

Letter to the Editor

Copper Levels and the Adriamycin Inhibition of Proliferating Cells

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Dear Sir:

Various studies indicate that copper binds to RNA and DNA [1] and that copper levels rise in neoplastic lesions [2, 3]. The present study was conducted to investigate the effect of high copper levels on the action of adriamycin, which inhibits DNA reduplication [4] in rapidly proliferating cells.

Batches of 50 embryonated white leghorn eggs were used in all the experiments, using the window technique [5]. Embryos harvested at 17 and 40 h were used as normal controls. In the positive controls, copper sulphate was injected into the subblastodermal space in a dose of 600 µg per embryo and adriamycin in a dose of 120 µg per embryo at 17-h incubation. In one batch, adriamycin was injected 45 min after reincubation, following the injection of copper sulphate; in another, adriamycin was injected before copper sulphate. All the experimental batches were harvested at 40 h of incubation.

Copper treatment gives rise to differentiation of the anterior part of the neural tube. The tube is wide and shows a fluted anterior neuropore. A prominent primitive streak is seen in the spinal region [6]. In embryos given adriamycin alone, there is normal differentiation in the anterior half but a hole replaces the spinal region. In comparison, there is complete neural tube formation by 40 h in control groups.

When adriamycin treatment is combined with copper the morphology is similar to copper-treated embryos, whether copper is given before or after the drug. Mitosis is present all over the disc. Morphometric measurements of the neural axis after combined treatment are comparable to those following copper but are significantly different from adriamycin-treated and normal 40 h controls (Table 1).

Thus, the morphology and morphometry with combined treatment simulate the effect of copper given alone. From these findings it is evident that high copper levels protect

proliferating cells against the effect of adriamycin. Chemotherapeutically, this indicates that the presence of high copper levels in rapidly proliferating tissues may lead to a resistance to adriamycin. Thus monitoring copper levels may be of importance in cancer chemotherapy.

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Table 1. The morphometric measurements of the embryonal axis after combined adriamycin and copper treatment

	AvL µm	P Cu	P N	NE-µm	P Cu	P N
Ad	1,736	$P < 0.001$	$P < 0.001$	697	$P < 0.001$	$P < 0.001$
Cu	2,590	—	$P < 0.001$	2,137	—	$P < 0.001$
CuAd	2,532	$P > 0.1$	$P < 0.001$	1,271	$P < 0.001$	$P < 0.001$
AdCu	2,773	$P > 0.1$	$P < 0.001$	1,906	$P > 0.1$	$P < 0.001$
40-h C	4,526	$P < 0.001$	—	4,526	$P < 0.001$	—

Ad, adriamycin; AvL, average length; NE, neuroectoderm; Cu, copper; µm, micron