

Influence of copper salts on gonococci

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Summary

No difference in the incidence of gonorrhoea was observed at a venereal disease clinic between women using a copper-coil intrauterine device (IUD) and women using oral contraceptives. Experiments *in vitro* demonstrated that copper sulphate has a deleterious effect on *Neisseria gonorrhoeae*, but the presence of serum protects the gonococci from the toxic effect of copper ions.

Introduction

Copper ions have been found to exert deleterious effects on *Neisseria gonorrhoeae in vitro* (Fiscina, Oster, Oster, and Swanson, 1973). Cohen and Thomas (1974) described three women with copper-bound intrauterine contraceptive devices who had been exposed to gonococci without having contracted the infection. They suggested that the inhibitory effect of copper ions on gonococci might also play an important role *in vivo*.

The aim of the present study was to investigate the suggestion that copper-bound intrauterine devices offer protection against gonorrhoea.

Material and methods

Study group

In the 3 months February to April, 1975, 392 women attended the Outpatient Clinic for Venereal Diseases, Sociala Huset, Gothenburg, Sweden. At the first visit, the patients were questioned about their reason for attending the VD Clinic, about contraceptives, and about drugs, especially antibiotics taken during the preceding 2 months. Each patient was examined three times at weekly intervals before she was considered free from gonorrhoea.

A diagnosis of gonorrhoea was made if either a smear or culture was positive for gonococci. Smears taken from the urethra, cervix, and rectum were considered positive if there was a collection of intracellular diplococci stained with methylene blue. Specimens for culture were taken from the urethra, cervix, rectum, and tonsils, and trans-

ported in a modified Stuart's medium (Möller, 1966) to the laboratory where they were processed within 5 hours after sampling. In this series all diagnoses made by positive smears were confirmed by positive cultures.

Studies on the influence of CuSO_4 on gonococci *in vitro*

Three recently isolated strains of gonococci were exposed to various concentrations of copper sulphate. The CuSO_4 was dissolved in physiological saline alone and also in a mixture of 50 per cent. physiological saline and 50 per cent. normal human serum heated to 56°C. for 30 min. The following concentrations of CuSO_4 were used: 10^{-5} M, 10^{-6} M, and 10^{-7} M.

Sampling was performed at regular intervals to determine the number of colony forming units.

Results

Oral contraceptives were used by 67 of the women and 27 (40 per cent.) of these were found to have gonorrhoea. Cervical cultures were positive in 26 of these 27 patients. A copper-coil intrauterine device was used by 47 of the women and nineteen (40 per cent.) of these were found to have gonorrhoea. Cervical cultures were positive in seventeen of these nineteen patients.

Further analysis showed that 28 of the 67 women using oral contraceptives had had intercourse with men who were known to have gonorrhoea. These women had been referred to the clinic either by the Public Health Officer or by their sexual partner. Of these 28 women, 21 (75 per cent.) were found to have contracted gonorrhoea.

Correspondingly, twelve of the 47 women using the copper-bound device had been referred to the VD clinic after having had intercourse with a man known to have gonorrhoea. Of these twelve patients, ten (83 per cent.) were found to have gonorrhoea.

The studies *in vitro* with gonococci exposed to copper sulphate demonstrated that gonococci are sensitive to the action of this compound when it is dissolved in physiological saline (Figure). However, the addition of serum markedly diminished the toxic effect of copper sulphate against gonococci; *e.g.*, in the presence of serum, 10^{-5} M copper sulphate

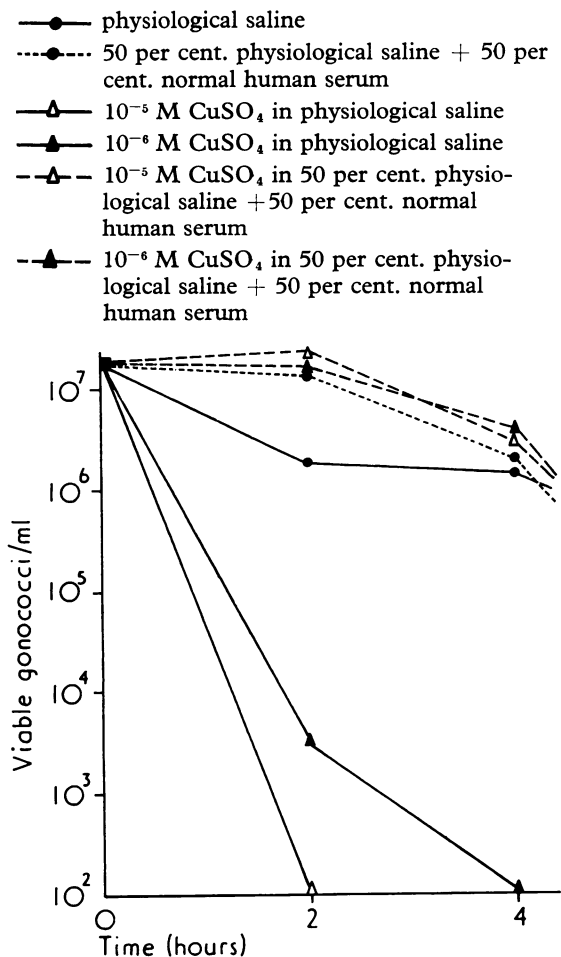


FIGURE 18-hrs-old gonococci grown on solid medium were harvested and suspended in physiological saline, and in a mixture of 50 per cent. physiological saline and 50 per cent normal human serum heated to 56° C for 30 min. These systems contained different amounts of copper sulphate. Viable counts were determined on a modified Thayer-Martin medium at regular intervals

caused a reduction in the number of viable bacteria approximating to that caused by physiological saline alone, whereas the same concentration of copper sulphate dissolved in physiological saline exhibited a pronounced killing effect. The strains displayed a

somewhat different sensitivity to copper dissolved in physiological saline, but the addition of serum invariably resulted in a pronounced reduction of the toxic effect.

Discussion

Copper sulphate is toxic to gonococci in certain concentrations (Fiscina and others, 1973). Further, copper ions are toxic to sperms (Odeblad 1974a). The copper concentration in cervical mucus was calculated by Fiscina and others (1973) to be at least $5 \cdot 10^{-8}$ M.

Hagenfeldt (1972) determined the copper concentration of cervical mucus to be higher during the proliferative phase than during the secretory phase after insertion of a Cu T device. Odeblad (1974b) showed that the copper concentration in cervical mucus is about 10^{-6} M in the upper part of the cervix. However, the concentration in the parts close to the external os is significantly lower than this. In cervical sinuses the concentration of copper is very low or absent (Odeblad, 1975).

Copper ions bound to organic ligand systems, for example alanin and histidin, are less toxic to sperms than non-organic copper salts (Odeblad, 1974a). The present results indicate that the presence of organic material such as serum protects gonococci from the toxic effect of copper ions. It seems plausible to assume that organic material present in cervical mucus might protect gonococci from the toxic effect of copper. If this assumption is valid, it offers an explanation of the fact that neither Spellacy, Hiser, and Birk (1974) nor we could demonstrate any protective effect of a copper-coil IUD against gonorrhoea.

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