LETTERS TO THE EDITOR

TOXICITY OF ARSENIC AND COPPER IN LIVER CIRRHOSIS

D. DHAWAN, AND D. V. DATTA
Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012, India.

ARSENIC and copper compounds can exert their harmful effects in many ways; arsenic compounds react with sulphydryl groups and thus inhibit the sulphydryl enzyme systems essential for cellular metabolism[1]. Copper acts as a cofactor in most enzymatic reactions and is stored in the liver as ceruloplasmin[2]. Several studies have shown an elevated level of copper in the plasma of patients with different types of liver cirrhosis[3-5]. Oral administration of arsenic leads to various abnormal changes in the liver of guinea pigs, rabbits and monkeys[6-8]. The present study was undertaken for a detailed understanding of the role of copper and arsenic in patients who died due to various liver abnormalities.

Liver samples of both normal and diseased human subjects were taken at autopsy from Nehru Hospital, Chandigarh. The normal samples were obtained from subjects, who died of diseases not involving liver or acute traumatic death. In all cases the liver samples were adjudged normal on the basis of histopathological examination. Depending upon the histopathological findings and clinical history, the patients were divided into five groups (a) Indian childhood cirrhosis (ICC), (b) Micro-nodular cirrhosis, (c) Macronodular cirrhosis, (d) Mixed cirrhosis, and (e) Alcoholic cirrhosis.

Liver samples obtained from the above groups were dried at 80° C to a constant weight and were then sealed in polythene bags which had previously been carefully washed with 0.1 N nitric acid and distilled water. The samples in duplicate were irradiated along with the appropriate amount of the standard at a neutron flux density of 10^{12}n$cm^{-2}s^{-1}$ for 10 hr in the Apsara reactor at Trombay. The irradiated samples and standards, which were treated earlier radiochemically were subjected to precipitation procedure described by Vogel[9] for separation of copper and arsenic. The samples were analysed in the Body Burden Measurement Section of Health Physics Division of Bhabha Atomic Research Centre, Bombay.

Table I shows the levels of arsenic and copper in the liver of normal subjects and the patients of ICC, micronodular cirrhosis, macronodular cirrhosis, mixed cirrhosis and alcoholic cirrhosis. The copper and arsenic values in normal liver tissues are consistent with previous reports[3,10,11]. Both arsenic and copper showed significant increase in the liver tissues of patients with different types of cirrhosis. Interestingly liver arsenic showed maximum increase in patients with alcoholic cirrhosis, while copper levels were maximum in the livers of patients of ICC. Previous reports have also shown the increased levels of copper in cirrhotic liver[12,13]. One report from this laboratory had shown the high level of arsenic in different organs of patients with ICC. The increase might be due to the fact that diseased liver does not allow the minerals their normal metabolic pathway and their excretion which is generally through the biliary duct, thus leading to raised levels in the liver. The present study suggests that high levels of arsenic and copper might be indicative of liver damage. From the therapeutic point of view also, these findings are of great importance, for we may not be able to treat some of these disorders with the aid of chelating agents such as penicillamine but may have to think in terms of preventing the occurrence of intoxication.

The authors would like to thank S. Somasundram and H. S. Dang of Health Physics Division, BARC, Bombay for their kind help in this study.

6 November 1981

TABLE I

Arsenic and copper levels (μg/g of dry tissue) in liver of normal and diseased human subjects

Subjects	Arsenic (μg/g)	Copper (μg/g)	
Normal (10)	0.041	0.01	12 ± 7
Indian childhood cirrhosis (12)	1.432	0.423[c]	237 ± 20[c]
Micronodular cirrhosis (7)	0.097	0.015[a]	120 ± 20[c]
Macronodular cirrhosis (8)	0.217	0.015[c]	89 ± 18[c]
Mixed cirrhosis (9)	0.431	0.052[c]	157.38[c]
Alcoholic cirrhosis (12)	4.92	1.37[c]	102 ± 29[c]

[a] P 0.05; [b] P 0.01; [c] P 0.001.

1. Datta, D. V., *J. Assoc. Phys. India*, 1978, **261**, 233.
2. Bowen, H. J. M., *Proc. Symp. Bled.*, 1972, I.A.E.A. Vienna, 393.

3. Hunt, A. H., Parr, R. M. and Taylor, D. M. *Br. Med. J.*, 1963, **11**, 1498.
4. Smallwood, R. A. and Williams, H. A., *Lancet*, 1968, **2**, 1310.
5. Worwood, M. and Taylor, D. M., *Br. Med. J.*, 1968, **3**, 344.
6. Ogeta, T., Beitr, Z., *Path. Anat. u.z. Alleg. Path.*, 1913, **55**, 236.
7. Stoefer, E., Beitr, Z., *Path. u.z. Alleg. Path.*, 1936, **97**, 367.
8. Datta, D. V. and Narang, A. P. S., *Bull. Post-graduate Inst., Chandigarh*, 1979, **13**, 189.
9. Vogel, A. I., *Text book of quantitative Inorganic analysis*, (London: ELBS), 1975.
10. Worwood, M. and Taylor, D. M., *Int. J. Appl. Radiat. Isot.*, 1968, **19**, 753.
11. Kingsley, G. R. and Schaffert, R. R., *Anat. Chem.*, 1951, **24**, 914.
12. Ritland, S., *Scand. J. Gastroent.*, 1977, **12**, 81.
13. Dang, H. S., Jaiswal, D. D., Wadhwani, C. M. and Somasundaram, S., *Proc. Symp. Bled.*, 1978, I.A.E.A., Vienna, 283.

ASCORBIC ACID LEVELS IN THE AMNIOTIC FLUID, CORD BLOOD, MATERNAL BLOOD AND NEWBORN URINE AT DIFFERENT GESTATIONAL PERIODS

K. P. MISTRY* R. V. BHATT† U. J. MODI‡
M. C. SHAH‡ AND B. K. MODI†
*Miles India Limited, Baroda; †Departments of Obstetric and Gynaecology; ‡Department of Paediatrics, Medical College, Baroda.
*Present Address: Kanwali Bhatwada, Wadi, Baroda 390 017, India.

DURING the last three decades only the dynamic nature of amniotic fluid is studied. Different constituents are studied in amniotic fluid like electrolytes, excretory products, enzymes, hormones, amino acids and phospholipids[1]. However, very few studies have been carried out on amniotic fluid vitamins. Corti and Murmori[2] found elevated vitamin A and carotene in amniotic fluid from the mothers of postmatured foetuses. Clarke[3] reported elevation of amniotic fluid vitamin B_{12} and folate levels in cases of severe toxemia associated with intrauterine deaths. Ostergard[1] noted that ascorbic acid concentrations were almost the same in amniotic fluid and maternal blood near term. However, no data are available on the ascorbic acid levels at different gestational ages.

Amniotic fluids of 129 normal pregnant women from S.S.G. Hospital, Baroda, were studied. They were mainly from middle and low socio-economic group. Their gestational ages varied between 8–40 weeks. The amniotic fluids were collected by suction, amniocentesis or artificial rupture of membrane. Suction and amniocentesis were performed in the women who desired abortion. For all the subjects included in the study, a previous written consent was taken before collecting amniotic fluid for ethical reasons. Out of 129 subjects, 15 subjects of 37–40 gestational weeks were also studied for their corresponding cord blood, maternal blood and newborn urine. The cord blood was collected from the placental side of the severed umbilical cord without squeezing it and maternal blood was collected within 30 minutes of delivery from the peripheral vein. The newborn urine was collected within two days of birth using urine collecting bags. All the fluids were collected in plain bulbs. In the cases of amniotic fluid and urine, they were first centrifuged, filtered and then analyzed. Ascorbic acid concentration was determined by dinitrophenylhydrazine method[4]. Within 2–3 hr of collection of fluids, their protein was precipitated by 6% trichloroacetic acid, the protein-free filtrates were treated with norite, filtered and stored in the deep freeze. Further process was continued within a week.

TABLE 1

*Ascorbic acid concentrations in amniotic fluid, cord blood, maternal blood and newborn urine (mg/dl)**

	Amniotic fluid							Cord blood	Maternal blood	Newborn urine
Gestational weeks	8–15	16–17	18 19	20 21	22-25	34–36	37 40	During 37–40 weeks		
	0.50	0.58	0.59	0.63	0.68	0.80	0.66	0.84	0.62	5.23
	± 0.36	0.32	± 0.35	± 0.39	± 0.37	± 0.44	± 0.60	± 0.57	± 0.61	± 4.19
	(5)	(12)	(25)	(35)	(10)	(6)	(36)	(14)	(12)	(15)

Mean, ± Standard Deviation; Figures in bracket give number of observations.