Epithelium in Tuberculous Pulmonary Lesions*, **
O. KANNER, M.D. and E. D. PEASLEY, M.D.
Oteen, North Carolina

During the last decade the availability of surgical material has stimulated morphologic observations of tuberculous pulmonary lesions not only for academic purposes, but also with a view to indications for surgery. This has led to divergent interpretations and inconsistent clinical conclusions. Contradictory explanations concerning epithelium, so frequently found in the lesions, have been the main cause of this divergence.

Based upon the material available at Oteen we have attempted to analyze the evidence which has led to such difference in opinion, and have met with facts not previously reported which tend to clarify the picture. This paper deals mainly with the formation and healing of tuberculous cavities. We are convinced that more consideration must be given to the bronchial tree than before. It appears that some still widely accepted views are no longer tenable.

Pagel and Simmonds1 believe that in one mechanism of cavity healing ingrowth of epithelium occurs after the tuberculous process has been replaced by ordinary granulation tissue and fibrosis. Auerbach et al2, 3, 4 support this view, and express the opinion that this type of healing is rare except following streptomycin therapy where it is said to be nearly constant. According to them “re-epithelialization” of the “broncho-cavitary junction” occurs regularly in the course of streptomycin therapy and “in some instances the epithelium extends far around the cavity wall,” preventing cavity closure. This is contrasted to non-streptomycin treated cases where they report that cavity closure follows bronchial occlusion, but Silverman et al5 find that this very mechanism of closure follows streptomycin therapy, and do not mention epithelialization.

Both Auerbach and Silverman agree that the cavity contents are potentially dangerous. However they disagree in the reasoning about the danger. Silverman, who claims that early cavity closure occurs with chemotherapy, is fearful about the subsequent retention of infectious material. Auerbach argues that the danger is brought about by non-closure of the cavity because of “re-epithelialization” induced by chemotherapy and is apprehensive about the infectious material because it can not be retained. Both conclusions cannot stand. Both authors have advised resection.

In addition, Silverman, et al suggest the possibility that a cavity may start in a bronchus, but add that by the time the specimen is seen there is too much parenchymal involvement to permit clarification of this point. They also express the belief that tuberculous bronchitis occurs mainly following caviation since none of their 22 cases had bronchitis

*From the Laboratory Service, Veterans Administration Hospital.
**Presented as part of an exhibit at the annual meeting, National Tuberculosis Association, Milwaukee, Wisconsin, May 23-27, 1955.
without cavitation.

According to Clegg,\textsuperscript{6} ulcero-caseous tuberculous bronchitis, progressing from the periphery to the hilus, is a very important mechanism in the development and spread of the disease. Bronchial stenosis leads to collapse when pneumonia does not occur. Coalescent lesions may produce bronchial cold abscess, either solitary or multiple, which may be evacuated leaving a cavity. He further says that it is often impossible to distinguish in a fully developed caseous lesion whether it arose from tuberculous pneumonia or bronchitis.

Previous authors have tacitly assumed that when epithelium lines structures devoid of muscle, cartilage and glands it is newly formed and hence its presence has been ascribed to epithelialization. It must be borne in mind that while the presence of the epithelium is a fact, the idea of epithelialization is speculative only and implies that the epithelium has not previously existed at the site where it is found. Our study has furnished evidence that epithelium alone identifies bronchial wall with as much certainty as does muscle, cartilage or glands. Our evidence is presented.

If epithelium can be used to identify bronchial wall, what appears to be a parenchymatous cavity lined by epithelium, may be an ectatic bronchus. Figure 1 is a schematic representation of mechanisms which,
according to our experience, produce such epithelialized structures. As a result of destructive endobronchial or parabronchial disease portions of the wall become ulcerated and weakened. Dilatation or distortion follows and irregular epithelial islands may remain. In this way the appearance of a more or less epithelialized cavity is created.

Of the specific bronchial structures, epithelium, glands, muscle and cartilage, epithelium may be the sole survivor because of its resistance to destruction. Even in contact with an acute caseating lesion, bronchial wall, and especially its epithelium, is not easily destroyed (Figs. 2, 3, 4, and 5). When epithelium is destroyed, regeneration depends upon the character of the bed which is to be covered. In acute disease such as influenza, regeneration of bronchial epithelium is so active that it may mimic a neoplastic process, as pointed out by Winternitz, et al.\(^7\) Regeneration occurs promptly over a well vascularized surface. However, when chronic inflammation has destroyed surface epithelium, re-epithelialization does not seem to occur. In the end stage of open-healed tuberculous cavities treated with or without chemotherapy the wall is composed of dense hyalinized fibrous tissue (Fig. 6A). In addition to such open-healed cavities, this inability to regenerate is observed in other conditions whenever an equally poor "bed" is provided. We have seen this phenomenon in abscess (Fig. 6B) and in infected bronchiectasis (Fig. 6C).

This view is supported by the experiments of Condon,\(^8\) who studied epithelial regeneration of the mucosa of the rat's trachea at various intervals following trauma. He found that the extent of regeneration at any interval was inversely proportional to both the depth of the injury and the amount of inflammatory reaction. These factors determined the

![FIGURE 2: Acute expanding lesion in a terminal bronchiole meeting resistant wall. Epithelium and muscle are preserved. 100×.](image-url)
properties of the surface over which epithelium must grow. The influence of the character of the bed to be epithelialized is thus demonstrated. Condon used healthy animals with small lesions, the epithelium regenerating over an otherwise physiological area. It is hard to conceive that epithelium would grow to line a tuberculous parenchymatous cavity because there the bed is extremely unfavorable. The prolonged and destructive stages of inflammation, caseation and fibrosis, create an almost avascular and impermeable structure, the typical lining of an open-healed tuberculous cavity.

When cartilage, muscle, or glands, singly or in any combination are present, no difficulty of identification of bronchial wall is met. Of these components, muscle is most often found. If a fairly intact segment of bronchial mucosa is seen in the wall of a lesion (Fig. 7), or if any other specific structure such as cartilage is present (Fig. 8), identification is certain. In the presence of epithelium only, it had been postulated by others that (a) the structure covered is not bronchial wall, and that (b) the epithelium is newly formed. No good cause was ever shown for this postulation.

Evidence to distinguish whether an epithelialized structure is bronchial wall or not seems to be missing when bronchial epithelium remains while cartilage, muscle, and glands are not seen. What determines

FIGURE 3: Tuberculous bronchitis. One side of the wall is destroyed; the opposite side shows preserved epithelium but no other specific structures. 50×.
whether bronchial wall is present or not in a given structure when only epithelium remains? Our observations have revealed the following:

1. The shape of even non-epithelialized structures may be such that recognition of bronchus is certain (Fig. 9).

2. The epithelialized structures sometimes contain scattered and minute remnants of identifying elements. In Fig. 2 bronchial wall at the edge of a caseating lesion is identified by the muscle. These structures which can be recognized by fragments of such specific elements are

FIGURE 4: A segment of columnar ciliated epithelium lines the capsule of a caseous nodule. 140×—FIGURE 5: Tuberculous bronchitis. Narrowed cavity with remnants of columnar epithelium. Without this epithelium identification is impossible. 60×. Insert 200×.
identical in all respects with those where they are absent (Fig. 3).

Assuming that an epithelialized structure has been identified as bronchial wall by the presence of a muscle fragment, would it not be incongruous to assert that the very same structure is not bronchus because no muscle fragment is seen in a neighboring section?

We believe epithelium to be an identifying element as are the others, and that all epithelium-bearing structures under consideration are bronchial walls. Alternate interpretations would require ad hoc postulation and would be more speculative.

The terms “broncho-cavitary junction” and “re-epithelialization,” we believe, have been inappropriately used by some. The broncho-cavitary junction can be defined only in a macroscopic sense as the place where a relatively narrow structure joins a wide one. Microscopic examination may reveal that a portion of the wider structure is still bronchial wall which has been ectropionized and dilated (Figs. 1 and 10). The term “re-epithelialization” was misused because the authors meant that epithelium had grown on a newly formed surface. The proper use of this term would infer replacement of pre-existing epithelium.

We do not believe that epithelium ever forms the lining of a parenchymatous cavity; that any epithelium found in an open cavity is best interpreted as an indication of underlying bronchial wall.

It may be interesting to note that more and more non-epithelialized cavities have been observed since the advent of chemotherapy, though they have been seen without chemotherapy. In the last stage of healing, giant cells are consistently present as a lining of the hyalinized fibrous tissue wall. They sometimes resemble epithelium (Fig. 6D).

FIGURE 6: 125 X. A. End stage of healing of a tuberculous cavity without chemotherapy. B. Healed post-abscess cavity wall, non-tuberculous. C. Healed Bronchiectatic "cavity" without "re-epithelialization." D. Tuberculous cavity. Nearly healed portion lined by giant cells. The structure is similar in all cases.
Conclusions

1. Bronchi participate extensively in tuberculous cavity formation.
2. The presence of epithelium in the lining of a "cavity" identifies bronchial wall.
3. Open-healing of tuberculous parenchymatous cavities does not lead to epithelialization.

FIGURE 7: A bronchial segment forms part of a tuberculous cavity wall. Mucous glands and columnar epithelium are preserved. 20 X. Insert 200 X. FIGURE 8: A caseous lesion originating from bronchitis. Without the chance finding of cartilage and desquamated epithelium, this lesion would be confused with a parenchymatous nodule. 40 X.
FIGURE 9: Y-shaped bronchial structure. The preserved limb permits identification. 10X.

FIGURE 10: "Broncho-cavitary junction." No chemotherapy. Muscle (arrow) identifies bronchial wall. In the absence of this or other identifying elements this frequently seen picture (note mechanisms, Figure 1) has been erroneously interpreted as "re-epithelialization" of the "broncho-cavitary junction." 76X.
SUMMARY

Epithelium found in the lining of tuberculous cavities has been generally interpreted as the result of epithelialization. Our evidence supports the concept that such epithelium is instead a remnant of bronchial wall.

Open-healed cavities are devoid of epithelium and remain so because the infection produces dense fibrous tissue which is permanently incapable of supporting epithelial growth. Similar situations prevail in non-tuberculous cavities (post-abscess and suppurative bronchiectasis). It is concluded that epithelium found on what appears to be cavity wall is not newly formed but identifies bronchial wall.

RESUMEN

El epitelio encontrado en la superficie de las cavernas tuberculosas se ha considerado generalmente como un resultado de la epitelización. Nuestras evidencias apoyan el concepto de que tal epitelio es un resto de la pared bronquial.

Las cavernas abiertas curadas carecen de epitelio y así permanecen porque la infección produce tejido fibroso denso que es permanentemente incapaz de soportar el crecimiento del epitelio. Situaciones semejantes se encuentran en las cavidades no tuberculosas (post-abscedales y bronquiectasias supurantes).

Se concluye que el epitelio encontrado en lo que parece ser la pared de la caverna no es nuevo, sino que se identificó la pared bronquial.

ZUSAMMENFASSUNG

Die Anwesenheit von epithelialer Auskleidung tuberkulöser Cavernen ist im Allgemeinen als das Resultat einer neuen Epithelialisierung gedeutet worden. Unser Befunde stützen aber die Auffassung, dass solches Epithel ein Überbleibsel von Bronchialwand ist.


REFERENCES