

also pertinent. Whatever the ultimate explanation for these observations, it is clear that in appropriate strain combinations a form of immunological tolerance can be achieved by parabiosis in mature animals. Although strains of mice used and the explanation of the phenomenon were somewhat different than that provided here, Rubin(10) using small number of mice has made similar observations.

Summary. 1) Tolerance of F_1 hybrid skin homografts in mice of their corresponding parent strains has been attempted by establishing " F_1 to parent" parabiosis. 2) Results were: a) Mice of either Z or Ce strain joined in parabiosis with $(Z \times Ce)$ F_1 hybrids became tolerant and accepted skin homografts taken from this hybrid. b) Tolerance of $(A \times Z)$ F_1 skin was also obtained in Z strain mice following parabiosis with $(A \times Z)$ F_1 hybrids. However, A mice joined to the same hybrids failed to develop tolerance and re-

jected the F_1 grafts in all instances. c) While 20% of Z mice became tolerant of $(Z \times C_{57}Bl)$ F_1 skin after being in parabiosis with this hybrid, none of $C_{57}Bl$ parent parabionts were susceptible of the hybrid skin grafts.

1. Martinez, C., Smith, J. M., Good, R. A., *Brit. J. Exp. Path.*, 1958, v39, 574.
2. Shapiro, F., Martinez, C., Good, R. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1959, v101, 94.
3. Mariani, T., Martinez, C., Smith, J. M., Good, R. A., *ibid.*, 1959, v101, 596.
4. Martinez, C., Smith, J. M., Shapiro, F., *ibid.*, 1959, in press.
5. Sauerbrück, F., Heyde, M., *Munch. med. Wochenschr.*, 1908, v55, 153.
6. Bunster, E., Meyer, R. K., *Anat. Rec.*, 1953, v57, 339.
7. Fox, A. S., *Ann. N. Y. Acad. Sci.*, 1958, v73, 611.
8. Egdaahl, R. H., Hume, D. M., *ibid.*, 1957, v64, 950.
9. Kamrin, B. B., *ibid.*, 1957, v64, 954.
10. Rubin, B. A., *Nature*, 1959, v184, 205.

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Delayed Repolarization in Smooth Muscles. (25484)

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A delay in repolarization following spike depolarization gives a plateau in heart muscle normally(1), in squid giant axons after injection of tetraethyl amine(2), and in myelinated nerve in presence of barium(3). The plateau in heart muscle can be varied in duration by a variety of treatments and appears to depend largely on a delayed rise in potassium conductance(4). The plateau in frog ventricular muscle is lengthened by barium(5). A plateau-type potential normally occurs in the ureter(6) but is unlike that in heart in being prolonged by quaternary ammonium compounds and shortened by epinephrine and low calcium(7). In other smooth muscles the spike normally shows equal rates of depolarization and repolarization(8,9,10).

Experimental. Action potentials were re-

corded from cat intestinal muscle by means of the sucrose gap electrode(11). When 0.1% barium chloride was added to the perfusing Krebs solution, 45 mv. spikes appeared which were soon transformed into plateaus (Figs. 1 and 2). The duration was increased from a spike of about 100 msec to depolarizations which persisted for as long as 70 seconds. The effect was reversible, as shown by washing out the barium (Fig. 1-c, d). The longer plateaus were usually characterized by oscillations, especially just prior to their termination (Fig. 1-b, Fig. 2-a, b, c).

Plateaus with trains of spikes on their crests were characteristically produced in cat longitudinal intestinal muscle by acetylcholine (10^{-6}) (Fig. 3-a, b). A higher concentration (10^{-5}) produced maintained depolarizations accompanied by spike activity (Fig. 3-c) as described for taenia coli(12). A critical con-

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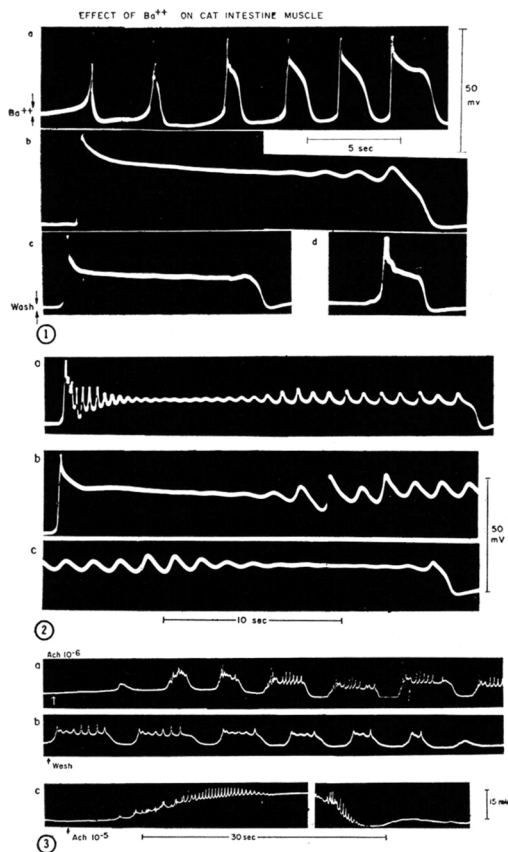


FIG. 1. Effect of 0.1% BaCl solution on cat intestine circular muscle. Sucrose gap technic. 37°C. a. Transition from normal to plateau type spikes during first 20 sec. exposure to barium. b. Typical plateau after 60 sec. c, d. Reversal of plateau to normal type spikes, 20 sec. and 50 sec. after washing out barium respectively.

FIG. 2. Examples of oscillations appearing on crests of barium (0.1%) induced plateaus. Cat intestine circular muscle. Sucrose gap technic. 37°C. a. Single plateau, with oscillations at beginning and end. b, c. Record of a single plateau during the first 25 sec. (b) and last 25 sec. (c). The central 15 sec. oscillation has been omitted.

FIG. 3. Effect of acetylcholine on cat intestine longitudinal muscle. Sucrose gap technic. 37°C. a. Development of plateaus topped by spikes during the first 50 sec. exposure to Ach 10^{-6} . b. Gradual reduction of plateaus on washing out Ach 10^{-6} . c. Maintained depolarization topped by spikes produced by Ach 10^{-5} . d. Repolarization on washing out acetylcholine by saline.

centration determines whether the response to acetylcholine is plateau-like or a maintained

depolarization with multiple spikes. In taenia coli, barium depolarizes as does acetylcholine without producing plateau-type spikes. In muscularis mucosae of pig esophagus both acetylcholine and epinephrine cause prolonged depolarization and spikes, but *not* plateaus.

Evidence is insufficient to decide whether the plateaus result from maintained Na conductance, from delayed K conductance or from a combination of both factors. The oscillations occurring on the crests of the plateau may indicate a delicate balance of Na and K permeabilities.

The reversible production of plateaus in intestinal muscle emphasizes the basic similarity of smooth muscle to many other excitable tissues.

Summary. Sucrose gap records from strips of cat circular intestinal muscle show under influence of barium a reversible transformation of spikes to plateaus lasting many seconds and topped by oscillations. Acetylcholine on cat longitudinal intestinal muscle may induce either rhythmic plateaus topped by spikes or a maintained depolarization, depending on concentration.

1. Brooks, C. W., Hoffmann, B., Suckling, E. E., Orias, O., *Excitability of the Heart*, 1955, Grune and Stratton, Philadelphia.
2. Tasaki, I., Hagiwara, S., *J. Gen. Physiol.*, 1957, v40, 859.
3. Greengard, P., Straub, R. W., *J. Physiol.*, 1959, v145, 562.
4. Weidmann, S., *Ann. N. Y. Acad. Sci.*, 1957, v65, 663.
5. Kleinfeld, M., Stein, E., Meyers, S., *Circ. Res.*, 1954, v2, 488.
6. Bozler, E., *Am. J. Physiol.*, 1942, v136, 543.
7. Prosser, C. L., Smith, C. E., Melton, C. E., *ibid.*, 1955, v181, 651.
8. Holman, M. E., *J. Physiol.*, 1958, v141, 464.
9. Burnstock, G., *ibid.*, 1958, v143, 165.
10. Burnstock, G., Prosser, C. L., in press.
11. Burnstock, G., Straub, R. W., *J. Physiol.*, 1958, v140, 156.
12. Bulbring, E., *ibid.*, 1957, v135, 412.

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