Table 1. Liver Uptake and Biliary Excretion of Copper-64

No. of rats	Copper pretreatment	Hours after ^{64}Cu injection	Activity* (percentage of injected dose) per ml. bile	per g liver
5	none	1	0·99 ± 0·24	5·66 ± 0·50
5	11 days	1	1·91 ± 0·77 (P < 0·05)	9·90 ± 4·00 (P < 0·05)
4	none	18	0·78 ± 0·27	1·25 ± 0·31
4	11 days	18	1·18 ± 0·41 (P < 0·20)	2·26 ± 0·93 (P < 0·10)

* Figures denote means and standard deviations.

is a consequence of the higher liver levels. The cause of the latter requires further investigation. Increased uptake of copper by the liver is in contrast to the decreased uptake reported in patients with Wilson's disease[5].

It appears that the capacity of the liver of copper-loaded rats to excrete a tracer dose of copper is not impaired. A similar finding has been reported in mice[6]. When large doses of the copper are injected some is retained, as shown by the increased liver copper-levels in copper-poisoned rats. The results recorded here suggest that the retention is not due to saturation or impairment of the normal excretory mechanism. A possible explanation for the retention is that in copper poisoning there is a diversion of part of the copper from the normal excretory pathway. The presence of copper-rich pigment in poisoned animals[4] suggests that the pigment may be the site of this diversion. Copper in pigment would only be slowly eliminated from the liver, possibly by mechanisms other than the normal pathway, for example, by renewal of liver cells.

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Dental Caries and the Fluoride Content of Olive Oil

Recent investigations have shown that the fluoride content of Greek teeth from the cities of Athens and Salonika was considerably high[1,2]. This may explain, at least in part, the low prevalence of dental caries observed in Greece[3]. However, the source of fluoride intake is not known. Water alone could not have been responsible, since the fluoride content of the water supplies of Athens and Salonika has been reported to be low: 0·04 p.p.m. and 0·5 p.p.m., respectively[1,2]. For an explanation, the opinion was advanced that the diet of the people may include some common foods, produced and consumed in Greece, which are rich in fluoride[1]. It has been proposed that one such food item, which is consumed in Greece apparently in considerable amounts, is salt produced by solar evaporation of sea water[4]. The fluoride content of sea salt has been reported to be about 40 p.p.m.[5].

With the exception of sea salt, however, the fluoride content of other foods commonly produced and consumed in Greece is not known. Consequently, it was thought of interest to investigate the fluoride concentration of olive oil produced in Greece. This food constitutes an indispensable item in the daily diet of the people of that country. The samples of olive oil used in this work were produced from olives grown in two districts of Greece, namely, the Island of Crete and the area of Kalamai in the Peloponnese. Fluoride was determined by a standard method[6]. The analyses showed that the fluoride content of olive oil from the Island of Crete was 0·36 p.p.m. and that from the area of Kalamai 0·63 p.p.m. The consumption *per capita* of olive oil in Greece is believed to be about 15 kg per year. On the basis of the foregoing, it appears that the inclusion of olive oil in the daily Greek diet does not make any significant contribution to the amount of ingested fluoride.

Thus, at present, sea salt remains an important source of dietary fluoride in Greece for protection against dental caries. This may well be the case in other countries, such as Taiwan, Ceylon and Lebanon, where because of local food customs the amount of sea salt consumed has been estimated to be considerable: about 16–20 g per person per day[7,8].

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PHARMACOLOGY

Dosage – Response Curves for the Teratogenic Activity of Trypan Blue

A teratogenic agent is one which, acting directly or indirectly on the developing organism, alters ontogenesis with consequent production of a malformed individual. In order to produce its characteristic effects the agent must be given within a specific dosage range, but this aspect of teratology is often neglected. Attempts have been made[1,2] to compare the teratogenic dose of certain substances with the adult LD_{50} and recently the fœtal LD_{50} has been considered useful[3]. This has led workers to relate embryotoxic doses of drugs with their therapeutic dose[4], and regression lines relating fœtal resorption to dose have been constructed for a number of drugs[5]. Here, dosage–response curves for the teratogenic dye trypan blue are constructed, and certain parameters relevant to teratogenic activity defined; these definitions may be widely applicable[6].

At 8·5 days of gestation (timed by vaginal smearing), inbred Wistar rats were injected subcutaneously with 5, 12·5, 25, 37·5, 50, 75, 100 or 200 mg/kg of trypan blue in the free acid form (control trypan blue (C)[7]). Controls received 5 ml/kg of isotonic saline. At 20·5 days the rats were killed, fœtuses examined for the presence of external malformations and fœtal resorption sites counted.

Results are shown in Table 1 and in Fig. 1. Percentage resorption and malformation rates given in columns 7 and 9 of Table 1 and in Fig. 1 represent the arithmetic means of the percentages of resorptions and malformations calculated for each individual litter, and are, therefore, not quite identical with percentages which could be calculated from columns 6 and 8 by reference to total implantations (column 3). By this means (assuming a normal distribution of proportionate response) the standard error of the mean resorptions and malformations can be introduced for each dose (Fig. 1).

For a given strain of animal the 'optimum teratogenic dose' is defined as that dose which, given at the appropriate stage of pregnancy, will produce the maximum number of malformed young at term. In the present experiment the optimum teratogenic dose for trypan blue is approximately 50 mg/kg. However, within the range 5–100 mg/kg, any dose is capable of producing malformed offspring, and this is defined as the 'teratogenic dose range'. It is arguable