

and some kaolinite, has been reported. The sediment on the floor of the Gulf of Mexico (12) is reported to contain illite, montmorillonite, kaolinite, chlorite, and mixed layer material. In general, it would appear (13) that illite (or hydromica), montmorillonite (or vermiculite), and chlorite, are prominent in submarine clays.

Terrestrial quick clays of marine origin might be expected to resemble submarine clays. Results of studies of the Norwegian (14), Swedish (15), and Canadian (16) clay types, confirmed by observations in the Columbia University mineralogical laboratory, indicate that illite in fine sizes is a prominent constituent of quick clays, while montmorillonite, chlorite, and kaolinite are present. Such fine clay (largely of grain size less than $2\ \mu$) with flaky texture and layer lattice structure, tends to develop unusual physical properties in large masses, behaving in what seems to be a somewhat thixotropic manner.

In quick-clay masses the loss of the natural electrolyte sodium chloride by fresh-water leaching (16), or the addition of a natural organic dispersant, such as tannic acid, or of calcium and magnesium ions (17) also acting as dispersants, increases the sensitivity of the clays. Clays in such a sensitive condition, or with such a high water content that the electrolytic factor is outweighed, appear susceptible to mass movement. Such clays, whether they are sensitive quick clays or sensitive submarine clays, are all similar in nature and appear susceptible to sliding action with an accompanying rafting action which moves associated heavy materials (18).

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References and Notes

1. D. B. Ericson, M. Ewing, B. C. Heezen, *Bull. Am. Assoc. Petrol. Geologists* **36**, 489 (1952).
2. R. A. Daly, *Am. J. Sci.* **31**, 401 (1936).
3. I. T. Rosenquist, "Guide to Excursion, 21st Session, International Geological Congress, Oslo" (1960).
4. J. Osterman, *Acta Polytech. Scand. Civil Eng. Bldg. Construct. Ser. No. 12* (1960).
5. R. F. Legget, *Roy. Soc. Can. Spec. Publ. No. 3* (1961).
6. C. Caldenius and R. Lundstrom, *Sveriges Geol. Undersokn. Ser. Ga No. 27* (1956), pp. 1-63.
7. V. P. de Smitt, *Trans. Am. Geophys. Union* **13**, 103 (1932).
8. K. Fredrickson, *Reports of the Swedish Deep-Sea Expedition, 1947-1948, No. 4* (1959), pp. 99-122.
9. M. F. Norton, thesis, Columbia (1958).
10. H. H. Murray and S. S. Sayab, *Natl. Acad. Sci. U.S. Publ. No. 395* (1954), pp. 430-441.
11. F. P. Shepard, R. Revelle, R. S. Dietz, *Science* **89**, 488 (1939).

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12. A. P. Pinsak and H. H. Murray, *Proc. Natl. Clay Conf., 7th* (1960), pp. 162-177.
13. S. K. E. Wakeel and J. P. Riley, *Geochim. Cosmochim. Acta* **25**, 110 (1961).
14. I. T. Rosenquist, *Am. Soc. Civil Engrs. Soil Technol. Paper No. 3187* (1961), pp. 743-767.
15. R. Soderblom, *Trans. Swed. Geotech. Inst.* **82**, 367 (1960).
16. —, *Proc. Intern. Conf. Soil Mech. Found. Eng.* **1**, 111 (1957).
17. —, *Trans. Swed. Geotech. Inst.* **81**, 727 (1959).
18. This study was conducted with the cooperation of the Cambridge Air Force Research Laboratories.

4 May 1962

Toxicity of Blood Clotting Factors

Abstract. Pure bovine thrombin was separated from autoprothrombin C, and the lethal intravenous dose for mice weighing 25 g was 0.4 ml of a solution containing 50 units of thrombin per milliliter. Autoprothrombin C was not toxic alone, but with crude cephalin it was fatal. The clotting time of human plasma was only slightly accelerated by autoprothrombin C alone; the clotting time was as short as 5 seconds with a combination of autoprothrombin C and cephalin.

When thrombin was first obtained in concentrated form, its intravenous infusion was found to be lethal when the dose was high (1). When the dose was smaller, a disseminated intravascular coagulation syndrome resulted, from direct clotting of the fibrinogen by thrombin. No other blood-clotting substance besides tissue extracts has been found to be toxic when infused intravenously. For instance, platelets and platelet degradation products were infused and clotting did not follow (2). Moreover, almost every conceivable concentrate of a procoagulant we have had in this laboratory has been tried (3). None has produced intravascular coagulation when given as a single substance or in combinations.

Recently autoprothrombin C was discovered in certain thrombin preparations (4), and we have separated it from thrombin so that purified thrombin and purified autoprothrombin C are available for intravenous infusion (5). Purified thrombin (6), shown to be homogeneous by several criteria, was assayed for its toxicity. Mice weighing an average of 25 g were given ether anesthesia, and the test material was injected into the tail vein rapidly by a technique previously described (7). The minimum lethal dose was 0.4 ml of a solution containing 50 units of thrombin per milliliter. Autoprothrombin C was not toxic in any of the concentrations tested. However, when it was combined with lipid material extracted

from brain tissue, autoprothrombin C was found to be fully as toxic as tissue extracts.

Autoprothrombin C was added to a saline suspension of crude cephalin, and 0.3 ml of the mixture was injected. The autoprothrombin C was purified, as previously described (5, 6), and crude cephalin was obtained from bovine brain by drying the macerated tissue with acetone, extracting with ether, evaporating the solvent, and suspending the lipid in saline. The minimum lethal dose of autoprothrombin C was about 300 units. Without cephalin, 3500 units of autoprothrombin C were tolerated well, and we suppose that even much larger quantities could be given without toxic manifestations. Evidently the lipid mixture normally in the plasma is not of sufficient potency to be of consequence as a procoagulant to function with autoprothrombin C. Platelet factor 3 functions as a procoagulant with autoprothrombin C, but when it is in the living circulating platelets it is not free to react.

We have emphasized that the autoprothrombin C functions with lipids to convert plasma prothrombin to thrombin. To evaluate this procoagulant power in test tubes, we used crude cephalin suspension, added autoprothrombin C, and then combined this with calcium and oxalated plasma. With excess lipid the rate of clotting was proportional to the concentration of autoprothrombin C (Fig. 1). By itself

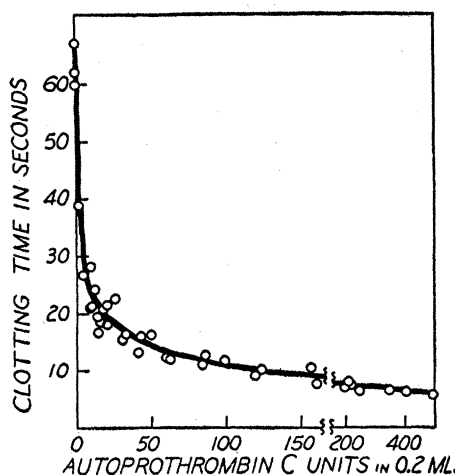


Fig. 1. Clotting time of normal human plasma in the presence of a constant quantity of calcium and lipid and of variable amounts of autoprothrombin C (at 37°C). The unit of autoprothrombin C has been previously described (5) in terms of kinetics of purified prothrombin activation. The reaction mixture consisted of normal plasma, 0.2 ml; crude cephalin (0.1 percent wt/vol), 0.2 ml; and autoprothrombin C (in CaCl_2 , 0.025M), 0.2 ml.

the lipid had only a weak procoagulant effect, and clotting was observed in 60 seconds. This small effect accounts for the survival of animals when this lipid is given alone. It is only a weak procoagulant and has been called a partial thromboplastin. Clotting occurred in 6 to 7 seconds when 300 units of autoprothrombin C were in the mixture with the lipid (Fig. 1). The 300 units of autoprothrombin C alone produced clotting in 50 seconds in another test. In animals or test tubes either procoagulant is weak by itself, but when the two are combined the mixture is a strong procoagulant. The test-tube experiments correlate so well with work on animals that the results from one can practically be used to predict results in the other (8).

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References and Notes

1. W. H. Seegers, E. D. Warner, K. M. Brinkhous, H. P. Smith, *Science* **89**, 86 (1939).
2. E. Epstein and A. J. Quick, *Proc. Soc. Exptl. Biol. Med.* **83**, 453 (1953).
3. E. R. Hecht, M. H. Cho, W. H. Seegers, *Am. J. Physiol.* **193**, 584 (1958).
4. H. Kowarzyk, E. Marciniak, B. Czerwinska, *Arch. Immunol. Terapii Doswiadczalnej* **9**, 719 (1961); E. Marciniak, *Bull. Acad. Polon. Sci.* **9**, 381 (1961).
5. E. Marciniak and W. H. Seegers, *Can. J. Biochem. Physiol.* **40**, 597 (1962).
6. W. H. Seegers, W. G. Levine, R. S. Shepard, *ibid.* **36**, 603 (1958).
7. C. L. Schneider, *Proc. Soc. Exptl. Biol. Med.* **62**, 322 (1946).
8. This study was supported by a research grant (H-5141) from the National Heart Institute, National Institutes of Health. One of us (E.M.) was a Rockefeller Foundation research fellow.

26 February 1962

Transfer Effects of Successive Discrimination-Reversal Training in Chimpanzees

Abstract. Chimpanzees receiving successive discrimination-reversal training on a single pair of stimuli transferred almost perfectly to two additional reversal tasks and to a "learning-set" series of 180 discrimination problems. A "win-stay, lose-shift" strategy, however it is acquired, seems to be a sufficient basis for one-trial discrimination learning.

Training on multiple discrimination problems results in progressive improvement in performance culminating in one-trial learning of single problems. This effect has been described as the formation of a learning set, and it has been studied most intensively in the primates. Although learning set has

been demonstrated in nonprimate forms, the rate of learning and asymptotic levels of performance are generally inferior to those achieved by primates (1). The sources of these phylogenetic differences have not been established; one possibility is that the primates are more capable of developing "hypotheses" or "strategies" which facilitate problem solution. Most of the theoretical and experimental work on learning-set formation, however, has focused on changes in the relative strength of responses to the physical properties and spatial relations of the stimulus objects as a function of training (2).

Restle, however, has suggested that the cues common to the correct stimulus objects in a series of discrimination problems, regardless of the physical attributes of the stimuli, are the properties of having been rewarded on the previous trial. According to this interpretation animals achieving consistent one-trial discrimination learning "use an abstract understanding of an LS [learning set] experiment, transcending the 'stimulus-response' rubric familiar in most theories of learning" (3). The behavioral contingencies through which this abstract principle is expressed may be described as a "win-stay, lose-shift" strategy. Levine (4) has shown that various strategies operate during learning-set formation. Furthermore, he has suggested that the gradual strengthening of a win-stay, lose-shift strategy by means of 100 percent reinforcement is largely responsible for learning-set formation.

If such a strategy is responsible for one-trial discrimination learning it should be possible to establish the strategy under one set of circumstances and transfer it to another. Accordingly, the present experiment was designed to determine whether chimpanzees given successive discrimination-reversal training on a single pair of stimuli would develop this strategy and show immediate transfer to a series of simultaneous discrimination problems with multiple pairs of stimulus objects (like those used in conventional learning-set experiments). It was further hypothesized that a second group trained on object-alternation would develop a "win-shift, lose-stay" strategy which would retard the formation of a learning set for conventional discrimination problems.

Chimpanzees were trained to displace a single stimulus object covering a food well before testing was begun.

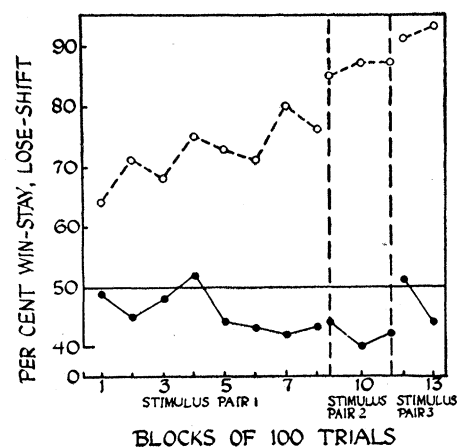


Fig. 1. Percentage of "win-stay, lose-shift" responses under two training conditions. Solid circles indicate progress of the discrimination-reversal group; open circles indicate lack of improvement for object-alternation group. Separation of data points indicates training on three different stimulus pairs.

Testing was conducted with a standard discrimination testing apparatus (5). The subject's task was to displace one of two stimuli (differing from each other in several dimensions) in order to obtain a food reward. The interval between stimulus presentations was 5 seconds. If the animal's initial choice was incorrect, it was allowed to displace the correct object after a 5-second delay.

The investigation consisted of two experiments. In the first experiment, seven experimentally naive adult chimpanzees were randomly assigned to two groups. One group ($N = 4$) received successive discrimination-reversal training on three stimulus pairs and the other group ($N = 3$) received alternation training on the same three stimulus pairs. The number of trials per stimulus pair for both training conditions is

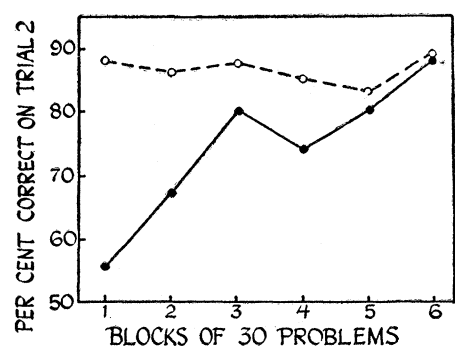


Fig. 2. Trial 2 performance on a learning set series of 180 discrimination problems after successive discrimination-reversal training (solid circles) and object-alternation training (open circles) on three stimulus pairs.