

development of the ventricular ectopic rhythm with tachycardia was unrelated to the arousal of the animal from anaesthesia.

While the spontaneous ventricular arrhythmia gradually disappeared over a period of 3 days, the exaggerated ectopic responses to noradrenaline persisted for about 7 days as shown in Fig. 1.

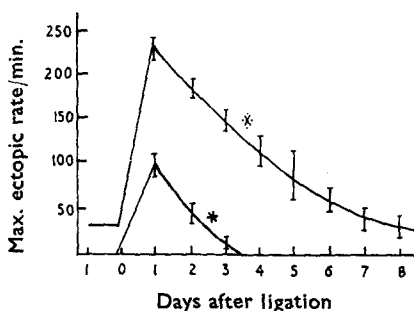


FIG. 1. Ectopic ventricular arrhythmia after coronary occlusion. Upper curve after noradrenaline, 8 µg./kg. i.v. Lower curve—spontaneous.

The 5 pigs developing the delayed ectopic ventricular arrhythmia in Group III survived, and were killed for histological study of the hearts. In the hearts of these animals, a month after ligation, the corresponding areas of the left ventricle were observed to have undergone a massive necrosis leaving a fibrotic thinned out part of the ventricular wall.

*Acknowledgement.* Part of this work was financed by the Indian Council of Medical Research, New Delhi-16.

Department of Pharmacology,  
All-India Institute of Medical  
Sciences, New Delhi-16, India.

R. B. ARORA  
D. S. SIVAPPA

February 19, 1962

#### REFERENCES

- Blumgart, H. L., Zoll, P. M., Freedberg, A. S. and Gilligan, D. R. (1950). *Circulation*, **1**, 10-27.  
 Florey, H. (1960). *Brit. med. J.*, **2**, 1329-1335.  
 Harris, A. S. (1950). *Circulation*, **1**, 1318-1328.  
 Winbury, M. M., Lorraine, M., Nicholas, A. and Zitowitz, L. (1960). *Fed. Proc.*, **19**, 88.

#### Observations on Conditioned and Unconditioned on- and off- Behavioural Responses to a Buzzer

SIR.—Responses occurring at the initiation of an afferent stimulation are called on-responses, and those occurring at its cessation, off-responses. Conditioned on- and off- responses have been studied at the behavioural level by Galeano, Roig, Segundo and Sommer-Smith (1959), Sommer-Smith, Galeano, Piñeyrúa-Payssé, Roig and Segundo (1962), Izquierdo and Östman (1961a,b) and Izquierdo (1962a). Further observations on the subject are added here.

The experiments were made on 17 adult albino rats. The noise of a buzzer acting during randomly variable periods separated by randomly variable silent

## LETTERS TO THE EDITOR

intervals, was the first indifferent, later conditioned stimulation. After a period of habituation, a shock to a metallic grid on the floor of the training box (square 0.1 m-sec./100 V pulses, 150/sec. during 0.5 to 2 sec.) was delivered 2-4 sec. after cessation of the buzzer as an absolute stimulus. After a number of such reinforcements, buzzes were again presented alone to extinguish the conditioned reflexes developed. Experiments were made in acute conditions (a single session lasting 60-130 min.; 10 buzzes for control; 50-80, reinforced with the shock; 10-30 for extinction) or in chronic conditions (daily sessions over a period of 6-14 weeks, at 10 or 20 buzzes per session; 100-300 for habituation; 200-500 reinforced; 50-300 for extinction).

Unconditioned on-responses to the buzzer were of three kinds. (i) Startle-defensive movements; (ii) investigative, orienting ones, and (iii) arrest, attention. Habituation was always difficult to achieve. In one experiment, after 1,000 buzzes in a chronic animal, no habituation occurred for any of these three kinds of responses. Group (i) reflexes were by far the most numerous; the defensive component (retraction, crouching) always habituated quickly but the startle seldom did so. Unconditioned off-responses to the buzzer were mostly group (iii); other off-responses were occasional and their habituation was extremely slow.

In chronic-treated rats, after the first few pairings of stimuli, dishabituation invariably occurred which lasted throughout the rest of the training schedule. Abortive, ill-defined, irregular and diverse on- and off-conditioned responses occurred at this early stage. Soon after, a clear-cut on-conditioned reflex occurred. When reinforcements were continued, however (2-10 sessions), only an off-conditioned reflex remained, and all other conditioned phenomena disappeared.

In acute-treated rats, the fate of unconditioned on- and off-responses was not studied in detail. Two kinds of conditioned reflexes appeared: an on- and an off- one (Izquierdo and Östman, 1961a).

Conditioned responses usually consisted of one or more of the following: squealing, running about, or standing up. These responses were qualitatively related but never equal to the absolute response to shock: shouting, running, tonic thrust, clonic movements. The percentage of conditioned responses never exceeding 60-80 in chronic and 80-90 in successive tenths in acute rat experiments.

Criteria for considering a particular response as conditioned were the following: (i) appearance during the reinforcement stage and not before; (ii) qualitative relationship to the absolute response; (iii) susceptibility to external inhibition and disinhibition; (iv) appearance after the conditioned signals; (v) internal inhibition by extinction. Of course, in the abortive early responses, these criteria were seldom completely considered.

Ten to 20 min. after the intraperitoneal injection of chlorpromazine (2-2.5 mg./kg.), both on- and off-conditioned reflexes were inhibited in 7 of 8 acute rats. Six of the chronic animals received 2 mg./kg. once and 2.5 mg./kg. twice, at intervals of four days between injections. In the 18 trials, the off-conditioned reflex was inhibited only twice. Difference between both groups was highly significant ( $P > 0.005$ ).

In a discussion of these data, it should be considered that both conditioned signals (on and off) reach the auditory cortex by a double route: one, via the classic primary sensory pathway; the other, via the reticular formation and its connections of the non-specific subcortical system. When employed at doses comparable to those used by us, chlorpromazine selectively blocks the collateral afferent inflow into the reticular formation (Bradley, 1959). As such blockade

## LETTERS TO THE EDITOR

affects early or acute conditioned reflexes but not chronic ones, it could reasonably be supposed that some sort of a "memory" mechanism develops by continued training at the acoustic cortex, which enables it to emit a conditioned message towards the motor area without receiving the reticular information; this, on the other hand, would be necessary in acute circumstances (Izquierdo, 1962b).

The existence of both an on- and an off-conditioned reflex in acute animals, and the final persistence of only an off-reflex in chronic ones, suggests that the acute experiments are equivalent to an early stage of the chronic one.

*Acknowledgement.* The valuable technical assistance of Mr. R. Östman is appreciated.

Cátedra de Farmacología Experimental,  
Facultad de Farmacia y Bioquímica,  
Junín 956, Buenos-Aires, Argentina.  
March 28, 1962

IVAN IZQUIERDO

### REFERENCES

- Bradley, P. B. (1959). In *Neuropsychopharmacology*, pp. 11-18, Editors: P. B. Bradley, C. Deniker and C. Radouco-Thomas; Amsterdam: Elsevier.
- Galeano C., Roig, J. A., Segundo, J. P. and Sommer-Smith, J. A. (1959). XXI Int. Cong. Physiol. Sci., Buenos-Aires; Abstr. of commun., p. 101.
- Izquierdo, I. (1962a). *Nature Lond.*, submitted for publication.
- Izquierdo, I. (1962b). *Med. exp.*, 6, in the press.
- Izquierdo, I. and Östman, R. (1961a). *Ibid.*, 5, in the press.
- Izquierdo, I. and Östman R. (1961b). *Rev. Soc. argent. Biol.*, in the press.
- Sommer-Smith, J. A., Galeano, C., Piñeyría-Payssé, M. M., Roig, J. A. and Segundo, J. P. (1962). *EEG Clin. Neurophysiol.*, in the press.

### Peroxide Value of Anhydrous Lanolin

SIR,—Anderson and Wood (1962) deduced that short periods of heating at 100° were sufficient to provide lanolin of low peroxide value for special purposes. We have found longer periods to be necessary for refined Wool Fat B.P., with concomitant increases in acid value and colour which make the method of little practical value. Another disadvantage is that the removal of peroxides

TABLE I  
CHANGES IN WOOL FAT B.P. HEATED AT 105°

Heating time hr.	Sample A				Sample B + 0.05 per cent BHA			
	Peroxide value (ml. 0.002N per g.)	Acid value	Colour (Lovibond)		Peroxide value	Acid value	Colour (Lovibond)	
			Yellow	Red			Yellow	Red
0	57.5	0.78	4.3	0.4	63.7	0.84	4.1	0.4
3	48.1	0.82	4.4	0.4				
4					46.5	0.88	4.5	0.5
6	24.6	0.86	4.9	0.5				
10.5					13.4	0.98	5.6	0.7
13	8.4	0.90	6.4	0.7				
17	5.7	0.92	7.2	0.8				
17.5					4.9	0.98	6.6	0.7
22.5					4.0	1.00	7.7	0.8
25	4.2	0.94	7.7	0.8				
30	5.1	0.96	8.3	0.9				
30.5					2.8	1.04	8.8	0.9
36	4.4	1.00	9.1	0.9				
37.5					2.9	1.06	9.9	1.0
44	3.8	1.04	10.0	1.0				
47					4.5	1.12	10.7	1.1