effects of acetylcholine on atrial muscle one must take into account not only its effects on membrane resistance (K+ permeability and rate of repolarization) but also the possible direct–indirect effects on depolarization mechanisms.

This research project was supported by the Life Insurance Medical Research Fund of Australia and New Zealand.

EDWARD A. JOHNSON
P. A. ROBERTSON

Department of Pharmacology,
University of Sydney.
Dec. 24.

[1] Trautwein, W., Kuffler, S. W., and Edwards, C., *J. Gen. Physiol.*, **40**, 135 (1956).
[2] Harris, E. J., and Hutter, O. F., *J. Physiol.*, **133**, 58*P* (1956).
[3] Johnson, E. A., and Robertson, P. A., *Nature*, **180**, 1483 (1957).
[4] Burn, J. H., "Functions of Autonomic Transmitters" (Williams and Wilkins Co., Baltimore, 1956).

Sites of the Physiological Breakdown of the Red Blood Corpuscles

IF erythrocytes labelled with iron-59 in their hæmoglobin are transfused from a donor rabbit to a sister animal, and, after a lapse of some hours, the labelled iron is located in the depot iron fraction, in the ferritin and hæmosiderin of organs, we can conclude that erythrocytes were broken down in these organs.

Since the plasma contains no radioiron, the only source of iron-59 present in the depot iron fractions is radioiron liberated from the transfused labelled red corpuscles.

This line of thought induced us to replace red corpuscles contained in 20 ml. of rabbit blood with the corresponding amount of washed red blood corpuscles all labelled with iron-59 from a sister animal.

The results of one of our experiments are given in Table 1.

Table 1. DISTRIBUTION OF IRON-59 IN THE DEPOT IRON (FERRITIN + HÆMOSIDERIN) OF ORGANS

Organ	Total depot iron (mgm.)	Total radio-activity of depot iron (c./min.)	Depot iron radioactivity per gm. organ (c./min./gm.)	Percentage distributed *
Liver	10·9	9,830	154	8·4
Spleen	0·681	2,340	2,600	2·0
Red bone marrow†	5·9	86,500	2,470	74·0
Kidneys	0·850	4,300	314	3·7
Lungs	0·590	9,250	1,050	7·9
Small intestine	0·807	4,600	79	4·0

* Total radioactivity of the depot iron of all organs investigated = 100 per cent.
† The total amount of the red bone marrow was assumed to comprise 1·1 per cent of the body-weight.

It is seen that the depot iron-59 content of 1 gm. of spleen is higher than that of an equal amount of any other organ studied. Considering the total organs, however, the red bone marrow contains more iron-59 than any other organ investigated. In seven other experiments the ratio of the depot iron-59 content of the red bone marrow and the spleen varied between 6 and 50, the corresponding ratio of the red bone marrow and liver figures being 0·6–9.

In view of the fact that the spleen of the rabbit is very small, its weight being only 1/35 that of the red bone marrow, we cannot expect the ratio of the amount of erythrocytes broken down in the bone marrow and the spleen to be as high in other mammalian species as it is in the rabbit. Our results suggest, however, that even in man presumably a third or more of the number of erythrocytes terminating their physiological life-cycle is broken down in the bone marrow.

Miescher[1] published results similar to those reported here. He transfused red corpuscles labelled with chromium-51 into rabbits and found that, after a lapse of 25–35 days, about 30–75 per cent of the chromium-51 was located in the bone marrow, 23–49 per cent in the liver and 6–40 per cent in the spleen. The finding of Miescher that the spleen accumulates a larger percentage of the chromium-51 than found by us is possibly due to a large part of the chromium-51 leaking out from intact erythrocytes. A part of this chromium may accumulate in the spleen. We arrived to the same conclusion as Miescher concerning the importance of the bone marrow for the physiological breakdown of the red corpuscles. In this connexion it is of interest to recall that Mann *et al.*[2] found that the main part of the bilirubin is formed in the bone marrow.

The interest taken by Prof. G. Hevesy in this investigation is gratefully acknowledged.

G. v. EHRENSTEIN
D. LOCKNER

Institute of Organic Chemistry
and Biochemistry,
University of Stockholm.
Dec. 17.

[1] Miescher, P., *Rev. d'Hématol.*, **11**, 248 (1956).
[2] Mann, F. C., Sheard, C., and Bollmann, J. L., *Amer. J. Physiol.*, **78**, 384 (1926).

Anticholesterol Activity of α-Lipoic Acid

SINCE α-lipoic acid is known to affect lipid metabolism, we have investigated the effect of this acid on the lipid content of plasma, liver and aorta from rabbits which had been fed on a diet containing an excess of cholesterol[1]. Rabbits weighing 2·5–3 kgm. were divided into four groups, each containing five animals. Group *A*, the control group, received a diet of ordinary commercial rabbit food. Each animal in groups *B*, *C* and *D* received this diet, supplemented for seven days with 1 gm. daily of cholesterol mixed with 9 gm. of shredded carrot. Group *B* received no further treatment. Group *C* received daily intramuscular injections of α-lipoic acid (5 mgm./kgm. of the sodium salt in saline). Group *D* received the same treatment as *C*, except that the injections were not started until the day after the high cholesterol diet had been stopped. After fifteen days from the start of the experiment, the animals were killed by bleeding, and samples of blood, liver and aorta were taken aseptically and weighed. Total lipids, phospholipids and neutral lipids were determined by the method of Bloor[2], and cholesterol by the method of Schoenheimer and Sperry[3].

The results (Table 1) show that the high cholesterol diet alone (group *B*) caused a clear-cut increase in plasma total lipids and cholesterol, and a less marked increase in plasma phospholipids and neutral lipids. The liver lipids showed a similar behaviour, but here the increase was larger for cholesterol and neutral lipids than for phospholipids. The aorta cholesterol was also increased, but phospholipids and total lipids were not much changed.