

*Between Auspitz and Kogoj:*

**WILLIAM DUBREUILH AND THE DEVELOPMENT OF  
DERMATOPATHOLOGY IN HIS TIME**

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The oncoming *World Congress of Dermatology in Paris* is a welcome opportunity to hail other centers of the field outside the *magna mater* of dermatology. *Bordeaux* is one of them and it is indeed famous not only for its wine, and William-Auguste Dubreuilh (1857-1935)<sup>1</sup>, son of the city, is a dignified representative of any historical perspective, also the first bordelais professor of dermato-venereology. For all those beyond the *banlieu* of the city and of French dermatology, Dubreuilh is remembered by any student of medicine for the *Mélanose circonscrite précancéreuse*<sup>2</sup>, - Melanosis circumscripta praeblastomatosa for those who are more familiar with the latinized term. This will be the focus of our presentation; the emphasis therefore will be on *dermatopathology* and its state of the art at the beginning of the 20<sup>th</sup> century.

Dubreuilh's first publicatory efforts appeared in Hermann Ludwig Eichhorst's volumes on general pathology and therapy (six editions between 1883 and 1907<sup>3</sup>.) Dubreuilh graduated MD in 1885 and in 1889 already there appeared a study on the problem of dermatitis herpetiformis Duhring (five years old by itself in that year as an entity). This is an area where early dermatopathologists used to apply their acumen ever since good microscopes exist. The dermatosis eponymically named after our hero is again one of dermatopathology, therefore we want to shortly foray into the development of this subspecialty.

Let us consider dermatopathology under the aspects of its *technical* (cutting and staining; optical equipment) and *semantical*, development, as a *subject of scientific treatises* and books, and as a process, - by anatomical metaphor, - *paving its way* through and along various layers of the skin<sup>4</sup>.

*Cutting and staining*: Only in the second half of the 19th century suitable stains were developed to differentiate clearly between various constituents of the cell and fibre network of tissue. And the same holds for cutting techniques. Early on last century, cutting was still done by hand resulting in a thickness of tissue layers which were not conducive to fine structural investigation. The very same must be said of microscopes. Only by mid-century the optical industry began to provide quality lenses for higher magnification beyond the hand-held lens.

*Semantical aspects*: As early as in the book of Daniel Turner (1667-1740) we find descriptions of the different texture of various strata of skin in his introduction. The term *dermato-pathologia* surfaced in Henry Seguin Jackson's book in 1792, applied in a different sense however, and decades later, was used in the sense of today, by Gilbert Breschet, in France, in 1835<sup>5</sup>, and Julius Rosenbaum, in Germany, in 1844<sup>6</sup>. First academic use of the term was made by Hebra in 1859 for the academic qualification (Habilitation) of Albert Reder-Schellmann, the later (and third) professor ordinarius at Vienna University<sup>4</sup>.

*Treatises and books* on the microanatomy of skin, viz. "dermatopathology" of today. In the first place Gilbert Breschet in Paris may be quoted, who demanded that tissue studies be a regular constituent of dermatologic investigations, thereafter Julius Rosenbaum in Halle and Gustav Simon in Berlin pointed out the same. ("Si on parvenait a localiser les maladies de la peau, et nous en concevons la possibilité, c'est-à-dire si l'on pouvait, prenant pour guide l'anatomie, indiquer le siège de chaque maladie cutanée, ce serait un véritable progrès pour la médecine et pour l'anatomie pathologique" Breschet 1835<sup>5</sup>, p.111, para 3, lin.1-5: Rosenbaum, 1844<sup>6</sup>, verso du frontispice et p.66, ref 58). Beyond these, there were early pioneers of tissue pathology like Oscar Wedl in Vienna, in whose lineage of students Salomon Stricker, Heinrich Auspitz, Moriz Kaposi and Paul Gerson Unna must be singled out for our perspective<sup>4</sup>. It was *Heinrich Auspitz* (1835-1886) (Fig.1) who deserves the greatest credit for his systematic and novel approach to the classification of dermatoses because in his "System

der Hautkrankheiten", dermatopathology played a greater role than in any previous text. *Acantholysis*, e.g. is his neologism traded down into our world of today<sup>8,9</sup>. This constitutes the reason why *his name* was chosen in the title. Unna in Hamburg in 1896 compiled the first comprehensive textbook. Suffice it to say, that it was Ernest Besnier in Paris, in 1885 who coined the term *biopsie*.

This was the world into which William-Auguste Dubreuilh was graduated MD in 1885.

*Now what about the general trend of dermatopathologic studies* during these decades of the *fin de siècle* and thereafter? The first texts on dermatopathologic subjects concerned solid proliferations, e.g. clavi, calli (plural of callus or callum), warts, condylomata acuminata, tumors, cysts, just because more or less solid, circumscribed epithelial structures were easier to cut by hand than bullae, pustules or soft connective tissue with vessels etc. and also because the epidermis was most easily accessible and constituted the proper terrain for dermatologists. The texts from Rosenbaum to Wedl to Isidor Neumann, i.e. from the 30ies to the 70ies of the 19th century bear witness for this fact. Next to solid proliferations, cavities within the epidermis attracted attention and as such were also located on "pure" dermatological ground. "Blisters" were subject of intense discussions in all schools of the field. But "blisters" could be clefts, vesicles, bullae, pustules of sort, may be intra- or subepithelial, have a deep or superficial level of separation. And here Heinrich Auspitz comes in, notwithstanding the fact that his "system" of skin diseases of 1881 was not appreciated by the dermatologic world. The suprabasal split in pemphigus (vulgaris), the more superficial in pemphigus foliaceus, especially the term "acantholysis" and its mechanism, were accepted and stand out as hallmarks of microscopic concepts ever since. Auspitz' texts were published in English in 1885, the same year Besnier used biopsy as a new term<sup>4</sup>.

If one observes the trend of new observations in epidermal pathology in the decades chosen for observation (about 1880 - 1930), the level of microscopic magnification goes up, the topics change from tumors (a *visible outgrowth*) to *dehiscence of the texture* of the epidermis (clefts, blisters), to the *array of layers* and further to the *order of individual cells* within these layers or throughout the whole epidermis. Eventually, the confines of the epidermis were transcended and the dermis became involved more strongly. This development had of course its influence also on more detailed observation of *cavities*: Hallopeau presented his .. "dermatite pustuleuse disséminée" in 1890, Munroe's (an Australian) microabscesses were described shortly before the turn of the century (just when he moved from Vienna to Paris), Kogoj's spongiforme pustule followed in the late twenties, Pautrier's microabscesses eventually came in 1937 and were called such in 1946. *Franjo Kogoj* (1895-1981) was chosen in the title of our presentation because he died only in 1981 and because one of us is from the place where he worked, i.e. Zagreb (SFF), the other knew him personally over many years (KH)<sup>10</sup> (Fig.2). Moreover the idea of a "spongiforme pustule" necessitated a so-to-say "two-dimensional" thinking, namely, the interlocking of epidermal and dermal pathology which we consider intriguing for the time.

*Dubreuilh* fits nicely into this mainstream of development of dermatopathology. Let us go and delve into this flow of papers.

Jean Darier described his "psorospermosis" as he called it and which bears his name eponymically which focuses on cellular details within the epidermis, in 1889. Dubreuilh entered this arena already in 1896 when he read a paper at the IIIrd International Congress in London entitled "*des hypérkeratoses circonscrites*" into which he counted arsenical keratoses, xeroderma pigmentosum, keratosis senilis, (extramammary) Paget, and others<sup>11</sup>. Very interestingly so, this paper of Dubreuilh's is mentioned right in the beginning of John

Templeton Bowen's classic of 1912 when he described what eponymically is called Bowen's disease<sup>12</sup>. In an subsequent paper of 1915 Bowen returns to the subject and mentions that Jean Darier first named Bowen's diseases by calling it such and introducing the American's name as an eponym<sup>13</sup>. To illustrate further these intertwining strands of observations let us now relate to Dubreuilh's classic from the very same year 1912 in the *Annales de Dermatologie: De la mélanose circonscrite précancéreuse*,<sup>2</sup> a lengthy treatise in which he sums up a series of 33 cases. In it he also comes back to his paper of 1896 at the London World Congress<sup>11</sup>. He explicitly states that he considers Paget's disease to be included (which cannot be upheld today) but calls it "*non-kératosique*", which is remarkable. At this point of time, "melanoma" was not a universally accepted term nor was its origin clear, this we must keep in mind. Also for this reason we do not enter the discussion on lentigo maligna vs. superficial spreading melanoma or any related differential diagnosis. We present here a historical *rapprochement* in honor of Dubreuilh and do not intend to offer clues for diagnosis of melanocytic lesions. And for this very reason there will be no discussion of Dubreuilh's precancerosis vis-à-vis Hutchinson's freckle of 1892 - by itself a story to follow up - nor against Hutchinson's melanotic whitlow of 1886<sup>14,15</sup>. In the present context, as we see, several famous authors dealt with the very same question in terms of dermatopathology, clinic and semantics and within the same decades from the mid 80ies of the 19<sup>th</sup> to the mid-teens of the 20<sup>th</sup> century: *Jean Darier, Jonathan Hutchinson, John Templeton Bowen and William Dubreuilh*

We should like to add two comments to this narrative of events in epidermal pathology:

- (i) a quotation from Dubreuilh's classic paper of 1912, namely a phrase from the last part of the commentary, p. 134, para 2, lines 1 ff: "*l'apparition d'un carcinome - (i.e. melanoma) - est une éventualité qui est toujours à craindre dans la mélanose, mais cette terminaison n'est pas fatale ou plutôt peut être indéfiniment reculée. L'évolution maligne peut se faire dès le début, c'est le carcinome d'emblée, au bout de quelques mois ou de quelques années, mais parfois elle peut n'apparaître qu'au bout de 20, 25, 30 ans davantage ; elle peut aussi ne jamais se faire...La tumeur n'apparaît pas toujours sur la tache elle-meme, elle peut aussi bien naître dans son voisinage, ...*" Thereby the precancerous character and its facultative progress to outright malignancy is stressed. This is an important fact because of the necessity of early preventive therapeutic measures and is in line with today's concept of "lentigo maligna melanoma".
- (ii) *disarray* within the epidermis, in a biological sense, i.e. in the direction of precancerous potential, was first alluded to by Unna with his sailors' skin, and by Dubreuilh more broadly and specifically, in the above mentioned presentation at the London ICD 1896<sup>11</sup>. It should be remembered that at this time melanoma of today was called mostly melano-carcinoma and that the production of melanin was ascribed to keratinocytes. Langerhans' cells "existed" in the literature since their first description in 1868 but melanocytes were not identified yet. We have tried to track down the naming of the *melanocyte* some years ago but could not unequivocally locate it. To the best of our knowledge this was done in the first decade of the 20th century, , in Nancy, by a female researcher, presumably of Russian origin. For the sake of completeness it shall be mentioned that the term "*mela(n)in*" was coined by Bartolommeo Bizio in 1825<sup>16</sup>.
- (iii) By describing his *Mélanose circonscrite précancéreuse* in 1912, Dubreuilh widened the concept of epidermal (pre)canceroses beyond the keratinocytes by including the melanin-producing cells and their lineage into this scheme. With his description it became clear that environmental influence may favor or accelerate

precanceroses and/or induce frank malignancy not only in the keratinocyte filiation. (The discovery of a "Langerhans cell tumor" took more than half a century till it was presumed in the mid-60ies, and was confirmed shortly after. The Merkel cell was described in 1875; as regards a Merkel-cell tumor it took till 1972 and still is a matter of some controversy today)<sup>17</sup>.

What we may conclude from all of the above is that William-Auguste Dubreuilh worked most of his years in Bordeaux, where he founded the *école bordelaise* of the specialty and his investigations were as much in the forefront of the field of dermatopathology as other studies were clinically focussed. Dubreuilh's results were as modern and up to date as were any in the metropolitan center of Paris at the time. And this is probably the greatest compliment to be made in favor of any French dermatologists outside the *Île de France*.

His contemporaries wrote<sup>1</sup> at the close of his academic career " *Il a fondé plus qu'un service, qu'un enseignement, qu'une chaire, il a fondé une école. Il serait délicat de chercher à déterminer quelle place cette école bordelaise occupe, grâce à lui, parmi les écoles de France et de l'Étranger, mais on peut dire, que cette place est importante.*"

*With this tribute we want to close.*

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