Letters to the Editor

On the Etiology of Clubbing of the Fingers

A common genesis for the development of clubbed fingers has long been sought. Its frequent occurrence in anoxic states, such as congenital heart disease with cyanosis, severe emphysema, chronic mountain sickness, etc., seemed to indicate anoxia as a basic cause. However, the development of clubbing in various chronic infections and in certain neoplastic states appeared to make the anoxia theory untenable, and as a result many theories have been proposed, the most recent based on increased peripheral flow (M. Mendlowitz. *Medicine,* 1942, 21, 269).

On the basis of readily observed clinical data, it is possible to postulate an anoxic factor in the infectious and neoplastic states, thereby offering a unified theory of pathogenesis. In these conditions the sedimentation rate of the blood is increased, which in turn is dependent on the formation of rouleaux. Intravascular rouleaux having been observed, it is apparent that the diffusion surface per unit of hemoglobin is reduced. The vasodilation incident to chronic anoxic states and the a – v anastamoses probably serve to facilitate the circulation of the rouleaux. With rapid rates of blood flow, tissue anoxia may exist in infections and neoplasms though the arterial saturation is normal. This provides the same mechanism (tissue anoxia) for clubbing in these states as in the classical cases of arterial anoxia.

An extension of these remarks will appear elsewhere.

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Exploration for "Big Bones" at Lower Blue Licks Spring, Kentucky

Proposing to continue the exploration for Pleistocene vertebrate fossils begun last year (*Science*, 1946, **103**, 58), a party from central northern Kentucky, southwestern Ohio, and southeastern Indiana led by Maj. Victor K. Dodge, gathered at the former old salt spring in the Licking River valley at Lower Blue Licks in Nicholas County, Kentucky, early on the morning of 15 September 1946. As on the previous occasion Maj. Dodge sponsored the project, paying all costs personally. The writer was present upon invitation of Maj. Dodge; other assisting personnel present were Charles E. Snow, anthropologist, and William G. Hagg, archeologist, both of the University of Kentucky, Lexington, Kentucky.

At 9: 00 A.M. a bulldozer with a 12-foot blade, engaged especially for the project, began the removal of the soft river bottom alluvium over a 40-foot strip about 18 feet N. 70° E. of the walled enclosure of the famous old salt spring, the flow of which ceased about 1897. At varying depths ranging from 18 to 26 inches in the first cut made by the bulldozer, a soft, yellowish, sandy, pebbly loam containing small limestone slabs, and rotten wood, all probably of early Recent age, gave up quite a number of scattered, disconnected, frequently fragmental buffalo, deer, elk, and other contemporary fossil bones. Beneath this a sharply defined bed of dark gray or blackish river sand containing small, occasional pebbles of chert and limestone and Pottsville quartz pebbles, produced a number of buffalo, deer, and perhaps other bones. This bed of loose sand was very evidently water deposited and of fluvial origin. Its dark color was evidently derived from a former, age-long impregnation of the sulphur-saline waters of the nearby old salt spring together with some amount of iron in solution.

Beneath this bed of sand and clearly separated stratigraphically from it was found 20–21 inches of a hard, blackish, sandy, fluvial gravel containing numerous rounded quartz and chert pebbles of small size and many small, smooth, and somewhat flattened limestone slabs of cobble size or slightly larger. This bed rests directly upon the smooth, somewhat broadly water-grooved, bedded and in-place lower Cynthiana limestone. It was this hard, black, coarse semiconsolidated gravel, lying just above the limestone, that produced the proboscidian bones found in Cuts No. 1 and No. 2 on the southwest side of the salt spring in the fall of 1945. In this first cut of 1946 this heavy black gravel bed produced only a scattering of bison, elk, and deer bones; the much desired osseous relics of the *Mastodon* and the *Mammoth* were not found. Cut No. 1 was 52 inches deep, as measured from the surface to the solid bedded limestone.

In the course of the day's exploration five separate cuts were made by the bulldozer. Each of these was 12 feet wide and from 30 to 50 or 60 feet long. Cut No. 2 was made 6 feet northeast of No. 1. It produced only the usual assortment of buffalo, deer, and elk bones. Cut No. 3, set 15 feet S. 35° E. of the walled spring, was similarly unproductive, turning up only one well-preserved but broken *Mastodon* molar. During the process of excavating Cut No. 3, which was abandoned at a depth of 57 inches, it became increasingly evident that it had been previously opened in part, probably by Thomas W. Hunter (deceased), by means of hand-dug trenches during the period 1897–1900. He procured many excellent bones and tusks of *Mastodon americanus* and *Elephas primigenius* as well as skeletal relics of the buffalo, deer, elk, and other animals, most of which are now on display in the nearby Blue Licks State Park Museum.

In midafternoon, Cut No. 4, located about 28 feet S. 35° W. from the walled curb of the old salt well, was opened in a narrow undisturbed area between Cuts No. 1 and No. 2 of 1945. This cut, 56 inches deep, turned out to be very productive of proboscidian fossils in the hard, black, coarse gravel bed overlying the bedded lower Cynthiana (Ordovician) limestone. Besides the usual assortment of buffalo, deer, and elk bones at upper levels, there were found in the bottom of the cut three large tusks, two large limb bones, several vertebrae and ribs, and one lower mandible with molar in place. Two of the tusks were evidently those of *Mastodon americanus*; one, larger and more curved, was probably derived from *Elephas primigenius*. The writer measured one of the highly curved—*Elephas*—tusks when about half excavated in the gravel bed at 56 inches. The recovered mandible, identified by the incased tooth, was that of the *Mastodon*. Other "big bones" recovered here in whole or as fragments may simply be loosely defined at present as proboscidian. Of the three tusks found, two were so soft and decayed that they fell into fragments during hand excavation. One, probably that of a young male *Mastodon*, was removed in two parts and presents a fine tip, which is frequently not well preserved. This tusk exhibits a small amount of planation, perhaps by running spring water a few inches from the tip. Toward the close of the day Cut No. 5, 18 feet N. 55° W. of the curbing of the old salt spring, was opened like the others but was unproductive.

In the course of the operation throughout the day each of the five cuts opened was refilled and the surface brought back nearly to normal as soon as the hand exploration was finished.

Altogether, 20 laboratory storage trays of the Museum of the University of Kentucky at Lexington are now filled with the vertebrate fossil material recovered during the one-day exploration of 15 September 1946. The individual bones and fragments of bones, as yet uncounted, probably number 200 or more. Besides these relics, which in time will be cleaned and prepared for museum, exhibition, and educational purposes, a considerable number of bones and some teeth of lesser consequence and value were picked up and removed by various individuals—mostly curiosity hunters—during the course of the exploration. As far as is now known no American Pleistocene species heretofore unknown to this area were found, nor were any undoubted Paleolithic artifacts discovered in the black, hard gravels.

It was estimated that between 600 and 650 people viewed this "fossil hunt."

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The Immunizing Effect in the Action of Trypanocidal Agents

The results recently reported by Mayer and Brousseau (*Proc. Soc. exp. Biol. Med.*, 1946, 62, 238) afford a confirmation of the viewpoint advanced by Reiner and Leonard (*Arch. int. Pharm.*, 1933, 44, 434) that, in the treatment of trypanosomiasis with certain trypanocidal drugs, a response of the host defense mechanism, an immunizing effect, contributes as a factor in the sterilization of the host. Reiner and Chao (*Amer. J. trop. Med.*, 1933, 13, 525) reported the immunization of rats to *T. equiperdum* by the use of vaccines of p-benzoquinone-killed and also of neoarsphenamine-treated trypanosomes. Strong trypano-agglutinins and lysins appeared demonstrable *in vitro* by their action on motile, virulent parasites. The immunity was shown to be strain specific. Immunized rats reinoculated with trypanosomes always survived longer than normal rats, but it was difficult to sterilize infected rats with the vaccines alone. A smaller than normal dose of an arsenical given in addition to the vaccine could, however, wipe out the infection. The serum of rats with progressed trypanosomiasis which were treated with arsenicals also showed the agglutinating and lytic effects, not shown by normal rat serum.

Mayer and Brousseau, working with mice, have apparently rediscovered this action of neoarsphenamine and have also found a similar immunizing action of an antimonial, melaminylphenylstibonic acid (Compound 122). The trypanocidal activity of this Sb compound has been reported by Friedheim and Berman (*Proc. Soc. exp. Biol. Med.*, 1946, 62, 131). Mayer and Brousseau, as in our earlier work, found only a temporary immunity conferred by their drug plus trypanosome injections, with a reappearance of trypanosomes in the blood after three days or later, and subsequent death of most of the infected animals. These workers have demonstrated a new point, namely, the transfer of passive immunity by injecting the serum of mice immunized by treatment of a progressed trypanosome infection into untreated, uninfected mice, followed by attempts to inoculate the latter.

Reiner and Leonard (*Arch. int. Pharm.*, 1932, 43, 10) demonstrated that *in vitro* treatment of *T. equiperdum* suspensions, in the presence of serum globulin, with arsenicals at drug concentrations failing to immobilize the parasites altered the virulence of the strain, so that rats inoculated with the treated trypanosomes were found to survive longer than controls inoculated with untreated trypanosomes.

The present writer has long held the view that trypanocidal drugs, even at concentrations failing to kill trypanosomes, can so alter the metabolism of the parasites as to make them more easily phagocytized, followed by an immunizing response of the host. That the immunization is only temporary may be due to a change in the character of the surviving parasites. Indeed, Friedheim and Berman note that the trypanosomes reappearing in mice after treatment with their Sb compound, followed by multiple reinfections, are atypical for mouse trypanosomiasis, the disease no longer showing the typical continuous, progressive blood-stream increase of parasites to death of the host, but rather an alteration to the chronic type infection seen in rabbits.

Finally, may we point out that no similar experiments seem to have been done to test whether such immune serum is obtainable after drug treatment of experimental treponeme infections. In view of the nature of the disease in rabbits (chiefly a tissue, rather than a blood-stream infection), this may be more difficult to demonstrate. But it would seem as if this could be tested *in vitro* by the action of rabbit sera on suspensions of treponemes from rabbit chancres. Such experiments might throw light on whether or not the Swift-Ellis subdural neurosyphilis therapy involves immunity factors, long a disputed point.

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