

## THE ACTION OF LEAD ON UNSTRIATED MUSCLE AND BLOOD VESSELS AND ITS RELATION TO HYPERTENSION

BY SUNITA IDERJIT SINGH, M.D. AND IDERJIT SINGH, F.A.Sc.

(From the Department of Physiology, Medical College, Agra)

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CHRONIC hypertension and arteriosclerosis may be associated with chronic lead poisoning, but it does not appear to be more common in lead workers than in others (see Sollmann, 1948, for references); nor they can be induced by long continued lead administration in rabbits and dogs. The blood pressure is not affected by lead poisoning, except during colic attacks when it rises. Intestinal spasm may be produced by intravenous injection of lead acetate and in excised intestines. It is by no means clear how it produces colic, although it is known that the disturbance is due to spasm of the intestine. Though some relief may be obtained in man and experimental animals by atropine, there seems to be no known agent which relieves lead colic. Certain authors (Aub *et al.*, 1925) assume that the action is due to the effect of lead on the envelope or membrane of smooth muscle cells, others (Grünberg, 1928), believe that it acts on the ganglion cells in the local plexus which control intestinal action.

Spasmodic contracture of the retinal vessels is known to occur in lead poisoning. The excised or perfused arteries are constricted by lead salts (Sollmann, 1948). This action is probably due to the action of lead on the excitatory system of smooth muscle.

It is universally accepted that the metabolism of lead and calcium are closely linked, so that the factor which would favour deposition of calcium in the media of the blood vessels, would also favour the deposition of lead, which might then act on the contractile mechanism of the smooth muscle of the blood vessels, and cause tonic spasm in this manner. The calcium content of the arteries increases in the aged, so that as the arteries have a special affinity for calcium, they may have a similar one for lead, though no analyses of the lead content of arteries are available. If they do, then lead will be especially present in increased concentration in the media of the arteries, and so produce a direct effect on the contractile mechanism of their smooth muscle. In the present research, therefore, the action of lead on the contractile mechanism of smooth muscle has been studied, in order to elucidate its possible role in hypertension.

### EXPERIMENTAL

The action of lead on the excitatory mechanism of unstriated muscle was studied by testing the effect of lead chloride on transverse muscle of the excised stomach of the dog and the frog, *Rana tigrina*. For testing the action on the contractile mechanism, transverse pieces of frog's stomach muscle were used, the action was tested on dying muscles the pieces of muscle being immersed in lead solutions for 24 hours (Singh and Singh, 1949, 1950), and on the heat killed frog's stomach muscle (Singh and Singh, 1954 *a, b, c*; 1955 *a*).

For studying the effect on the contractile mechanism of the smooth muscle of the blood vessels, the dog's hind limbs were perfused and the rate of flow recorded before and after immersion for 24 hours (Singh and Singh, 1955 *b, c, d*).

Direct microscopic observations on the arterioles of the guinea pig's mesentery were made before and after immersion for 24 hours.

### RESULTS

*Action of lead on the excitatory mechanism.*—Saline which was saturated with lead chloride, was used. Other lead salts, such as acetate, nitrate, though more soluble, were not used as the anions have a stimulating effect on unstriated muscle. Lead chloride does not produce any contraction of dog's and frog's stomach muscle. In dog's stomach muscle, it produces only relaxation.

Arterioles of the dog's hind limb are constricted, as shown by immediate retardation of flow in concentrations of lead chloride from 1 in  $10^5$  to 1 in  $10^4$ . The arterioles of the guinea pig's mesentery are also constricted.

Lead therefore acts on the excitatory mechanism of smooth muscle. Lead increases the excitability to alternating current and potassium in small concentrations, and in higher concentrations, it increases the excitability to alternating current and decreases that to potassium (Singh and Singh, 1946).

*Action of lead on the contractile mechanism.*—The contractile mechanism of unstriated muscle is affected by lead. In dying muscles, immersed for 24 hours, lead chloride causes contraction, in concentrations up to 1 in  $10^5$  (Table I). Heat killed muscles are contracted by concentrations up to 1 in 1000 (Table II). Dying arterioles are also affected similarly; concentrations up to 1 in  $10^5$  causes them to contract, as shown by perfusing dog's hind limbs (Fig. 1).

TABLE I

*Frog's stomach muscle. Contraction produced by lead chloride in dying muscle, immersed for 24 hours*

Contraction produced by lead chloride, saturated saline					
No. of Experiment	Per cent. of initial length		No. of Experiment	Per cent. of initial length	
	Effect of lead	Control		Effect of lead	Control
1	83	91	7	90	96
2	78	90	8	90	85
3	71	100	9	62	90
4	80	115	10	74	80
5	90	110	11	74	90
6	71	98	12	75	85
Effect of lead, 1 in 10 <sup>4</sup>					
1	90	96	4	74	80
2	90	85	5	74	90
3	62	90	6	75	85
Effect of lead, 1 in 10 <sup>5</sup>					
1	81	90	4	85	100
2	80	90	5	75	100
3	79	110	6	70	90

TABLE II

*Frog's stomach muscle, killed by heating to 50° C. for 10 minutes. Contraction produced by lead chloride, immersed for 24 hours*

Contraction produced by lead chloride, saturated saline					
No. of Experiment	Per cent. of initial length		No. of Experiment	Per cent. of initial length	
	Effect of lead	Control		Effect of lead	Control
1	93	100	4	90	102
2	90	105	5	90	108
3	95	105	6	98	108
Effect of lead 1 in 1000					
1	100	104	4	103	106
2	95	100	5	90	98
3	104	110	6	95	105

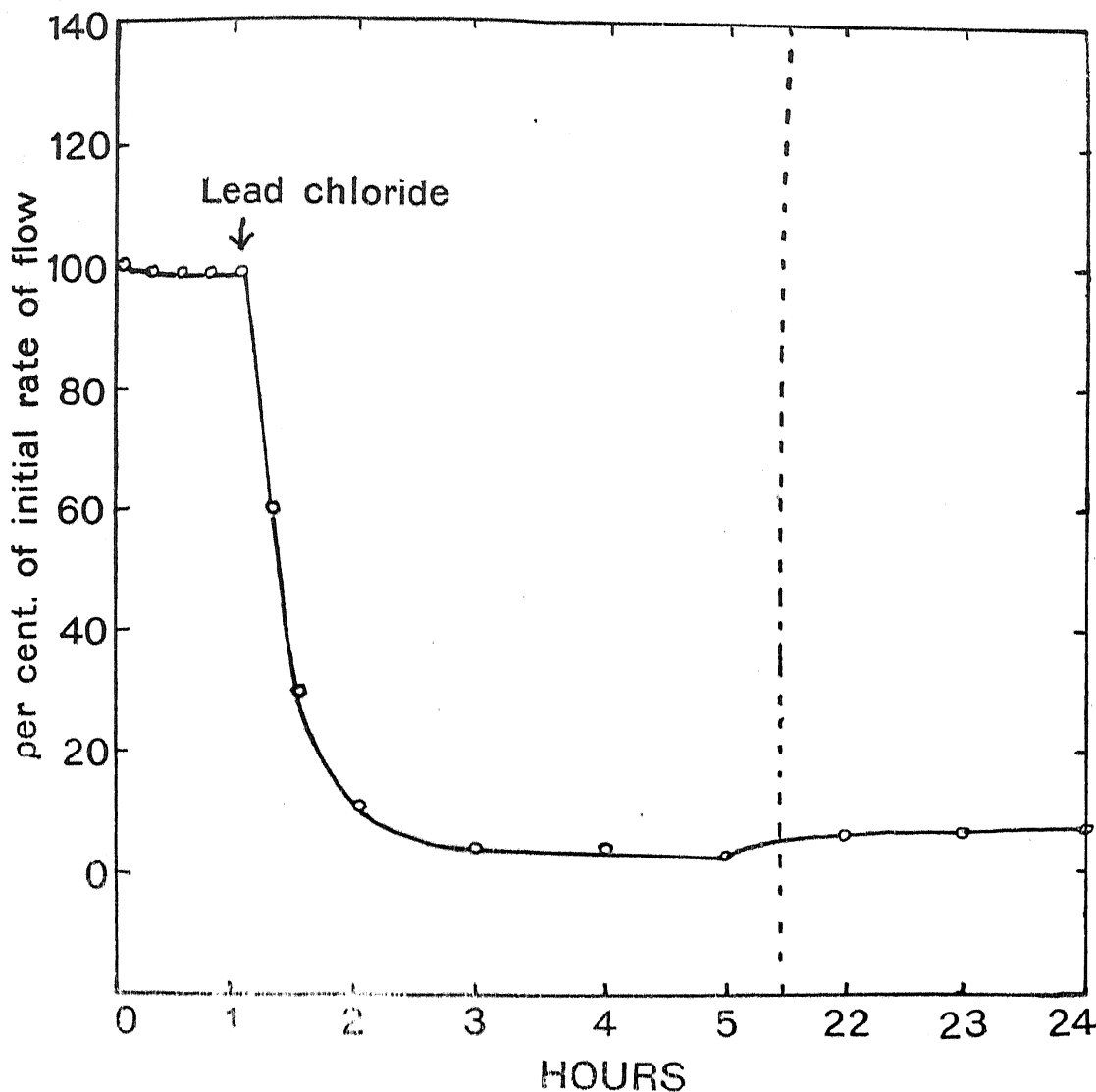


FIG. 1. Dog's hind limbs. At first they were perfused with unbuffered mammalian saline, and then with saline saturated with lead chloride.

#### DISCUSSION

Lead may affect the smooth muscle in the body by acting on the excitatory or the contractile system. In the latter case, the spasm will not be amenable to drugs. If the metabolism of lead follows that of calcium, then lead is likely to be concentrated in the arteries, just as calcium, and thus persistent hypertension may result. It is however doubtful whether such action of lead occurs in the body.

#### SUMMARY

1. The action of lead on the excitatory and contractile mechanism of smooth muscle is described. The latter has been determined by testing the effect of lead on dying and heat killed muscles.

2. Lead causes contraction of smooth muscle and arterioles by direct action on the contractile mechanism. This action may be of significance in producing contraction of smooth muscle in the body and in producing hypertension.

## REFERENCES

- Aub, J. C., Fairhall, L. T., Minot, A. S. and Reznikoff, P. *Medicine*, 1925, 4, 1. Quoted from W. T. Salter, *A Text Book of Pharmacology*, W. B. Saunders, London, 1953, p. 983.
- Grünberg, F. W. .. *Ztschr. f. d. ges. exper. Med.*, 1928, 62, 649. Quoted from Salter.
- Singh, S. I. and Singh, I. .. *Proc. Ind. Acad. Sci.*, 1946, 23, 301.
- \_\_\_\_\_ .. *Ibid.*, 1949, 30, 270.
- \_\_\_\_\_ .. *Ibid.*, 1950, 32, 12.
- \_\_\_\_\_ .. *Ibid.*, 1954 b, 40, 125.
- \_\_\_\_\_ .. *Ibid.*, 1954 c, 40, 145.
- \_\_\_\_\_ .. *Ibid.*, 1955 a, 41, 183.
- \_\_\_\_\_ .. *Ibid.*, 1955 b, 42.
- \_\_\_\_\_ .. *Ibid.*, 1955 c, 42.
- \_\_\_\_\_ .. *Ibid.*, 1955 d, 42.
- \_\_\_\_\_ .. *Curr. Sci.*, 1954 a, 23, 126.
- Sollmann, T. .. *A Manual of Pharmacology*, 7th edition, 1948, p. 989, W. B. Saunders, London.