

Devitalizing effects of phenol on bone marrow cells

Histologic study on cadaveric animal vertebrae

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The devitalizing effects of 5–90 percent phenol for 30 seconds on bone marrow cells were examined on vertebral bodies of fresh animal cadavers. Evaluation was made by measuring the width of the zone of

necrotic cells. The zone increased with rising phenol concentration up to 75 percent, reaching an average width of 0.75 mm. However, when protected by bone trabeculae, the cells escaped devitalization.

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The application of phenol to the curetted bone cavity in the treatment of tumors or tumor-like lesions has been reported by Dahlin and Ivins (1972), Campanacci (1985), Capanna et al. (1985), and Eckardt and Grogan (1986) without information on the concentrations used. Also in the literature, we have not found experimental studies on the effects of various phenol concentrations.

We have examined the necrotizing effects of various phenol concentrations on bone marrow cells.

Material and methods

We used the spines of four calves and one spine of a pig that had just died of cardiorespiratory or gastrointestinal diseases at the Department of Veterinary Medicine of the University of Vienna. The animals were between 3 months and 1 year of age. The investigations were performed 1 hour after harvesting.

After making a longitudinal incision into the fresh spine, we constructed a 1 × 1, 0.5-cm-deep defect in each vertebral body by using a chisel with a 1-cm-wide blade; the 0.5-cm depth was achieved with a curette. Swabs soaked in phenol were applied to these defects for 30 seconds and in three test series for 2 minutes.

Phenol (Ebewe Co.) was used in six different concentrations: 5 percent phenol in an aqueous solution, 10 percent phenol in 14 percent ethanol, 25 percent phenol in 20 percent ethanol, 50 percent phenol in 25 percent ethanol, 75 percent phenol in 20 percent ethanol, and 90 percent phenol in an aqueous solution.

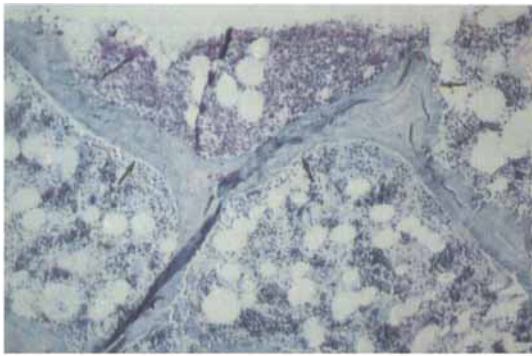
Ten minutes later, we neutralized with a swab soaked in sodium bicarbonate. In addition, one vertebral body per test series was treated with 0.9 percent sodium chloride as the negative control. Then, sodium bicarbonate was applied to determine its effect on the bone marrow cells. A further test series was made with 14, 20, and 25 percent ethanol corresponding to the phenol concentrations. In addition, we examined the thermic effects of curetting on six vertebral bodies. The cavities of each spine were processed separately for histologic studies. The material was fixed in 8 percent neutral formalin, embedded in methyl methacrylate, and stained with Giemsa in three thick sections.

The cellular effects of the various treatments were evaluated visually, whereas the thickness of necrosis was measured under the microscope using the average of five measurements. The measurements were statistically compared using the Fisher PLSD and the Scheffe *F*-test.

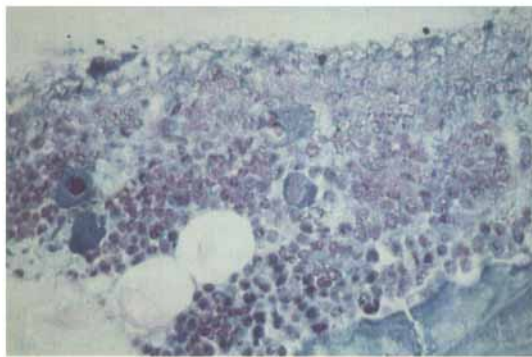
Results

Macroscopically, we observed a small seam with grayish brown staining along the margins of the phenolated cavities from a concentration of 10 percent upwards. At 10–25 percent concentration, the vertebral bodies showed a moderate change of color and from 50 percent upwards a definitive change of color.

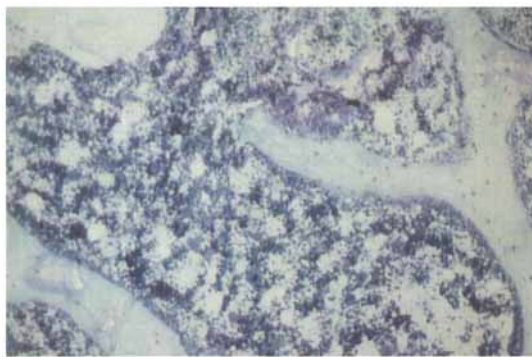
As an effect of phenol on the bone marrow cells, we observed in the margins of the cavities that the nuclei were practically structureless (mostly swollen and



A. Treatment with 75 percent phenol, uniform devitalized marginal area. The cellular layers separated by trabeculae (arrow) are all vital (Giemsa, $\times 10$).



B. Treatment with 75 percent phenol. Devitalized cellular layer with loosened, swollen nuclei; the margins of the cells can only partially still be differentiated. Types of cells not identifiable (Giemsa, $\times 40$).



C. Treatment with 0.9 sodium chloride. No changes in the bone marrow cells (Giemsa, $\times 10$).

Figure 1. Vertebral body of a calf.

loosened up) and were hardly stained; further, the cellular margins were blurred, and the individual cell types could no longer be discriminated (Figure 1).

Table 1. Mean thickness of the devitalized zone with different phenol concentrations

Phenol concentration (%)	Thickness (μ)	SD
10	235	88
25	398	155
50	630	60
75	747	47
90	566	51

These changes could only be determined in "exposed" bone marrow cells. Trabeculae located at or along the margin of the defect or bone marrow cells separated from the cavity by trabeculae showed no histologic changes.

A five percent phenol solution had little or no effect on the bone marrow cells. Ten and 25 percent phenol concentrations definitely changed the staining and/or the structures of the nuclei started to dissolve. However, a circular zone of necrosis did not appear at these concentrations.

Fifty and 75 percent concentrations of phenol caused a uniform and a mean 630-747- μ -wide zone of devitalization of the bone marrow cells; but with the exception of those areas where trabeculae lay at the surface, this zone was circular. The differences in the width of the zone of necrosis were not as conspicuous between 50 and 75 percent concentrations as they were between 25 and 50 percent concentrations.

The 90 percent phenol solution caused a smaller devitalization zone of the bone marrow cells than did the 75 percent solution (Table 1). The differences between the groups were significant at the 95 percent level with the exception of the 50 percent phenol concentration as compared with the 90 percent concentration. Finally, 0.9 percent sodium chloride (Figure 1), sodium bicarbonate, and ethanol solutions, as well as mechanical curetting, had no effects on the bone marrow cells.

When lower concentrations of phenol were used, 2 minutes of application led to only a slightly higher number of devitalized cells than 30 seconds of application.

Discussion

Chemical cauterization of bone cavities for the prevention of local recurrences after curettage of the tumor-simulating condition, as well as benign and potentially malignant bone tumors, represents an adjuvant, "ancient" method of therapy (Bloodgood 1910).

Although in the newer literature the application of phenol has been rejected because of possible impeding effects on the repair processes and revascularization of bone transplants (Neer et al. 1973), the majority of authors have reported a decrease in the number of recurrences without an increase in the infection rate or obstruction of the repair processes in the treatment of juvenile and aneurysmal bone cysts (Campanacci et al. 1985) and giant cell tumors (Eckart and Grogan 1986, Schiller et al. 1989). Capanna et al. (1985) reported a series of 125 benign bone lesions with local recurrences in 7 percent upon application of phenol compared with 41 percent in the control group treated with only curettage. Yet, with the exception of Schiller et al. (1989), who used a 5 percent phenol solution, nothing was mentioned about the phenol concentration reported in the literature.

Being a low-level acid, phenol leads to protein denaturation without coagulation. The optimum phenol concentration is reached when a sufficiently thick and continuous zone of necrosis develops. In addition, care has to be taken that the phenol concentrations are not too high when applied to rather large surfaces of the bone cavities, because this could lead to toxic effects.

We assume that our material was viable, because the cells could be seen very well in the histologic slide preparations. This is why we consider the experiment on fresh cadaver bone acceptable. For technical reasons the cavities were made with a curette in our series of tests. Intraoperatively, the surgical cavities were curetted before cauterization. Mechanical manipulation and the development of heat could also cause damage to the bone marrow cells. In the six additionally curetted vertebral bodies, we did not observe any impairment of the bone marrow cells: viz., that curetting has no devitalizing effects on residual tumor cells

in the marginal area of the surgical cavities. However, subsequent cauterization of the surgical area with phenol may lead to overt damage of the bone marrow cells in the marginal area at a depth of 0.7-0.8 mm.

We would like to stress that the damaged zone of bone marrow cells was very narrow, i.e., only small remains of a pathologic process, consisting of a few cells, were damaged by phenol after a mechanical surgical intervention. Moreover, this only occurred in lesions with abundant cells without appreciable intercellular substance. Whether or not this small necrotic zone, even after the use of 75 percent phenol in 20 percent ethanol, would be adequate to prevent a local recurrence cannot be answered.

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