free and within macrophage. Red blood corpuscles, some of which are crenated, provide a comparison for size. Phase-contrast microscope. Times 1000." The caption for Fig. 3 in the paper by Pande *et al.* reads: "Extracellular forms in the impression smear of peritoneal exudate of mice. Note the crenated erythrocytes (phase-contrast × 1500). [May-Grunwald-Giemsa]."

We apologize to our readers for this unfortunate event, thus following the precedent set by the Editorial Board of the *Journal of Infectious Diseases* (*3*) in a similar case in which at least five of the six figures used to document an article (*4*) "were taken from the previously published work of other authors."

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Phagocytized Platelets: A Source of Lipids in Human Thrombi and Atherosclerotic Plaques

Abstract. Phagocytosis of lipid-rich platelets by monocytes and the transformation of such cells into lipophages containing fat was observed in human thrombi. The lipophages are similar to lipophages in atherosclerotic plaques. This observation supports the idea that some atherosclerotic plaques are organized mural thrombi.

Recently, in this laboratory, the conversion of autologous pulmonary arterial thromboemboli to typical fibrofatty atherosclerotic plaques containing foam cells (lipophages) was observed in the rabbit (*1*). The lipophages were derived from monocytes that had phagocytosed and digested lipid-rich platelets within the thromboemboli. After this experiment with the rabbit, a study was made of human in vivo and in vitro thrombi to determine whether or not phagocytosis of platelets could be found.

Thrombi made in vitro (*2*) from human plasma were incubated at 34° to 37°C for 1 to 6 days. The thrombi were composed of clumps and columns of aggregated platelets surrounded by monocytes and by granulocytes, and bound together by strands of fibrin. Phagocytosis of platelets by monocytes within the thrombi occurred on the second day of incubation (Fig. 1*a*), and the transformation of such cells to lipophages containing fat occurred by the fifth day (Fig. 1*b*). The cytoplasm of the phagocytic monocytes was filled with numerous platelets, and the nucleus was displaced to an eccentric position. Swollen platelets could be distinguished in the monocytes in the early stages of fatty change. However, by the sixth day many of the phagocytized platelets had become lysed and were replaced by fatty vacuoles characteristic of foam cells.

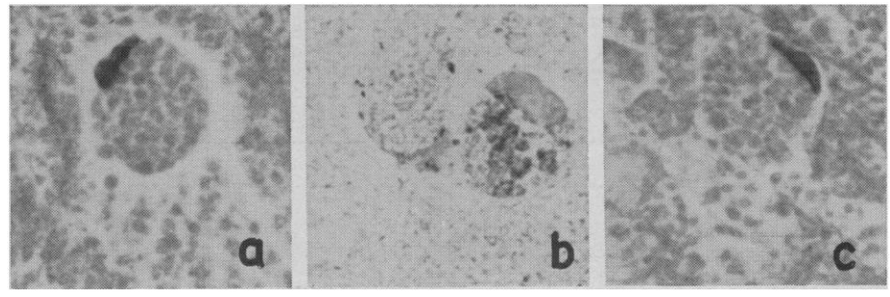

Fig. 1. Phagocytized platelets (× 400) in monocytes of in vitro thrombi (*a*, *b*) and an in vivo thrombus (*c*). Note the similarity of the phagocytic monocytes in *a* and *c* (hematoxylin and eosin stains). Two monocytes in *b* contain platelets. The platelets in the cell on the right are undergoing fatty change (Fettrot fat stain; fat is black in photograph).

The degree of phagocytosis and fatty change varied from cell to cell. Some monocytes that had not phagocytosed platelets accumulated fine droplets of fat. These cells retained their normal size and could be easily distinguished from the large monocytes that contained phagocytized platelets and fatty vacuoles. In some thrombi a few unphagocytized platelets underwent fatty change.

In each experiment 10 ml of venous blood was collected in a plastic tube (*3*), and plasma was obtained by centrifugation of the blood in the collection tube at 650 to 700 rev/min for 5 to 10 minutes. The plasma was transferred in 1-ml portions to each of three polyvinyl chloride tubes 20 cm long by 0.140 inch in internal diameter. The ends of the tubes were joined with outside plastic collars to form a circle. Then the tubes, filled approximately half with plasma and half with air, were rotated at 17 rev/min on inclined turntables (Fig. 2) until thrombi formed (15 to 20 min).

The contents of one circular tube—the thrombus in its own plasma—were incubated in each experiment. Before incubation, the tube was further sealed with paraffin at the junction, and the air in the tube was replaced with a mixture of 95 percent oxygen and 5 percent carbon dioxide by means of inlet and outlet needles. The remaining two tubes were stored at 5°C, and the plasma was used for replacement of the autologous media in the incubated tube on the second and fourth day of incubation. After each plasma exchange, the gas mixture was also replaced.

The thrombus was incubated at 34°C for 2 days and at 37°C for the next 1 to 4 days. A temperature of 34°C was used for the first 2 days because in earlier experiments initial incubation at 37°C caused much multiplication of monocytes and minimal phagocytosis of platelets by the monocytes. The circular tube was rotated on a vertical turntable at 1 rev/min during incubation so that the thrombus was carried alternately through the plasma and the

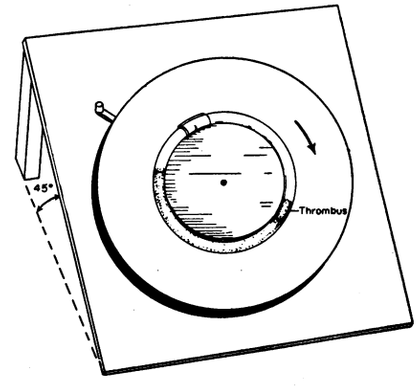

Fig. 2. Inclined turntable. The thrombus forms in the plasma as the column of plasma flows through a circular tube that rotates on the turntable.

gas. In order to prevent the thrombus from floating in the plasma, the lumen of the tube was constricted at one point by an outside metal clip. Aseptic sterile technique was used throughout the experiment.

A total of 165 experiments were performed on the plasma of blood obtained from adult patients of the outpatient clinic of the Eugene Talmadge Memorial Hospital of the Medical College of Georgia. Samples were taken from most of the patients before and after an operation or delivery. Several variations in the experiment were tried initially. Sixty-seven experiments were done as described above, and lipophages were identified in 28 of 45 thrombi that were stained for fat. All thrombi were examined histologically.

Human in vivo thrombi in the early stages of degeneration and organization also contained lipophages similar to those in atherosclerotic plaques. Phagocytosis of platelets was observed in 58 of 134 venous and arterial thrombi that were obtained at autopsy and varied in estimated age from a few hours to several weeks (Fig. 1*c*). Phagocytosis was most pronounced in the first 2 weeks. In some thrombi transitional cells containing both fat and platelets were observed.

The concept that some atherosclerotic plaques are mural thrombi altered by degeneration and organization is supported by many investigators who have traced the conversion of fibrin to fibrous intimal plaques in both human and experimental thrombi (*4*). Since fibrin is a fibrous protein that contains no lipid (*5*), it does not account for fat in plaques. However, platelets are rich in lipids, including cholesterol (*6*), and are a principal constituent of arterial thrombi (*7*).

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6. B. Maupin, *Les Plaquettes Sanguines de l'Homme* (Masson, Paris, 1954), p. 102. Lipids including neutral fats, phospholipids, and cholesterol constitute 19 percent, dry weight, of platelets; cholesterol accounts for 3.9 percent; proteins, including lipoproteins, total 57 percent.
7. This work was supported in part by a grant (H-3973) from the U.S. Public Health Service. We wish to thank Marion Hutson, Teresa Klett, and Mrs. David Fulghum for their technical assistance.

12 June 1961

Continuous Compensatory Tracking by a Cebus Monkey

Abstract. A cebus monkey was trained to hold a continuously moving voltmeter needle on-target for 60 seconds to obtain a food-pellet reinforcement. The task confronting the animal was relatively complex in that the high-frequency error voltage fed to the voltmeter needle was nulled by the animal by means of a joystick physically separated from the stimulus display.

The investigation reported here was designed to determine whether a cebus monkey could be trained to perform continuous compensatory tracking in one dimension with (i) food reward as a positive reinforcement, (ii) a relatively complex tracking task, and (iii) a control stick physically separated from the stimulus display. Such a response would be invaluable for providing precision monitoring of animal behavior in studies where conditions such as drug states, space flights, and so forth, would preclude the use of human subjects.

The apparatus as seen by the monkey is shown in Fig. 1. A potentiometer attached to the bottom of the self-centering control stick (*A*) provided a voltage change proportional to stick position. A ½-inch target zone (*D*), in the center of the milliammeter (*B*), was illuminated by a red 6-volt bulb any time the needle (*C*) entered the zone.

A cam-generated forcing function produced an irregular needle deflection of ±1 inch, and had a frequency of approximately 10 cy/min. The potentiometer attached to the stick enabled the animal to null the cam-generated error voltage and receive a reinforcement (food pellet). The error voltage drove a pen on a multichannel recorder, and, when reduced by the monkey to a sufficiently low magnitude, started a synchronous timer and actuated the on-target light in the center of the meter face. When the animal held the needle on target for the length of time set into the synchronous timer, a 0.67-g pellet of whole-diet food was delivered to the food cup by a mechanized food dispenser (see *E* in Fig. 1).

To prevent the monkey from obtaining free food pellets during early training stages as the needle passed through the target zone, the needle was set to fluctuate about a point 2 inches to the right or left of the target zone (see trace *A* in Fig. 2).

Although the animal was unrestrained and free to move the stick at any time, the food delivery equipment was energized only 1 hour in the morning, 1 hour at noon, and 1 hour at night. Since the monkey was not fed at any other time, it was under 16 hours of food deprivation in the morning, and under 4 hours of deprivation before each of the other two sessions. At feeding times (which were controlled automatically by a 24-hour timer), the room lights were shut off, the small light behind the face of the meter was turned on, and the multichannel graphic recorder was started. If the stage of practice required it, the forcing-function cam was also started at this time. After 1 hour, the apparatus was automatically turned off and the room lights were automatically turned on.

With the exclusion of delays due to apparatus failures and experimenter error, it is estimated that the training lasted approximately 30 days, or 90 experimental hours. In the first phase of training the monkey was taught to compensate for a discrete deflection of the display needle. Initially, any deflection by the control stick that caused the needle to cross the target zone was rewarded no matter how small an amount of time it remained in the target zone. The delivery of the food pellet was accompanied by an audible click of a relay and the illumination of the red

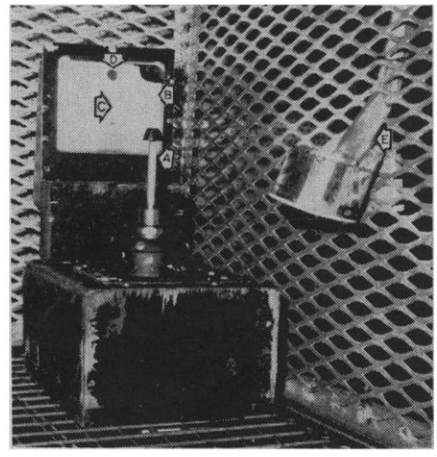

Fig. 1. Apparatus as seen by the monkey (*A*, control stick; *B*, meter; *C*, needle; *D*, target zone; *E*, food dispenser).