## Regional Variation in Copper Content of Arterial Wall

Copper is unique in biological systems, as it forms an integral part of the electron-transfer oxidase which catalyze the reduction of molecular oxygen to water<sup>1</sup>. This element also promotes lipid autooxidation and thereby atherosclerosis<sup>2</sup>. Contrary to Ito<sup>2</sup>, Schroeder et al.<sup>3</sup> reported a significant decline in the concentration of copper in aorta with increasing age and degree of atherosclerosis. Recently Rao<sup>4</sup> observed a significant variation in the magnesium content of different arteries. With these considerations the present work was undertaken.

Arterial samples removed at autopsy of 18 cases were analyzed. Each sample was roughly 1.5-2 cm in length. Aorta was taken about 2 cm above the origin of left renal artery. Pulmonary, renal, common carotid and illiac arteries of right side were also removed. Cross grading of

the rate of lipid peroxidation in geriatric subjects. Serum copper level is also elevated in various vascular diseases <sup>10, 11</sup>. Recently Waisman et al. <sup>12</sup> have shown that animals kept on a copper restricted diet survived with scarred vessels, but demonstrated a tendency towards premature atherosclerosis. Interestingly enough, in the present study copper content of all arteries decreased linearly with the increase in the degree of atherosclerosis. Moreover, copper content was highest in the pulmonary artery which had minimal degree of atherosclerosis, and was lowest in aorta and illiac arteries which exhibited severe grades of atherosclerosis.

The present study indicates that, though copper promotes atherosclesosis<sup>2</sup>, its concentration in the arterial wall declines with the increase in the grade of atherosclero-

Number of specimens of various arteries (shown in bracket) and mean average of copper-content of various arteries as related to degree of atherosclerosis of aorta. Copper-content in mg per 1000 g of FFDW of arteries

Grade of atherosclerosis	Aorta	Pulmonary	Illiac	Carotid	Renal
Grade I Grade II Grade III	9.31±0.34°°° (7) 8.9±0.45 (6) 7.4±0.5 (5)	13.2±0.2°,f (7) 12.24±0.6 (5) 11.54±1.54 (5)	9.56±0.34 (6) 9.0±0.6 (5) 9.6±0.42 (5)	9.84±0.6 (5) 9.7±0.7 (6) 9.9±0.5 (4)	9.56±0.49 (6) 9.35±0.34 (6) 9.75±0.6 (4)
Average of 3 grades	8.64±0.41°° (18)	12.43±0.71 (17)	9.35±0.45°,8 (16)	9.52±0.67°,8 (15)	9.39±0.49°, g (16)

 $<sup>^{</sup>a}$  P < 0.05.  $^{b}$  P < 0.005.  $^{c}$  P < 0.001.  $^{d}$  Between grade I and III of aorta.  $^{c}$  Between aorta and pulmonary-artery.  $^{c}$  Between grade I and III of pulmonary-artery.  $^{c}$  Between pulmonary-artery and illiac, carotid or renal arteries.

atherosclerosis of all arteries was done by  ${\rm I}{\rm To}$ 's  $^2$  modification of W.H.O. classification.

From the arterial samples, adventitia was removed and fat-free extracts of each of them were prepared by the methods described 5, 6. These were then weighed and ashing was carried out 4. Dry ashing was preferred to the wet, as the latter has many disadvantages like contamination and lesser degree of accuracy 7. Copper is a non-volatile element and hence dry ashing is a reliable procedure. Ash so obtained was dissolved in 3 ml of hydrochloric acid and copper content was determined 8. Final results were calculated for copper content in 1000 g of fat-free dry weight of artery (FFDW) and the differences were statistically evaluated by Students' t-test (Table).

HARMEN<sup>9</sup> reported that the serum copper shows a linear rise with age and suggested that this change may increase

sis in various arteries. The mechanisms which either mobilize copper from arterial wall or inhibit its entrance into it are yet unknown.

Résumé. La teneur en cuivre dans l'aorte et les artères pulmonaire, rénale, illiaque et carotide a été déterminée. Une corrélation inverse entre le degré d'athérosclérose et celui du cuivre a été observée. La cause de ce phénomène reste à ètre établie.

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- <sup>1</sup> J. SCHUBERT, Copper and Peroxides in Radiobiology and Medicine (C. C. Thomas, Springfield, Ill. 1964).
- <sup>2</sup> T. Ito, Jap. Circulation J. 33, 25 (1969).
- <sup>3</sup> H. A. Schroeder, A. P. Nason, I. H. Tipton, J. J. Balassa, J. chron. Dis. 19, 1007 (1966).
- <sup>4</sup> J. N. Rao, Thesis for M. D., University of Indore, Indore (1970).
- <sup>5</sup> S. R. Rosenthal, Arch. Path. 18, 473 (1934).
- <sup>6</sup> R. C. Buck, Arch. Path. 51, 319 (1951).
- 7 H. Schroeder, personal communication (1970).

- <sup>8</sup> C. J. Gubler, M. E. Lahey, H. Asbenbrucker, G. E. Cartwright, M. M. Wintrobe, J. biol. Chem. 196, 209 (1952).
- <sup>9</sup> D. HARMEN, J. Geront. 20, 151 (1965).
- <sup>10</sup> G. C. Sepaha, J. D. Khandekar, D. P. Mukerji, C. V. Res. VI World Congress of Cardiology (1970), 283.
- <sup>11</sup> J. D. KHANDEKAR, G. C. SEPAHA, D. P. MUKERJI, New Engl. J. Med. 283, 319 (1970).
- <sup>12</sup> J. Waisman, P. A. Cancilla, W. F. Coulson, Lab. Invest. 21, 648 (1969).

## Potentiation of Fever, Produced by Intravenous Leucocyte Pyrogen, Following the Injection of Paraffin Oil in the Cerebral Ventricles of the Unanesthetized Rabbit<sup>1</sup>

When leucocyte pyrogen<sup>2</sup> is injected into the brain of unanesthetized rabbits, the greatest increases in temperature, with the shortest latency, occur following injections into the anterior hypothalamic region<sup>3,4</sup>. There is recent evidence to suggest that leucocyte pyrogen, when

given intravenously, enters the hypothalamus directly from the blood stream rather than via the cerebrospinal fluid (CSF)<sup>5</sup>. We now present evidence to suggest that fluid flow in the cerebral ventricular system could play a role in the termination of the febrile response.