I shall put off for another occasion references to what I regard as internal and visceral naevi or naevoid conditions, including naevoid abnormalities of the blood cells.

A great difficulty experienced in dividing naevi into groups is that many of them, according to various methods or aspects of classification, are found to belong to more than one group. Local developmental deficiency or excess of epidermis, dermis, or subcutaneous tissue (and subcutaneous fat) and of local blood supply and lymphatics may explain some naevi, but "naevus anaemicus" (Voerner) may occasionally be associated with haemangiectatic naevus (cf. Weber and Harris, 1932; Weber, 1933; Wakeley and Weber, 1936). So, also, a pigmented naevus may, as is well known, be surrounded by an area of hypochromic or achromic skin. The first example I saw of this, rendered specially remarkable by the fact that the patient also had chronic obstructive jaundice, was shown by H. D. Rolleston (1910) before R. L. Sutton (1916) described his two cases of "leucoderma acquisitum centrifugum" (cf. Weber, 1924).

Atavistic Naevi.—Piebaldism is perhaps the most striking example. Some pigmented and hairy naevi may well have an atavistic or "simian" origin—for instance, the extensive hairy naevi of bathing-drawers localization. Many congenital cysts and sinuses are atavistic (branchiogenic, etc.)—that is to say, they are developed from remnants of structures which were normal in distant ancestors or at certain stages of human foetal life. An os penis in human beings has an atavistic explanation.

*Communicated to the Annual Meeting of the British Association of Dermatology, Oxford June 30, 1951.

Mongoloid pigmentary patches, especially over the lower sacral region, are perhaps to be regarded as atavistic, and so are the common pigment spots or papules representing supernumerary nipples.

Somewhat allied to atavistic naevi are the *organoid tumours*, the best-recognized example of which is the *glomus tumour* ("glomangioma"), which is a "hamartomatous" dysplasia of the glomus organ of Masson, sometimes occurring in situations where a normal glomus organ would not be expected.

Personally I regard Pringle's sebaceous adenomata as organoid tumours of sebaceous glands (cf. Weber, 1950a). As in glomus tumours the degree of vascularity may vary greatly, so in sebaceous adenomata the relative proportion of blood vessels and sebaceous cells may differ widely in different specimens.* The association of sebaceous adenomata with tuberous sclerosis of the brain is well known, but they (Pringle's sebaceous adenomata) may occur in apparently otherwise normal individuals—in fact, as the only sign of "epiloia." (A post-mortem examination after some fatal accident may nevertheless reveal the unexpected presence of tuberous sclerosis of the brain.) Fibrous naevi of the skin and naevi of abdominal viscera may also constitute a feature in epiloia.

Naevi as Local Non-progressive Variants of Generalized Diseases

Neurofibromatous Naevi.—Many otherwise normal individuals have one or two molluscous fibromata or one or two *café-au-lait* patches of cutaneous pigmentation. These I would term neurofibromatous naevi. There is a congenital or developmental naevoid type of *cutis verticis gyrata*, or "bulldog scalp," the microscopical structure of which is neurofibromatous. It deserves to be included as a neurofibromatous naevus (cf. Weber, 1950b). I shall return to this subject further on.

Naevi Due to Local Abnormalities of Intracellular Metabolism

Xanthomatous Naevi.—It seems to me that as xanthelasma palpebrarum may appear in young persons—sometimes in more than one individual in the same family—without ever leading to serious xanthomatous disease, it may well be regarded in such cases as a local naevoid condition, due to a local abnormality of intracellular cholesterol metabolism, which remains confined to the affected region and never involves other and more important parts of the body. (The spots in children which have been termed "xantho-naevo-endotheliomata" by J. E. R. McDonagh in 1912 should also be mentioned here.) Mr. Eugene Wolff (1951) thinks that xanthelasma palpebrarum is due to a lipid change in the cells or in a down-growth from the cells which he regards as unicellular sebaceous glands in the basal layer of the epidermis at the inner part of the eyelids; in these altered cells he finds doubly refractile lipid material. I do not think that this view—whether right or wrong—affects what I have said about the probable naevoid nature of xanthelasma palpebrarum in young persons, but I shall refer to this subject further on.

*If I were asked whether I wished to include all glandular adenomata under the term "organoid tumours" I would reply: "No, only those in which the 'tumour' consists not only of the derivatives of the glandular cells but also of vascular and other non-glandular constituents of the gland in question." Thus, in the sebaceous adenomata of Pringle the non-glandular blood-vascular element may sometimes be the chief constituent, causing it to resemble a small haemangioma.

Calcinosis Naevi

Multiple calcifying lesions may be present in the skin and subcutaneous tissue of young children without involvement of other parts of the body or of the general health. In such a case (that of a little girl) one of the lesions was seen to be present at birth. Chronic calcareous discharge occurred from one or two of the lesions when the child was 2 years old, without any disturbance in her general development or health. It seems a legitimate suggestion that the lesions in question are due to a local abnormality of intracellular calcareous metabolism. For being permitted to see this unique case I am greatly indebted to Dr. G. B. Dowling. Though no biopsy was possible, I think one may practically exclude the diagnosis of calcifying epithelioma, which I regard as also naevoid in nature.

Primary local amyloid "tumours" (naevi) of the tongue, conjunctivae, nose, etc., and *primary generalized amyloidosis*, notably the cases with *amyloid macroglossia* (Lubarsch-Pick syndrome), should be mentioned here (cf. Weber, 1949).

Connexion Between Haemangiectatic Naevi and Associated Hypertrophy of Limbs or Neighbouring Tissue

What I called haemangiectatic hypertrophy of limbs in 1918 (Weber, 1918) is now fairly well known as a developmental naevoid condition (cf. Reichenheim, 1943), and it is certain that parts other than the extremities may be occasionally analogously affected. There is some justification in using the term "haemangiectasia hypertrophicans, Klippel-Trenaunay-Parkes Weber" (see Ciarrocchi, 1950). In this class of cases are not rarely present developmental phlebarteriectasis and arterio-venous communications which I regard as themselves naevoid conditions. So-called "congenital varicose veins" are sometimes developmental conditions of the same naevoid nature.

In the various types of angiokeratosis (haemangiokeratosis) there seems to be a causal connexion between the epithelial overgrowth and the haemangiectatic basis. Angiokeratomata of the fingers are, I think, rarer than the multiple very small angiokeratomata of the scrotum (I have not heard of analogous angiokeratomata of the vulva), which constitute a condition similar to the very rare haemangiokeratomatosis (multiple angiokeratoma) involving the trunk and thighs. Allied to these cases are, I think, the various developmental conditions of patchy hyperkeratosis of the hands, feet, or other parts on an erythematous or telangiectatic basis.

Naevi and Age

It is still held by some that naevi must be present at birth or appear during the early years of life, but, according to my definition, this is not so. Naevi may first appear during middle life or during old age, as in so-called sebaceous naevi. There is occasionally a form of senile "degenerative" venous naevus of the tongue or lips in old persons.

I now believe that the condition described by Parkes Weber and Hellenschmied (1930) as "telangiectasia macularis eruptiva perstans" should be regarded as a form of naevus. The crops of spots appear especially (but not only) in obese middle-aged women, without any obvious cause, and persist. As this disease is intimately allied to, if not actually a telangiectatic variant of,

urticaria pigmentosa with little pigmentation and little urtication, I regard urticaria pigmentosa also as a naevoid condition. In the naevoid group I feel likewise inclined to place "inborn urticaria factitia" and inborn dermographia (pruritus not necessarily present). Minute "pruriginous naevi" (spots of idiopathic pruritus), appearing in adult life, might constitute the bases on which by repeated scratching prurigo nodularis ultimately develops (cf. Elford, Weber, and Lowenberg, 1950).

Naevi and Mutation of Somatic Cells

I would of course agree that many of the developmental conditions referred to in this paper are, like numerous developmental abnormalities in the osseous and other systems, to be regarded as originally due to gene-mutation in germ cells; but I think also that there are acquired minor dermatological abnormalities, such as "ruby spots," which might be regarded as results of mutation in somatic cells, if it could be proved that such take place. *Ruby spots* (Campbell de Morgan's spots), though present in practically all adults (and some children), tend to be more numerous in elderly persons. I regard them as minute telangiectatic naevi which are possibly due to spontaneous mutation of somatic cells. Any adult who has not one or more ruby spots is a rare exception—in fact, in this respect abnormal (Weber, 1946). They are not to be confused with the rarer spider telangiectases—"stellate naevi"—which may be congenital, though they are often associated in some way with liver disease.

Spontaneous Disappearance or Partial Disappearance of Naevi

It is well known that, in children, capillary vascular naevi may after birth fade or partially or completely disappear spontaneously. "Ruby spots" and minute telangiectatic naevi may sometimes disappear (? by spontaneous thrombosis or atrophic closure of blood vessels). McDonagh's xanthonaevio-endotheliomata in children may spontaneously disappear. I have known one case in which slight but definite xanthelasma palpebrarum disappeared spontaneously. So-called mongoloid patches may disappear in early life. Some other naevi in elderly persons may, I think, diminish or necrose spontaneously.

Naevi and Malignant Neoplasms

The occasional supervention of malignant neoplasms on moles is well known ("naevocarcinoma"). Seborrhoeic naevi in elderly persons may occasionally become carcinomatous and malignant melanomata may develop from pigment naevi. In the rare familial recessive mendelian disease *xerodermia pigmentosa* (xeroderma pigmentosum) the skin is excessively sensitive to exposure to sunlight, which gives rise to warty lesions which ultimately become carcinomatous. Equally well known is the supervention of fatal malignant disease in cases of familial polyposis of the intestine (notably colon) which may be regarded as a familial intestinal naevoid condition (cf. Cockayne, 1927; Dukes, 1930; Lewis, 1941).

Here I would allude to the rare *syndrome of melanin spots (pigment naevi) on the lips and oral mucosa with intestinal polyposis which may lead to intussusception*. The first known examples were in twin sisters described by Sir Jonathan Hutchinson (1896) and J. T. Conner (1895). Afterwards by the kindness of Dr. Conner I

was able to examine one of the twins (Weber, 1919), but no evidence of intestinal polyposis was discovered till later. Jeghers, McKusick, and Katz (1949) collected their own and all known cases bearing on the subject in a paper entitled "Generalized Intestinal Polyposis and Melanin Spots of the Oral Mucosa, Lips and Digits: A Syndrome of Diagnostic Significance." An excellent example of this syndrome with gastric as well as jejunal polyposis was shown by N. C. Tanner (1951) at the Royal Society of Medicine (Clinical Section) on December 8, 1950. Similar familial pigment spots of the lips and mouth without known intestinal polyposis have been published, from time to time. The complete syndrome may be regarded as a fifth kind of "phakomatosis" in J. van der Hoeve's use of the term (Weber, 1951)—see below.

Naevus and Naevoid Diseases and the "Phakomatoses" (Naevus Tumour Diseases) of van der Hoeve

J. van der Hoeve (1938) has grouped the four developmental diseases—Recklinghausen's neurofibromatosis, Bournville's disease (tuberous sclerosis, epiloia), the Lindau-Hippel disease, and the Sturge-Kalischer-Weber disease—as what he terms "phakomatoses." The Greek word φακός (lentil,* birth-mark) is medically equivalent to the Latin *naevus*. I think one must agree that van der Hoeve's phakomatoses are of naevoid nature. So what I have termed neurofibromatous naevi would be included under the heading "neurofibromatosis, a developmental naevoid disease." But if what I have termed "xanthomatous naevi" be regarded as minor localized and non-progressive forms of the developmental metabolic disease xanthomatosis, then xanthomatosis must be accepted as also "naevoid" in nature. This consideration would lead to the question: Are all "inborn errors of metabolism" (A. E. Garrod) to be regarded as naevoid in nature? I am not prepared to go so far, but obviously the whole difficulty is partly one of terminology. To assert that all inborn errors of metabolism are of naevoid nature would be like saying that all conditions resulting from gene abnormalities are of naevoid nature.

"Naevus" and "Naevoid"

In the present state of knowledge I think it is permissible to use the words "naevus" and "naevoid" (that is to say, like a naevus) synonymously. Instead of "naevoid," strictly speaking one should of course say "phakoid," using two Greek words instead of a Latin and a Greek word joined together. However, in this paper I have used the word "naevoid" in respect of conditions which are generally regarded as not naevus, but which I suggest are of naevus-like nature. I speak of a neurofibromatous "naevus," though I regard the whole disease, neurofibromatosis, as "naevoid"—that is, as van der Hoeve would say, a "phakomatosis." Similarly, I would speak of a Pringle's naevus; but the whole disease, epiloia, I would call a naevoid disease—that is, a phakomatosis (van der Hoeve). From my point of view, I would speak of diseases like *telangiectasia macularis eruptiva perstans* and *urticaria pigmentosa* and *inborn urticaria facititia* (which are not generally regarded as naevus conditions) as of naevoid nature. The Sturge-Kalischer-Weber disease or syndrome often presents a trigeminal vascular naevus as a striking feature, but many would object to call the whole syn-

drome a naevus condition, though I think it is obviously of naevoid nature, a phakomatosis of van der Hoeve.

[NOTE.—A list was added of most of the external and some of the internal conditions which Dr. Weber would (often doubtfully) classify as naevi or naevoid, but there was not time to read it.]

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AN EXPLANATION OF THE "PRIMARY ATYPICAL PNEUMONIA" SYNDROME

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In the course of the past two years we have seen over 500 cases of a condition which we believe to be an aspiration pneumonia, the pulmonary lesions of which are confined to certain local regions of the lung. This, both clinically and radiologically, is similar to descriptions of primary atypical pneumonia and to many of the so-called virus pneumonias. We wish to dispel much of the mysticism associated with this group of conditions and to destroy the concept of atypical pneumonia as at present described.

The features of our own cases are described; the reported features of primary atypical pneumonia are reviewed, and the two are compared. Reasons are given for our attack on the present conception of atypical pneumonia, and the significance of the altered point of view is discussed.

Present Series

Material.—The cases have been drawn from young men who had already been passed by a medical board and who were undergoing the first few weeks of initial

*Phakos (lentil) is of course used also to mean the crystalline lens of the eye. When I first heard of "phakoma" (naevus "tumour") I was puzzled concerning what a tumour of the crystalline lens could be.