of autolysates was negligible: not more than 100 aerobic bacteria and 10 to 20 anaerobes were found per milliliter of autolysate during the process of autolysis. Thus we conclude that the autolysis of normal animal tissues, as of baker's yeast (*5*), leads to production of appreciable quantities of toxohormone, at least in the cases tested. In our opinion the phenomenon of autolysis may be the origin of the small quantity of toxohormone that can be isolated from all normal tissues (*8*). Likewise we suggest the possibility that the presence of toxohormone in tumor-bearing organisms is closely related to the processes of autolysis in the malignant cells or in the tissues invaded by them.

J. OLIVARES
V. CALLAO
E. MONTOYA

Department of Microbiology, Estación Experimental del Zaidin, Granada, Spain

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Wrinkling of Molar Crowns: New Evidence

Abstract. *We submit that wrinkling of molar crowns in Primates is a phenomenon of genetically controlled activity of the inner enamel epithelium that is grossly evident soon after initial calcification of the tooth occurs. The amount and pattern of this wrinkling are characteristic of the species before they are evident in the enamel surface itself.*

In 1887 Schlosser (*1*) called attention to the occurrence of wrinkles in the enamel covering of the molars of fossil Hominoidea (namely *Dryopithecus*); he considered this feature to be of phylogenetic significance within the primate order. Even earlier, however, the arrangements of these enamel folds among the living Hominoidea were well known: in the gibbon this trait is the most attenuated, while in the orangutan it reaches its most profuse expression. The other anthropoid apes and man fall between gibbon and orangutan in this respect. The phylogenetic interpretation of this trait has been disputed in the literature: on the one hand, Adloff (*2*) dismissed wrinkling as a diagnostic taxonomic aid, since he considered this phenomenon to be simply a haphazard and inconstant accident of the calcification process; on the other hand, Korenhof (*3*) and Weidenreich (*4*), both of whom comprehensively reviewed both sides, felt that wrinkling in hominoids is at least as old as the Miocene and has phylogenetic and racial significance. Korenhof based his argument upon the fact that wrinkling appears on the surface of the dentino-enamel junction, which he regarded as a structure representing an earlier or "more original stage" of the tooth than does the enamel surface of the crown. The presence of wrinkling on the junction had been established as early as 1917 by Aichel (*5*); later by Schwarz (*6*). Weidenreich (*7*) put it this way: "As the dentine, regarded from the morphological viewpoint, is the most integral constituent of the tooth, its surface relief cannot be considered as a purely accidental feature with no morphological significance."

Since the problem of wrinkling is important not only in comparative primatology, hominoid evolution, and race differentiation, but also in dental embryology, we were moved to observe directly the status of the crown surface before, during, and after the calcification process. This we did by extracting the appropriate tooth buds from term fetuses of gorilla (*Gorilla gorilla gorilla*), orangutan (*Pongo pygmaeus*), and man, and by comparing them to the unworn crowns of the corresponding erupted molars of juvenile specimens of the three primate groups.

Figure 1 shows the mandibular right first permanent molars of gorilla, orangutan, and man in the unworn state. The characteristic profuse wrinkling of the crown surface of the orangutan contrasts with the relatively smooth surface of the human molar and with the rugged marked ridges, with the high cusps, on the gorilla molar. Figure 2 shows the mandibular right second primary molars (dm2) of the three species from the distal occlusal view; all three were removed from full-term fetuses. Only in the gorilla is the crown surface not entirely covered by calcified tissue; at this stage of development the enamel is immature and relatively shallow in depth. The crown surfaces were carefully dried before photography to eliminate highlights. The extensive wrinkling on the surface of the orangutan molar is quite obvious but less pronounced than in the completed tooth (Fig. 1). In the human molar the cusps are much steeper and the ridges descending from them are more strongly developed, but there are very few accessory ridges as in the orangutan. In the gorilla, sharp ridges occur on the slopes of the cusps, but at the bases of the cusps there is very little wrinkling.

The first permanent molars of the same full-term fetuses are shown in occlusal view in Fig. 3. In the gorilla three cusps have begun calcification: the mesiobuccal (Protoconid), mesiolingual (Metaconid), and distobuccal (Hypoconid). In the orangutan the same three cusps, plus the distolingual cusp (Entoconid), have commenced to calcify. In the human all five cusps are in various stages of calcification. In none of the molars, however, has coalescence of enamel between cusps occurred. The uncalcified portions of the crown show interesting differences. In the orangutan the surface is covered with minute ridges suggestive of the final crown form. In the gorilla there are fewer but heavier ridges located mainly on the steep slopes of the cusps. In the human the basin is broader and flatter and shows no wrinkling whatever.

It is apparent that wrinkling is not a phenomenon initiated in the enamel-formation process; it commences in the inner enamel epithelium. Presumably the wrinkling begins soon after initial calcification of one or more cusps in gorilla and orangutan. In man, wrinkling has not been observed in the molars even after all five cusps have calcified and coalesced; apparently any folding of the inner enamel epithelium that does take place occurs immediately in advance of the calcification process, and then only on the slopes of the cusps.

We agree with Weidenreich that the enamel folds and wrinkles found on primate molars do not result from fortuitous piling-up of enamel, although his reasons for asserting that these minute structures are integral parts of the tooth were based upon a commonly held notion of the significance of the dentino-enamel junction. Contrary to Schour's opinion (*8*) that the junction is the "blueprint pattern" for the final morphology of the tooth, it has been shown that in fact the surface of the dentin, underlying the enamel, is in itself a final product of changing growth (*9*). The structures observed on the dentin surface after removal of the covering enamel were developed at different times: a cusp is uplifted long before the small ridges, and wrinkles develop on the slopes or in the intercuspal valleys.

Although Weidenreich seemed to subscribe to the idea that the enamel wrinkles were a consequence of dentino-enamel junction prototypes (that is, of precalcification wrinkling of the crown surface), he nevertheless continually likened the calcification process to the "flow and solidification of lava . . . over an uneven surface" (*7*); but in the orangutan, unlike the gorilla, the "enamel stream" descends from the cusps more slowly and "with a greater tendency to divide into smaller, secondary streams over plane [*sic*] areas at the base of the cone" (*7*). Weidenreich was careful to state that this was a simile, but obviously he had let it become for him the explanation of the mechanism of calcification and ultimate crown morphology. Calcification, however, does not in fact proceed like the flow of volcanic lava, although one is tempted to describe it so. Initially the deposition of dentin and immature enamel can only follow the surface contours of the inner enamel epithelium.

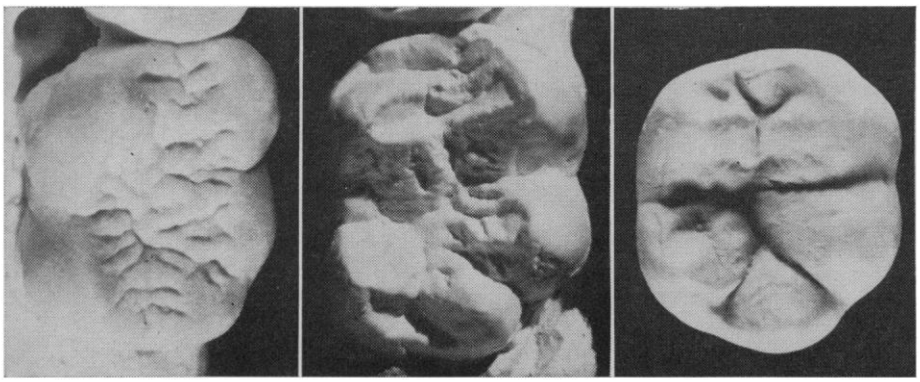

Fig. 1. Casts of mandibular right first permanent molars of juvenile hominoids (× 3.5). Left to right: orangutan, gorilla, and man.

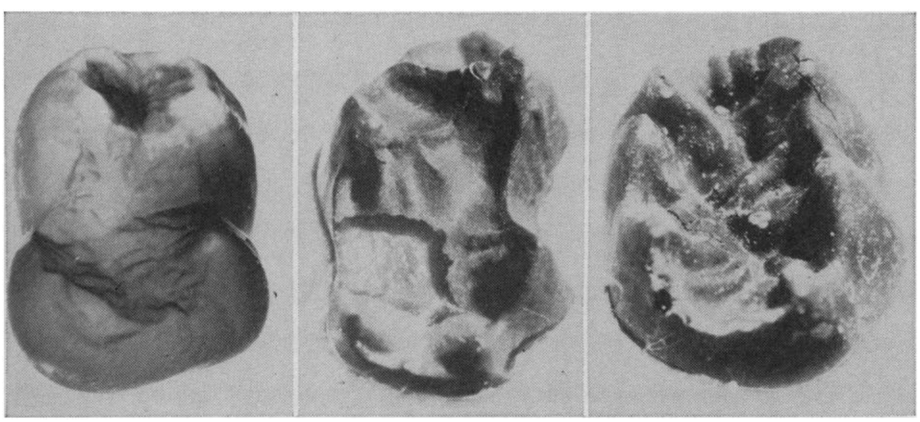

Fig. 2. Mandibular right second primary molars of full-term hominoid fetuses (× 4). Left to right: orangutan, gorilla, and man.

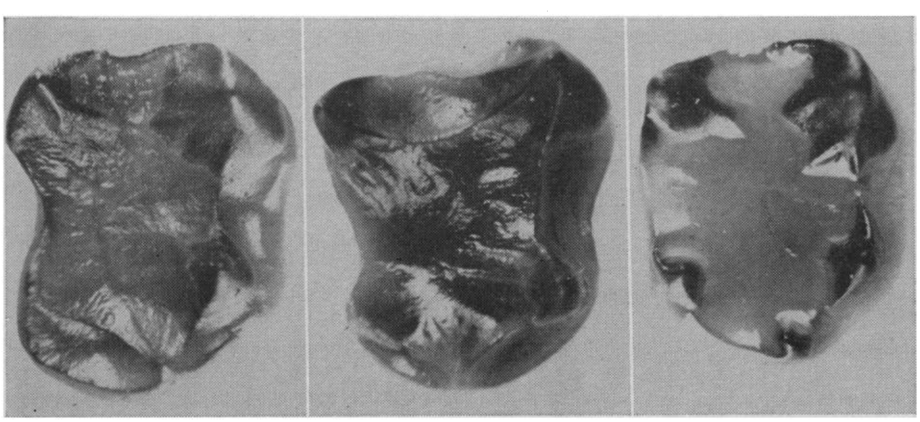

Fig. 3. Mandibular right first permanent molars of full-term hominoid fetuses (× 5). Left to right: orangutan, gorilla, and man.

Two possible explanations suggest themselves for the uplifting of the inner enamel epithelium into what later, during the calcification process, results in the so-called wrinkles on the occlusal surface of the molar. On the one hand, rapid mitotic activity within the epithelial layer in valleys may outstrip the increase in breadth of the crown with the result of crowding, hence folding. The fact that this process would be primarily fortuitous fails to explain the complete concordance in detail in monozygotic human twins in patterns of ridges, grooves, and wrinkles. On the other hand, the folding may be an endogenous process similar to that which results in the uplift of the future cusps, a process that is always orderly and species specific.

Thus we contend that wrinkling, in its various forms and degrees, is a phenomenon of genetically controlled activity of the inner enamel epithelium that is grossly evident soon after initial calcification of the tooth occurs. The amount and pattern of this wrinkling are characteristic of the species before they are evident in the enamel surface itself.

BERTRAM S. KRAUS
SEISHI W. OKA
Cleft Palate Research Center, University of Pittsburgh, Pittsburgh, Pennsylvania

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