

# THE HISTOGENESIS OF MOLLUSCUM CONTAGIOSUM \*

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In a paper by Wile and Kingery, presented at the last annual meeting of the American Dermatological Society, were detailed a series of experiments directed toward a demonstration of the etiologic agent of molluscum contagiosum. As a result of their studies, these authors were able to show that the lesions of this disease can be produced experimentally from the sterile filtrate of molluscum lesions, thereby justifying their conclusion that molluscum contagiosum is caused by a filterable virus. The technic of these experiments, as carried out on themselves and their assistants, was comparatively simple. Molluscum lesions were removed by curettement, ground up in a mortar containing a small amount of sterile saline, and the resultant mash passed through the finest Berkefeld filter under negative pressure. The filtrate thus obtained, which produced no growth on all ordinary culture mediums, was injected intracutaneously into human subjects, at the points of predilection for the development of this disease. After an incubation period varying from twelve days to three weeks, definite papular lesions developed at the sites of the injections. These lesions rapidly took on the clinical characteristics of molluscum contagiosum. Those examined histologically, after a developmental period of eight weeks, presented the unmistakable picture of the disease, including the so-called "molluscum bodies." The subjects of these experiments were under daily observation and histologic study was undertaken at short intervals during the entire evolution of the lesions. In this way material was obtained including every developmental phase of the lesions, from the earliest pinpoint papule, up to the mature stage with its waxy appearance, the central umbilication, etc. The material thus studied offered an unusual opportunity for the investigation of lesions whose histogenesis has been a debated question since the time of Bateman's original description of the disease. It is on a critical examination of this material that the present study is based.

## TWO THEORIES REGARDING ORIGIN OF MOLLUSCUM CONTAGIOSUM

The opposing views of many leading investigators, regarding the peculiar histologic picture presented by molluscum contagiosum, are

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found recorded frequently in the literature on this disease. Out of these controversies two preeminent theories have been developed, which are today used in an attempt to explain the origin of these lesions.

*Theory of Pilosebaceous Origin.*—The first of these views to be advanced was to the effect that the lesions of this disease are related to the pilosebaceous apparatus. Engel<sup>1</sup> was among the foremost to take a definite stand on this interesting phase of the question. As the result of a series of observations, he stated his belief that the molluscum tumor was to be regarded as an enlarged sebaceous gland. This view

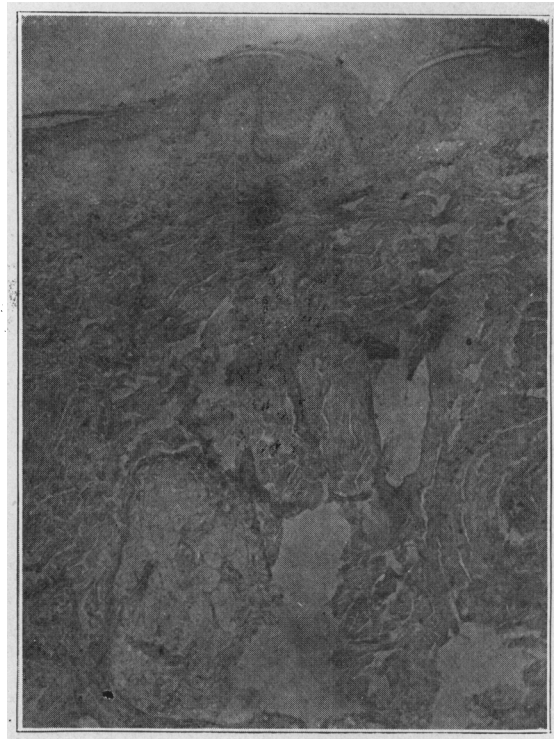


Fig. 1.—Early pinpoint size experimental lesion, showing beginning localized acanthosis and related gland structures.

was strengthened a few years later, when Virchow<sup>2</sup> published the results of his investigations of this disease. He interpreted the histologic picture as a lobulated glandular epithelioma, arising from the hair follicle. He further likened the molluscum bodies to fat-like

1. Engel: Ztschr. d. k. k. Gesellschaft der Aerzte in Wien **2**:408, 1844; abstr. White and Robey: Molluscum Contagiosum, J. Med. Research **7**:25, 1902.

2. Virchow: Molluscum Contagiosum, Berl. med. Gesellschaft Sitzung, Dec., 1864; Berl. klin. Wchnschr. **2**:34, 1865.

globules surrounded by a double-contoured rim, which resisted the action of water and acids. A few years later Kaposi's<sup>3</sup> views were published. He was one of the first to agitate the contagiousness of the disease and at the same time he stated his firm belief in the follicular origin of the tumors. The following year Vidal<sup>4</sup> likewise expressed himself as believing the tumor to be of pilosebaceous origin, and added the suggestion of a colloid degeneration of the cells. The papers of Renault,<sup>5</sup> Crocker,<sup>6</sup> Hebra,<sup>7</sup> and Benda<sup>8</sup> appeared shortly afterward, in which each, while placing different interpretations on the molluscum bodies, firmly stated his belief that these tumors arise always in connection with the pilosebaceous apparatus. Among the list of supporters of this view must also be included the names of Erasmus Wilson.<sup>9</sup>



Fig. 2.—Experimental molluscum lesion, a few days later; acanthosis more marked.

3. Kaposi: Ueber das sogenannten Molluscum Contagiosum, Vierteljahresschrift f. Dermat. u. Syphilis **4**:333, 1877.

4. Vidal: Soc. de Biol., Seance du 15 juin, 1878, Progres méd. **0**:478, 1878.

5. Renault: Anatomie pathologique de l'acne varioliforme, Ann. de dermat. et syph. **1**:397, 1880.

6. Crocker: Diseases of the Skin, London, H. K. Lewis, 1893, p. 479.

7. Hebra, F.: Diseases of the Skin, Including the Exanthemata **1**:131, trans. by H. Fagge, London.

8. Benda: Untersuchung ueber die Elemente des Molluscum Contagiosum. Dermatol. Ztschr. **2**:195, 1895.

9. Wilson, E.: Diseases of the Skin, London, 1842, p. 341; *ibid.*: Diseases of the Skin, Philadelphia, 1863, p. 653.

Rokitansky,<sup>10</sup> Tilbury Fox,<sup>11</sup> Hutchinson<sup>12</sup> and others. Minor differences of opinion are to be found in the publications of these investigators; yet, in the main, it is to them that we owe the belief, still shared by many authorities, that the lesions of this disease are always, in some way, related to the pilosebaceous apparatus of the skin.

*Theory Regarding Origin of Molluscum Contagiosum in Rete Layer of Epidermis.*—Coincident with the studies and investigations mentioned above, however, other and equally reputable investigators placed an entirely different interpretation on the microscopic picture of these tumors. For them the lesions were never related either to the follicles or the sebaceous glands, but were due to a pathology concerning only the rete layer of the epidermis. As early as 1848, only a few years after the article by Engel, von Barenprung<sup>13</sup> described the bodies making up these tumors as epidermal cells which had undergone a peculiar degeneration. He furthermore stated his belief in their non-follicular origin. A few years later Retzius<sup>14</sup> concluded, after a series of observations, that the tumors were never related to the pilosebaceous apparatus, but owed their origin entirely to the epidermis. Shortly thereafter Boeck,<sup>15</sup> after a careful study, entirely denied the sebaceous origin of the lesions, because fat is never detected in the cells. This reasoning, however, is hardly more tenable than would be a similar objection to the origin and relation of a tumor of the pancreas because of the absence of pancreatin in the cells of such a new growth. The absence of fat might be more easily explained by the changes through which the cells must pass before molluscum bodies are obtained. The papers of Lukomsky<sup>16</sup> and O. Simon<sup>17</sup> then followed, and offered separately, as an explanation, an enormous proliferation of the rete cells, resulting in the peculiar tumor formation seen. A few years later the subject was carefully presented in a paper by Geber,<sup>18</sup> in which

10. Rokitansky: *Pathologische Anatomie*, Ed. 3, Vienna, Braumuller, **2**: 79, 1856.

11. Fox, T.: Case Report, Clinical Society of London, April, 1872, *Brit. M. J.* **2**:538, 1872.

12. Hutchinson, J.: *Lectures on Clinical Surgery*, London, J. and A. Churchill, 1878.

13. Von Barenprung: *Beitrag zur Anatomie und Pathologie der Haut*, Leipzig, 1848, p. 43.

14. Retzius: *Ueber Molluscum Contagiosum*, *Deutsch. Klin.* **23**:450, 1871.

15. Boeck: *Ueber Molluscum Contagiosum und die sogenannten "Molluscumkorper," Vierteljahresschrift f. Dermatol. u. Syphilis* **2**:23, 1875.

16. Lukomsky: *Ueber Molluscum Contagiosum*, *Virchows Archiv.* **65**:145, 1875.

17. Simon, O.: *Ueber Molluscum Contagiosum*, *Vierteljahresschrift f. Dermatol. u. Syphilis* **3**:400, 1876.

18. Geber *Ein Fall von Epithelioma molluscum (Virchow) universal mit besonderer Rücksicht auf das Wesen dieser Krankheit* *Pest. Med. chir. Presse*, Budapest, 1882, pp. 685, 703.

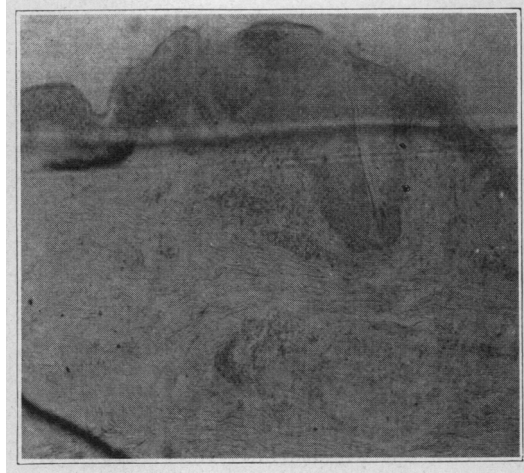


Fig. 3.—Early experimental molluscum lesion, showing involvement of follicle, hair remnants and related gland.



Fig. 4.—Continuation of follicular acanthosis and beginning cellular degeneration.

he attempts to trace the evolution of the rete cells into the molluscum bodies. Still later Neisser,<sup>19</sup> 1882, Stanziale,<sup>20</sup> 1890, and McCallum<sup>21</sup> in 1892, published papers, and among other observations stated their firm belief in the nonfollicular origin of the tumors. In 1896 Unna's<sup>22</sup> histopathology appeared with a most thorough elucidation of the subject. In this Unna suggested the term "epithelioma contagiosum," and stated that he did not believe the tumors to be of sebaceous origin because he had never seen any sebaceous material in the tumor tissue. This reason, however, seems to prove the point no more than that offered by Boeck and is, I believe, open to the same objections. Finally, a most scholarly review of the subject, presenting previous and contemporary opinions, has more recently been published by White and Robey.<sup>23</sup> Besides those mentioned above, the names of Campana,<sup>24</sup> Torok,<sup>25</sup> Klebs and Kromayer<sup>26</sup> must be added to those who believe in the nonfollicular origin of the lesions of the disease.

Such, then, have been the theories of the histogenesis of molluscum contagiosum up to the present time. Two explanations, one almost diametrically opposed to the other, yet each supported by more than one of the leading investigators of their time. Similarly, differences of opinion have arisen through attempts to explain the derivation and origin of the so-called "molluscum bodies." This, and other questions, have not been included in the present study, in which the subject of histogenesis only has received consideration. So far as the literature reveals, the opportunity for investigation of material similar to that of the present study has never presented itself in the past. This fact, it is believed, justifies a fairly detailed account of the changes as observed in the development of lesions experimentally produced.

19. Neisser: Ueber das Epithelioma (sive Molluscum) contagiosum, Vierteljahresschrift f. Dermatol. u. Syphilis **15**:553, 1888.

20. Stanziale: Gior. Internazionale de Sc. Med. n. s. 1890, n. s. **12**: 321, 1 pl. Contributo sperimentale anatomo-patologico e batteriologico all studio del mollusco contagioso di Bateman.

21. MacCallum: Histology of Molluscum Contagiosum, J. Cutan. & Gen-Urin. Dis. **10**:93, 1892.

22. Unna: Histopathology, Diseases of the Skin, Walker's trans., Edinburgh, W. F. Clay, p. 793.

23. White and Robey: Molluscum Contagiosum, J. Med. Research **7**:255, 1902.

24. Campana: Sui globi del Mollusco contagioso, Gior. ital. d. mal. ven. **21**:37, 1886.

25. Torok and Tommasoli: Ueber das Wesen des Epithelioma Contagiosum. Monatsh. f. prakt. Dermat. **10**:149, 1890.

26. Klebs: Psorospermien im Innern von thierschen Zellen, Virchows Arch. f. path Anat. **16**:188, 1859.



Fig. 5.—Experimental lesion few days older, showing early cavity formation and cellular changes.

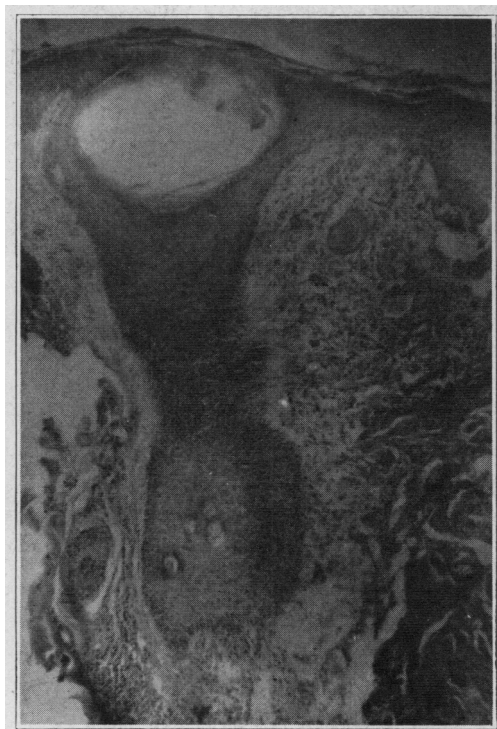


Fig. 6.—Experimental lesion, showing epithelial pocket formation, definite papular element and changes, including follicle and gland.

STUDY OF MOLLUSCUM CONTAGIOSUM EXPERIMENTALLY  
PRODUCED

As stated before, the development of these lesions was under daily observation, so that clinical and histologic examinations were possible as frequently as developmental changes warranted. Approximately twelve days following the injection of the sterile filtrate, one of the patients developed small papular lesions, surrounded by a slightly erythematous zone. These rapidly took on characteristics, making a clinical diagnosis possible. One of several lesions excised at this time are shown in Figures 1 and 2. Apparently, the first change occurring



Fig. 7.—Experimental lesion showing early umbilication, epithelial pocket formation, cellular debris, and related glandular structures.

is that of an extremely small, localized acanthosis, the process resulting in a downward bulging of the epithelium, the increase in thickness being due chiefly to malpighian changes. Apparently, this change continues for some time, the acanthosis becoming more marked, the rete pegs being gradually obliterated, and the process encroaching on the underlying cutis. A few days later, however, serial sections show a factor not present in Figures 1 and 2, i. e., that this acanthotic change involves the follicular wall, a fact evidenced by the hair sheath remnants present and the glandular structures deeper in the section (Fig. 3). Sections a

short time later show a still more extensive involvement of the follicular apparatus (Figs. 4 and 5). The experimental lesions developed fairly rapidly in certain instances, and by the twenty-first day, in one case, had assumed definite papular proportions, presented a waxy appearance, and in not a few a central umbilication was evident. Again serial sections were examined (Figs. 6, 7 and 8). In addition to the

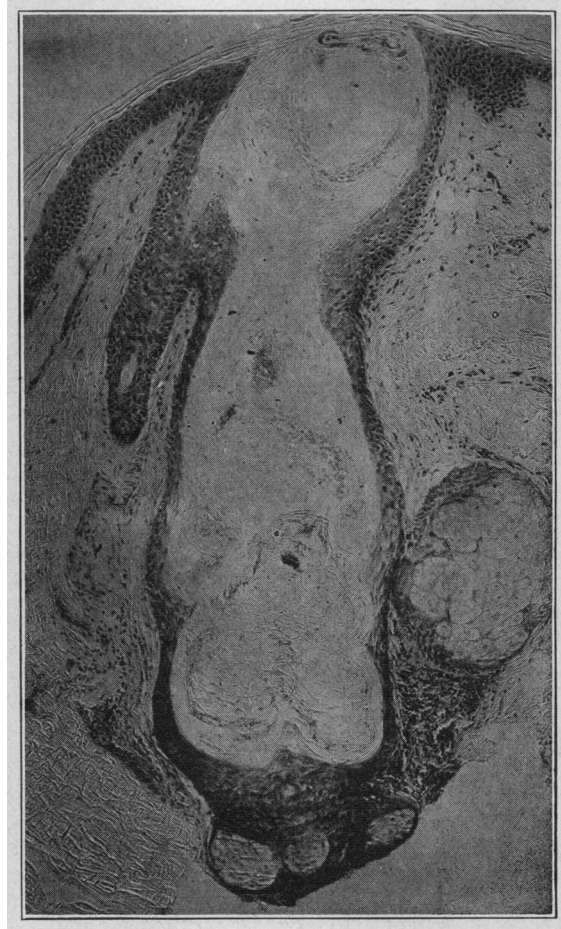


Fig. 8.—More extensive follicular involvement, marked epithelial pocket formation, etc. A lesion clinically typical of molluscum contagiosum.

follicular acanthosis above described, a peculiar cellular degeneration had begun to appear in the central portion of the process. At first these changing cells stain not unlike those undergoing hyperkeratinization. Soon, however, these centrally located, deep-staining cells undergo further degeneration, and in the course of a few days the

process assumes the true outline of molluscum lesions (Figs. 9, 10, 11, 12 and 13). In section, the basal cell layer remains apparently unchanged and intact, and in addition there is epithelial pocket formation with a central cavity containing for the most part cellular debris. Apparently, the so-called molluscum bodies develop relatively late in the disease, as in none of the specimens examined up to this time were the bodies present, although the lesions were clinically typical of the disease. Objective change was gradual from this time on. The lesions slowly increased in size, and one after another, without exception, took on the peculiar waxy color, developed a central umbilication, and from

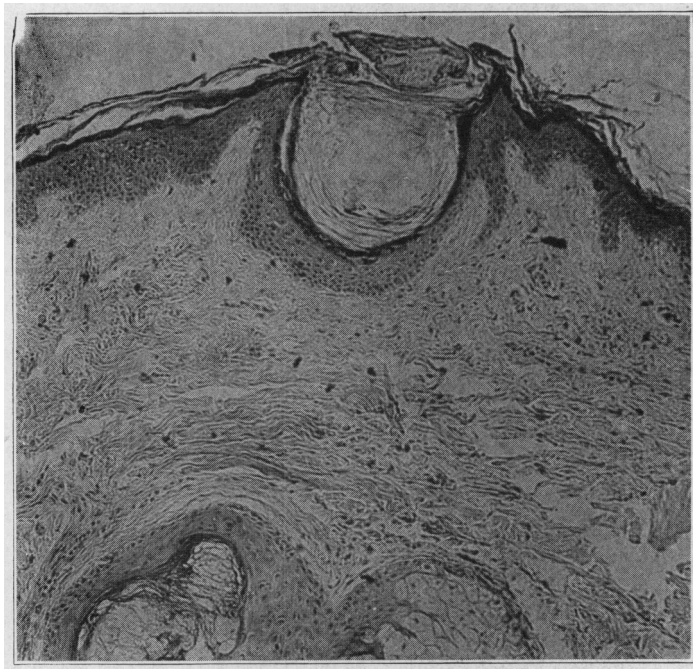


Fig. 9.—Somewhat later stage, well formed capsule, cellular degeneration, pilosebaceous structures.

time to time the patients complained of pruritis. It was also an interesting observation that new lesions began to appear outside the sites of injection, an occurrence suggestive of the contagiousness of the condition and its dissemination by the trauma incidental to scratching. The lesions at this time were in the sixth week of development, and as the picture had apparently changed so little, biopsies were suspended for a number of days. Approximately eight weeks following the beginning of the experiment, a few more clinically typical lesions developing at the sites of injection, were removed. Sections of these

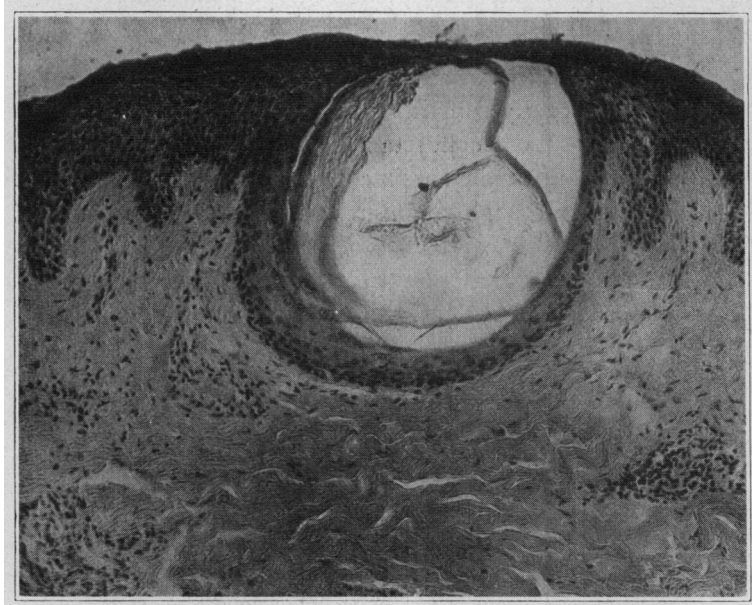


Fig. 10.—Slightly older lesion, showing gradual growth of epithelial pocket.

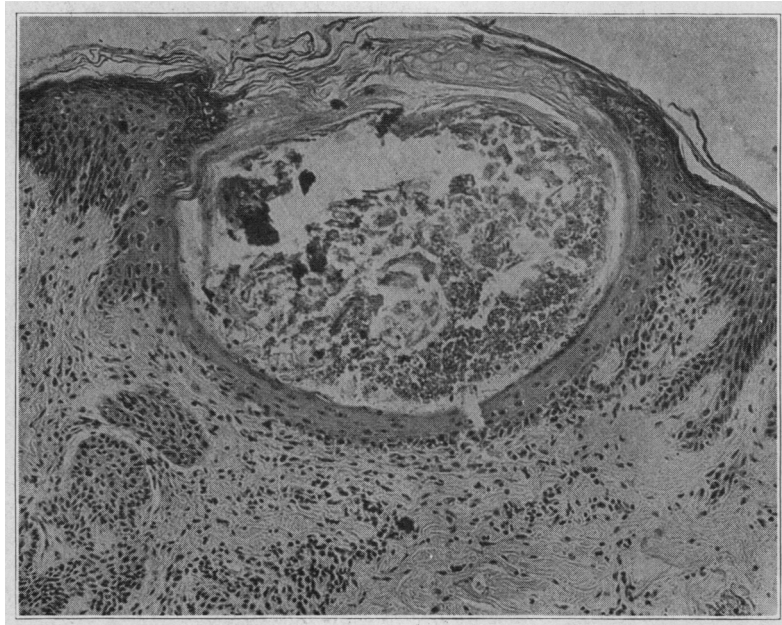


Fig. 11.—Well formed experimental lesion of molluscum contagiosum, typical except for absence of true molluscum bodies.

lesions are shown in Figures 14 and 15. A detailed description of these typical lesions is unnecessary. In Figure 14 the peculiar degeneration of this disease appears below the surface, being attached by an epithelial pedicle of unchanged cells. In the tumor itself, the basal cell layer is apparently little changed, the peculiar metamorphosis becoming more evident as the central portion is approached. The epithelial pedicle extending downward from the surface, in view of the relation shown in previous earlier sections is, I believe, the unaffected portion of the



Fig. 12.—Experimental molluscum lesion, showing relation of pilosebaceous apparatus.

follicular wall, in tangential section. In Figure 15, a more central section, the process extends to the surface, umbilication is evident, and the adult stage is evidenced by the presence of the molluscum bodies.

To review briefly, the observations recorded above are from lesions developing at the sites of injections of the sterile filtrate of the lesions of molluscum contagiosum. The described changes are as seen in the

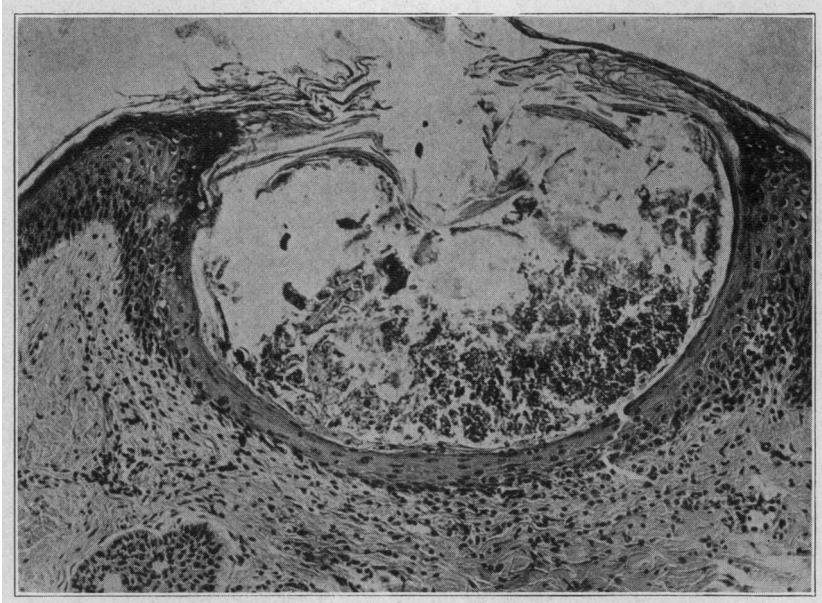


Fig. 13.—Experimental molluscum lesion, approximately six weeks old, the typical picture, lacking only the molluscum bodies, not yet formed, and again showing related pilosebaceous apparatus.



Fig. 14.—Well developed experimental lesion, eight weeks old with epithelial pedicle.

sections, and these, together with the study of many hundreds of sections not reproduced, have continually emphasized a relation with the glandular and follicular structures of the skin.

#### STUDY OF SIMILAR DISEASE IN ANIMALS

In spite of this experimental evidence, which is, without exception, in favor of the pilosebaceous origin of the disease, the opinion of those renowned investigators who believed otherwise, cannot be well ignored. Not entirely satisfied, therefore, an investigation of other experimental work suggested itself, with findings worthy of consideration. From time to time, experimental studies and observations have been carried out on a disease, clinically and pathologically identical with molluscum contagiosum of man, occurring in the lower animals.

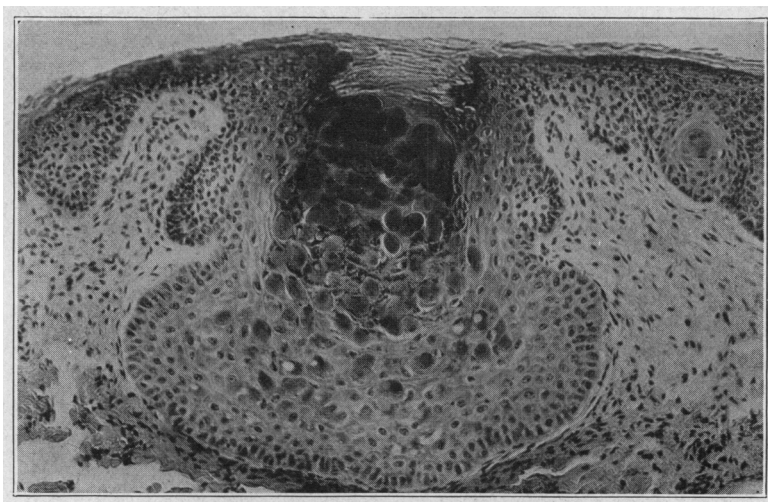


Fig. 15.—Adult lesion a few days older, presenting typical bodies, central umbilication.

As long ago as 1873, Bollinger<sup>27</sup> reported successful inoculations and transplantations in an investigation of the etiology of “Epithelioma Contagiosum” of domestic fowls. He was able to satisfy himself of the contagiousness of the condition, suggested as sites of predilection the comb, wattles, external ears, eyelids and feet of domestic fowls, and lastly he identified the histologic picture with that of molluscum contagiosum of man (Fig. 16). Hutchinson,<sup>28</sup> MacKenzie,<sup>29</sup> and

27. Bollinger: Ueber Epithelioma contagiosum beim Haushahn und die Sogenannten Pocken des Geglugels, Arch. f. path. Anat. u. Physiol. **58**:349, 1873.

28. Hutchinson: Molluscum Contagiosum, etc., Clin. J. **5**:323, 1894-1895.

29. MacKenzie: Molluscum Contagiosum in the Field Sparrow, Canadian Pract. & Rev. (Toronto) **26**:83, 1901.

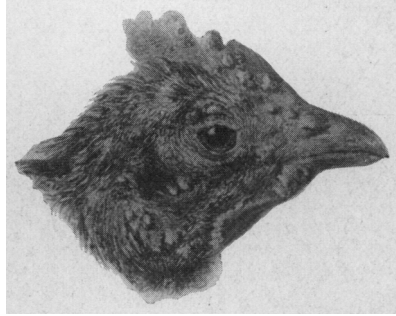


Fig. 16.—Lesions of “epithelioma contagiosum” occurring on combs, wattles, etc., of domestic fowl.

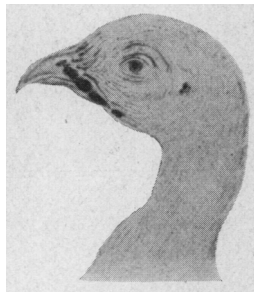


Fig. 17.—Case of “molluscum contagiosum” involving head and extremities of fowl reported by Fox.

Shattock,<sup>30</sup> a few years later, recorded individual observations of what they termed "molluscum contagiosum in both wild and domestic fowls." In 1898, Colcott Fox<sup>31</sup> presented to the Pathological Society of London, a case of "molluscum contagiosum" occurring in a young fowl (Fig. 17), and called attention to the identity of the clinical and pathologic picture, with that of molluscum contagiosum occurring in the human subject. And lastly, Marx and Sticker,<sup>32</sup> and Mariani,<sup>33</sup> have published the results of separate investigations of "Epithelioma Contagiosum of Fowls." The former were able to produce lesions histologically typical of molluscum contagiosum by rubbing the material from lesions of epithelioma contagiosum into the scarified combs of

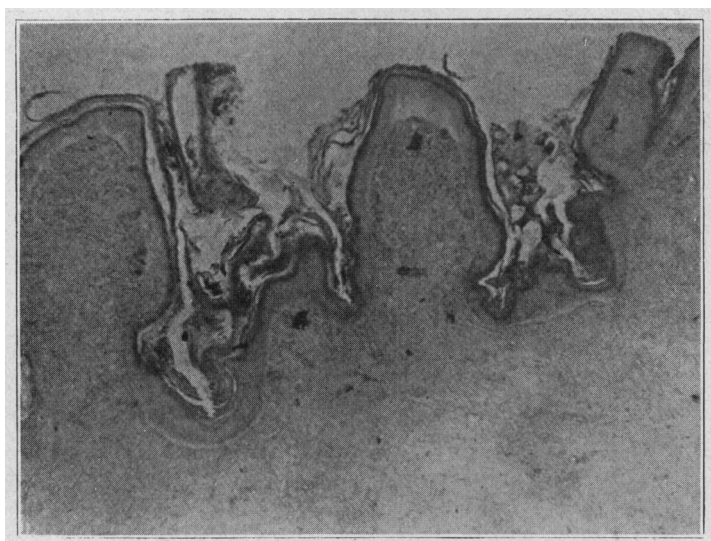


Fig. 18.—Section from comb of domestic fowl. Note absence of pilosebaceous structures.

pigeons and chickens. Mariani points out in particular the similarity of the contagioseness of the two conditions and the identity of the histologic pictures. The foregoing and numerous other references in the

30. Shattock: Molluscum Contagiosum in Two Bunting Sparrows, *Trans. Path. Soc. London* **49**:394, 1898.

31. Fox, C.: Molluscum Contagiosum of Legs, Feet and Head of the Chicken, *Trans. Path. Soc. London* **49**:393, 1898.

32. Marx and Sticker: Untersuchungen über das Epithelioma contagiosum des Geflügels, *Deutsch. med. Wchnschr.* **28**:893, 1902.

33. Mariani: Beitrag zur Aetiologie und Pathologie des Molluscum Contagiosum des Menschen und des Epithelioma Contagiosum der Vogel, *Arch. f. Protistenkunde* **21**:213, 1911.

literature leave no doubt that a disease, clinically and pathologically similar to molluscum contagiosum in man, occurs in the lower animals.

In not a few of the above studies certain sites of predilection were emphasized and an investigation of the comparative histology of these parts was undertaken (Figs. 18 and 19). A critical search of serial sections taken from the combs and feet of fowls has in no instance revealed the presence of sebaceous or other glandular structures, nor the suggestion of any analogue. It would seem that this is a point of extreme interest in the light of the interpretations of English investigators; Hutchinson, Fox, MacKenzie, and Shattock, each have reported their observations on what they have elected to term "molluscum con-



Fig. 19.—Section from leg of domestic fowl. Note absence of pilosebaceous structures.

tagiosum" in lower animals. Shattock, in particular, urges the identity of the two conditions, and gives as evidence, besides his microscopic findings, isolated cases of probable transmission of the disease from animals to man. For these investigators, the clinical and pathologic similarity, and the presumptive evidence of transmission, has warranted the use of identical nomenclature. Whether or not these two conditions are identical, as presumptive evidence would lead one to believe; or whether the virus causing these lesions has a certain specificity for the host invaded; are questions that must await the results of future investigations. For the present, one may go only so far as to say that the

analogue of molluscum contagiosum in man does occur in the lower animals, with clinical, pathologic and etiologic characteristics in common. Further, it may be said that the lesions of this disease are capable of developing independent of the pilosebaceous structures.

If we may consider the preexisting theories in the light of the present study, it would appear that each were correct in part. With sections exhibiting but one phase of development, or perhaps obtained from but one case, the reason is patent for previous views having limited themselves to a follicular or nonfollicular origin of the disease. Without doubt, certain cases or at least certain lesions present a pathology which exactly limits itself to the pilosebaceous apparatus. In addition, such a contention may be well supported by the lobulated outline often assumed, the clinical symptom of pruritus, and lastly the ease with which an etiologic agent might gain entrance through the follicular openings of the glabrous skin. To other investigators it may well be that only epithelial changes were evident. There were no glandular structures related in the sections studied and the usual tests for fat, when applied to the so-called molluscum bodies, were negative. If, however, one goes a step further, it may be recalled that embryologically the surface epithelium, the hair follicle and the sebaceous gland and duct have a common anlage. The outer layer of the embryo consists only of ectoderm, from which downward invagination, and subsequent proliferation, result in the pilosebaceous apparatus of the adult, while from the surface portion develops the cutaneous envelope. Embryonically, and we may almost say potentially, therefore, these structures are similar, and given favorable soil, i. e., susceptible individuals, it is but reasonable to believe that the same causative factor may result in changes pathologically similar, whether it be implanted one place or the other.

#### CONCLUSIONS

1. Studies by Wile and Kingery have shown the development of experimental lesions of molluscum contagiosum to be limited to pilosebaceous epithelium.
2. An abundance of clinical and pathologic evidence favors the existence of the analogue of molluscum contagiosum in fowls.
3. Absence of pilosebaceous epithelium in the combs and feet of fowls and pigeons, where lesions of molluscum epitheliale often occur, justifies the conclusion that the lesions of this disease can develop independent of pilosebaceous structures.
4. Presumptive evidence points to the identity of molluscum contagiosum in man and molluscum epitheliale in lower animals. Final proof of the development of molluscum contagiosum from the surface

epithelium, therefore, must depend on the establishment of the identity of these two conditions. This identity will be proved only by the successful inoculation of molluscum contagiosum into fowls, and of molluscum epitheliale into human subjects.

5. Experiments directed toward this end have been undertaken in this laboratory.

For the privilege of undertaking this work and for constant and invaluable advice during its completion, I wish to express my indebtedness to Prof. Udo J. Wile.

#### ABSTRACT OF DISCUSSION

DR. J. M. KING, Nashville, Tenn.: In 1904 Dr. Crocker of London received a parrot from South America. The bird had papules all over the body, neck and head. The case was diagnosed by Dr. Crocker and Dr. Pernet as molluscum contagiosum. I do not know what the laboratory reported.

DR. WALTER J. HIGHMAN, New York: I was taught that molluscum starts in the malpighian rete. The relation of the growth to the pilosebaceous glands is clearly brought out in Dr. Kingery's paper and is quite at variance with the older ideas. Is the disease found in fowls known as "pigeon epithelioma"? Prowazek thought he had found the cause of pigeon epithelioma and he considered the disease closely allied to molluscum contagiosum in man.

DR. LYLE B. KINGERY, Ann Arbor, Mich.: So far as I know, while the investigators believed the disease to be of parasitic origin, they were unable to cultivate or demonstrate a specific organism.