

## Influence of Sex Hormones on Total Serum Copper.\* (25155)

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Previous studies(1,2) suggested that total serum copper level increases in pregnant women. Estrogen therapy(3) has shown an increase in total serum copper in certain diseases. The pathway and relationship between hormones and serum copper is unknown, and it is not clear what part release of hormones plays in mobilization of serum copper. We were particularly interested in studying the influence of parenterally administered androgenic and estrogenic hormones on total serum copper in geriatric patients. We found that 200 geriatric patients showed a mean value of  $99 \pm 15 \mu\text{g}/100 \text{ ml}$  as compared with a mean value of  $110 \pm 13 \mu\text{g}/100 \text{ ml}$  serum as reported by several other authors for middle aged subjects(6).

**Method.** Eighteen female and 21 male subjects were selected, ranging from 66 to 95 years of age. All subjects were ambulatory, with no acute or debilitating disease and with no hypercupremia. The subjects were divided into 2 groups. Group A was composed of 5 females who received 2 mg of estradiol benzoate<sup>†</sup> 3 times a week for 7 weeks, and 5 females and 11 males who received the same medication for 4 weeks. Group B was composed of 8 females and 10 males who received 25 mg testosterone propionate<sup>†</sup> twice weekly for 10 weeks. The subjects received no

other drug therapy during entire period of study. Duplicate total serum copper analyses were made prior to, and at termination of, administration of hormones, and 8 weeks after discontinuance of therapy. Blood for analysis was secured with necessary precautions to avoid contamination. All patients were in basal state. Total serum copper was determined colorimetrically, using the method of Greenleaf(4) with modification by one of the authors (NCJ).

**Results.** Table I shows mean total serum copper in the control period, at the end of therapy, and 8 weeks after discontinuance. In all instances there was an increase in total serum copper which was significant at the 1% level in all groups except for males in Group B on androgen, who showed an increase which was significant at the 2% level. Total serum copper returned to, or near, its preadministration value 8 weeks after hormone therapy was terminated. No correlation could be found between amount of increase in serum copper values and intensity of changes in vaginal smears after sex hormone administration.

**Discussion.** Several investigators observed (1,2,3) an increase in total serum copper in pregnancy, menstrual cycle, and estrogen therapy. Investigations have also shown that day-to-day changes in serum copper level are

TABLE I. Total Serum Copper Levels before and after Sex Hormone Therapy ( $\mu\text{g}/100 \text{ ml}$ ).

	Duration of therapy (wk)	Control period	End of therapy	8 wk after discontinuance
<i>Group A</i> (2 mg estradiol benzoate 3 times weekly)				
5 females	4	$111 \pm 18$	$137 \pm 15$	$108 \pm 12$
5 "	7	$110.6 \pm 22$	$154 \pm 30$	$99 \pm 15$
11 males	4	$104 \pm 18$	$135 \pm 19$	$99 \pm 20$
<i>Group B</i> (25 mg testosterone pro- pionate twice weekly)				
8 females	10	$114 \pm 15$	$153 \pm 17$	$113 \pm 13$
10 males	10	$106 \pm 18$	$137 \pm 18$	$105 \pm 18$

All values expressed as mean  $\pm$  S.D.

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<sup>†</sup> Generously supplied by Schering Corp.

not significant (p greater than 20%) and week-to-week changes are very small(1,5,6). According to these reports and our own experience, we cannot consider the changes observed in our study as normal variations in serum copper level, as all individuals showed definite increases. Since both androgen and estrogen increased serum copper content in both male and female, there must exist some relationship between sex hormone level in the body and serum copper content.

**Summary.** 1. Administration of testosterone propionate or estradiol benzoate to healthy elderly males and post-menopausal women increased significantly their serum copper content. 2. Eight weeks after discontinu-

ance of androgen or estrogen administration, serum copper values dropped back to, or very close to, preadministration levels.

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## Transplantation of Polyoma Virus Induced Tumor in the Hamster. (25156)

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Polyoma virus was isolated from cell-free extracts of parotid gland tumors which had been produced by inoculation of newborn mice with similar extracts from leukemia #60 or spontaneous AKR leukemias(1). The demonstration that this agent would multiply in monkey kidney tissue culture(2), cause cytopathic lesions in mouse embryo tissue culture(3), and hemagglutination of guinea pig rbc(4) have made experiments with this virus practical. The virus is capable of producing a variety of tumor types when inoculated into newborn mice(5) and hamsters(3) but no evidence of tumor production or infection in adults except production of antiviral antibodies. This is a report of the successful transplantation in adult Syrian hamsters of a sarcoma produced by inoculation of a newborn hamster with polyoma virus, cultivation of the transplantable tumor in tissue culture and the relationship of virus and viral antibody to its growth.

**Methods.** (a) *Transplantation.* Healthy appearing areas of tumors were removed and minced with scissors in Eagle's tissue culture

medium to give a heavy suspension of tumor fragments and 0.2 ml inoculated subcutaneously into the right scapular area of either newborn or adult hamsters. Animals were observed twice weekly for signs of tumor development. (b) *Demonstration of virus.* Either mouse embryo tissue cultures were inoculated and observed for cytopathic effect and development of hemagglutinins (HA) or 5 adult mice were inoculated intraperitoneally, bled 3 weeks later and their serum tested for hemagglutinin inhibiting antibodies(HI). (c) *HA and HI tests.* The technic and criteria described by Eddy, *et al.*(4) were used. (d) *Tissue culture.* Standard procedures of trypsinization and planting in T30 flasks were used with 10% calf serum Eagle's medium for growth and 2% horse serum Eagle's for maintenance. Maintenance medium was changed twice weekly.

**Results.** (a) *Transplantation series.* Hamster C474, kindly supplied by Dr. Bernice Eddy, had a subcutaneous sarcoma of approximately 5 weeks' duration, measuring 3 x 6 inches. Its serum had an HI titer of 640.