gene (AdCMVlacZ) and the therapeutic efficacy of adenovirus-mediated transfer of the thymidine kinase gene of the herpes simplex virus (HSV-tk) followed by ganciclovir (GCV) administration. DENA was very effective in inducing HCC but also stimulated nontumor cell replication, as shown by proliferating cell nuclear antigen (PCNA) staining. The study of in vivo gene transfer efficiency in tumor-bearing rats showed that nontumor tissue and small tumor nodules were transduced effectively whereas a poor transduction rate was noted in large tumor nodules. Concerning therapeutic efficacy, three groups of rats with established HCC were studied: group A and B received intraportally recombinant adenovirus carrying HSV-tk (AdCMVtk) or AdCMVlacZ, respectively, and 2 days after GCV was given intraperitoneally for 9 days; group C received only saline. Of the rats from groups B and C, 100% and 93% respectively, exhibited multiple HCC tumor nodules at end of the study. In contrast, a complete regression of tumor was observed in 63% of animals from group A. This group showed significant elevation of serum transaminases and a diffuse hepatotoxic lesion in liver tissue; histological signs of regeneration were observed in surviving animals. Nine out of 19 rats from group A died during the treatment period. We conclude that (i) in the DENA model of HCC, tumoral cells can be destroyed in vivo by the HSV-tk/GCV system despite poor transduction of large tumor nodules, suggesting that toxic metabolites generated by nontumor cells may exert a bystander effect on tumor tissue; (ii) significant hepatotoxicity and a high mortality rate occurred in HSV-tk/GCV-treated rats; these side effects appear to be due to the fact that in DENA-treated livers enhanced cell proliferation was present not only in tumor nodules but also in nontumor parenchyma, leading to GCV sensitization of both tissues; (iii) our results have implications concerning the efficacy and potential risks of the HSV-tk/GCV system in the treatment of human HCC.

Measurement of bone lengthening forces; an experimental model in the lamb

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Abstract of:
Clinical Biomechanics Vol. 12 No 1, 17-21, 1997

Objective: To obtain the mechanical behaviour pattern of the lengthening process.

Design: In vivo measurement of forces during bone lengthening in lambs.

Background: A series of parameters of a mechanical and biological nature have a bearing on all lengthening processes, and most of them are not fully understood.

Methods: A strain-gauge-monitored unilateral fixator was designed and used to obtain data about the changes which took place in the forces of elongation at a rate of 1 mm/day in four lambs while a 3 cm progressive lengthening of the left tibia was being performed, analysing how these forces behaved from day to day, and how they changed in the course of a single day.

Results: The maximum forces in all the animals each day occur after distraction, and the forces reach their greatest magnitude between days 21 and 25 after surgery, attaining values of slightly over 8 kg (40-50% of the animal’s weight). The maximum daily force starts to drop 1 h after distraction, and continues to decrease gradually throughout the day until it reaches a value slightly greater than the initial force on the previous day.

Conclusion: This pattern is due to the distraction of soft tissues which gradually adapt to their new situation, thereby reducing the level of stress.