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ABSTRACTS

Page 3 of 4

Continued from Page 2

Lactoferrin

In vitro antiviral activity of lactoferrin and ribavirin upon hantavirus.

Bovine lactoferrin (LF) and ribavirin (Rbv) were tested as antiviral agents against Seoul type hantavirus (SR-11 strain) in vitro. Hantaviral foci number in Vero E6 cells infected with SR-11 was reduced with LF treatment by 5 days post infection to obtain a 50% effective dose (ED50) of 2500 microg/ml, while pretreatment with LF was highly efficacious having an ED50 of 39 microg/ml. Conversely, 1 h pretreatment with Rbv revealed no inhibition of viral focus formation but could significantly reduce the number of viral foci (ED50: 10 microg/ml) when used from the time of viral infection. One hour pre-treatment of the cell monolayer with LF and subsequent addition of Rbv revealed a synergistic anti-hantaviral effect against SR-11, <20 FFU/ml as compared to 10(5) foci/ml in the control. One hour treatment of SR-11 with LF prior to cell inoculation gave an ED50 of 312.5 microg/ml. Whereas, washing the LF-pretreated cell monolayer with PBS demonstrated minimal focus reduction, suggesting LF lightly adheres to cells. These results indicate that LF has anti-hantaviral activity in vitro and inhibition of virus adsorption to cells which play an important role in revealing the anti-hantaviral activity of LF. This paper reports for the first time the anti-hantaviral effect of LF.

Arch Virol 2000;145(8):1571-82

Human lactoferrin and peptides derived from a surface-exposed helical region reduce experimental escherichia coli urinary tract infection in mice

Lactoferrin (LF) is a multifunctional immunoregulatory protein that has been associated with host defense at mucosal surfaces through its antibacterial properties. The antibacterial and anti-inflammatory properties of LF were further explored with an animal model of experimental urinary tract infection. Bovine LF (bLF), human LF (hLF), and synthetic peptide sequences based on the antibacterial region of hLF (amino acid residues 16 to 40 [HLD1] and 18 to 40 [HLD2]) were given orally to female mice 30 min after the instillation of 10(8) Escherichia coli bacteria into the urinary bladder. The control groups received phosphate-buffered saline or water. C3H/Tif mice were treated with hLF or bLF, and C3H/HeN mice were treated with bLF only. The numbers of bacteria in the kidneys and bladder of C3H/Tif and C3H/HeN mice were significantly reduced 24 h later by the LF treatments compared to the findings for the control group. The hLF-treated group showed the strongest reduction compared with the vehicle-treated-group (P values were 0.009 and 0.0001 for the kidneys and bladder, respectively). The urinary leukocyte response was diminished in the hLF-treated group. The hLF treatment also significantly reduced the urinary interleukin-6 (IL-6) levels at 2 h and the systemic IL-6 levels at 24 h after infection (P values were 0.04 and < 0.002, respectively). In the bLF-treated animals, no such strong anti-inflammatory effects were obtained. In another series of experiments, C3H/Tif mice perorally treated with HLD1 or HLD2 also showed reduced numbers of bacteria in the kidneys compared with the vehicle-treated mice, although the results were significantly different only for HLD2 (P < 0.01). Analysis of urine from hLF-fed C3H/Tif mice showed that hLF was excreted into the urinary tract at 2 h after feeding. Testing of the in vitro bactericidal activity of LF (1 mg/ml) or the peptides (0.1 mg/ml) in mouse urine against the E. coli bacteria revealed moderate killing only by HLD2. In conclusion, these results demonstrate for the first time that oral administration of hLF or peptides thereof is effective in reducing infection and inflammation at a remote site, the urinary tract, possibly through transfer of hLF or its peptides to the site of infection via renal secretion. The antibacterial mechanism is suggested to involve bactericidal capacities of LF, fragments thereof, or its peptides.

Infect Immun 2000 Oct;68(10):5816-23

Oral administration of bovine lactoferrin for treatment of tinea pedis. A placebo-controlled, double-blind study.

A clinical study was conducted to evaluate the effectiveness of lactoferrin, which is a protein component of cow's milk, in the treatment of tinea pedis. Doses of either 600 mg or 2000 mg of lactoferrin, or a placebo was orally administered daily for 8 weeks to 37 adults who were judged to have mild or moderate tinea pedis. Dermatological improvement and antifungal efficacy were

assessed. In the analysis of all subjects, dermatological symptoms scores in all groups decreased but the differences were not statistically significant comparing the three groups. However, in the analysis limited to subjects with moderate vesicular or interdigital tinea pedis, dermatological symptoms scores in the lactoferrin-treated groups decreased significantly in comparison with the placebo group ($P < 0.05$). The organisms isolated were *Trichophyton rubrum* and *Trichophyton mentagrophytes*. A mycological cure was not seen in any of the subjects. In the 37 subjects there were no adverse events and no subject withdrew from the study because of an adverse event. These results suggest that orally administered lactoferrin can improve the dermatological symptoms in some subjects. The potential usefulness of lactoferrin as a functional food material for treating tinea pedis was seen for the first time in this study.

Mycoses 2000;43(5):197-202

Mercury Toxicity

Maternal-fetal distribution of mercury (^{203}Hg) released from dental amalgam fillings.

In humans, the continuous release of Hg vapor from dental amalgam tooth restorations is markedly increased for prolonged periods after chewing. The present study establishes a time-course distribution for amalgam Hg in body tissues of adult and fetal sheep. Under general anesthesia, five pregnant ewes had twelve occlusal amalgam fillings containing radioactive ^{203}Hg placed in teeth at 112 days gestation. Blood, amniotic fluid, feces, and urine specimens were collected at 1- to 3-day intervals for 16 days. From days 16-140 after amalgam placement (16-41 days for fetal lambs), tissue specimens were analyzed for radioactivity, and total Hg concentrations were calculated. Results demonstrate that Hg from dental amalgam will appear in maternal and fetal blood and amniotic fluid within 2 days after placement of amalgam tooth restorations. Excretion of some of this Hg will also commence within 2 days. All tissues examined displayed Hg accumulation. Highest concentrations of Hg from amalgam in the adult occurred in kidney and liver, whereas in the fetus the highest amalgam Hg concentrations appeared in liver and pituitary gland. The placenta progressively concentrated Hg as gestation advanced to term, and milk concentration of amalgam Hg postpartum provides a potential source of Hg exposure to the newborn. It is concluded that accumulation of amalgam Hg progresses in maternal and fetal tissues to a steady state with advancing gestation and is maintained. Dental amalgam usage as a tooth restorative material in pregnant women and children should be reconsidered.

Am J Physiol 1990 Apr;258(4 Pt 2):R939-45

An estimation of the uptake of mercury from amalgam fillings based on urinary excretion of mercury in Swedish subjects.

Mercury is released from amalgam fillings in several forms, i.e. as elemental vapour, ions and in fine particles. Despite many investigations there is still considerable uncertainty concerning the uptake of such mercury. Most available estimates have calculated the pulmonary uptake of mercury vapour based on measurements of concentrations intra-orally or in expired breath. Presented estimates vary by an order of magnitude from approximately 1 to 20 micrograms/day. The possibility of estimating this uptake based on levels of mercury in a biological index medium has received comparatively little attention. The purpose of the present work is to estimate the uptake of mercury from amalgam fillings based on urinary concentrations of mercury. It is estimated that the average uptake of mercury from amalgam fillings in Swedish subjects is within the interval 4-19 micrograms/day. This interval was arrived at after a detailed evaluation of the uncertainties in the data used and in the different assumptions. Notwithstanding the considerable range of this estimate it indicates a higher uptake than several other estimates, some of which have had a large impact on the scientific debate concerning this issue.

Sci Total Environ 1995 Jun 30;168(3):255-65

Mercury concentration in the mouth mucosa of patients with amalgam fillings.

Mercury concentrations were measured in specimens of oral mucosa taken during oral surgery from 90 patients (53 men, 37 women, mean age 42 +/- 16 years); 30 of the patients had no amalgam fillings. All the mucosal specimens extended for at least 2-3 mm from the epithelium of the gingival margin and were clinically and radiologically normal. Thirteen patients without metallic fillings of any kind had mercury concentrations of 118.4 +/- 83.7 ng/g tissue, and in 17 patients with precious metal fillings but no amalgam the mean mercury concentrations were 144 +/- 290 ng/g tissue. Seventeen patients with 1-3 amalgam fillings had an average of 1975 +/- 4300 ng/g tissue and in 26 patients with 3-6 amalgam fillings the average concentration was 1158 +/- 2500 ng/g tissue. In 17 patients with more than six amalgam fillings the mean mercury concentration was 2302 +/- 5600 ng/g tissue. Although these results demonstrate a considerable degree of transfer of mercury from the amalgam fillings to the oral mucosa, it had not resulted in any clinically detectable mucosal lesions.

Dtsch Med Wochenschr 1992 Nov 13;117(46):1743-7

Influence of chewing gum consumption and dental contact of amalgam fillings to different metal restorations on urine mercury content.

It had been shown previously by various authors that contact of amalgam fillings to metal fillings of different type can increase the electrochemically caused amalgam corrosion in vitro thus leading to an elevated release of mercury. So it was recommended to renounce of a dental contact of amalgam to metal fillings of other type. One aim of the present study was to evaluate possible influences of this contact in vivo on the urinary mercury contents in human volunteers. Neither approximal nor occlusal contacts had any influence on the urinary mercury excretion in comparison to a reference group with similar amalgam status. Furthermore, the influence of gum chewing on urinary mercury levels was taken into account. It could be shown that the consumption of chewing gum resulted in a significantly higher mean urinary mercury content in probands with amalgam fillings in comparison to people with similar amalgam status (gum chewers: 1.36 Hg/24 h vs. non-chewers 0.70 microgram Hg/24 h). Thus, gum chewing has to be considered as important parameter of influence on the urinary mercury levels of people with amalgam fillings.

Zentralbl Hyg Umweltmed 1996 Nov;199(1):69-75

Long-term use of nicotine chewing gum and mercury exposure from dental amalgam fillings.

In experimental studies, chewing gum has been shown to increase the release rate of mercury vapor from dental amalgam fillings. The aim of the present study was to investigate the influence of long-term frequent chewing on mercury levels in plasma and urine. Mercury levels in plasma (P-Hg) and urine (U-Hg), and urinary cotinine were examined in 18 subjects who regularly used nicotine chewing gum, and in 19 referents. Age and number of amalgam surfaces were similar in the two groups. Total mercury concentrations in plasma and urine were determined by means of cold vapor atomic absorption spectrometry. Urinary cotinine was determined by gas chromatography-mass spectrometry. The chewers had been using 10 (median) pieces of gum per day for the past 27 (median) months. P-Hg and U-Hg levels were significantly higher in the chewers (27 nmol/L and 6.5 nmol/mmol creatinine) than in the referents (4.9 nmol/L and 1.2 nmol/mmol creatinine). In both groups, significant correlations were found between P-Hg or U-Hg on the one hand and the number of amalgam surfaces on the other. In the chewers, no correlations were found between P-Hg or U-Hg and chewing time per day or cotinine in urine. Cotinine in urine increased with the number of pieces of chewing gum used. The impact of excessive chewing on mercury levels was considerable.

J Dent Res 1996 Jan;75(1):594-8

Impact of nocturnal bruxism on mercury uptake from dental amalgams.

The mercury (Hg) release from dental amalgam fillings increases by mechanical stimulation. The aim of this study was to investigate the possible impact of nocturnal bruxism on Hg exposure from dental amalgams and to evaluate the effect of an occlusal appliance. 88 female patients from an orofacial pain clinic with a complete maxillary and mandibular dentition, a normal frontal vertical overbite with cuspid guidance, and at least 4 occlusal amalgam fillings in contact with antagonists in intercuspital position, were examined with the Bruxcore bruxism monitoring device to measure the level of on-going nocturnal bruxism. Based on the degree of abrasion recorded, the subjects were divided into a group defined as bruxists, (n = 29), another group defined as non-bruxists, (n = 32), serving as controls, the intermediate group being discarded. The Hg exposure was assessed from the Hg concentration in plasma and urine, corrected for the creatinine content. In a regression model with bruxism as the only explanatory variable, no significant effect of bruxism was found, but when the number of amalgam fillings, chewing gum use, and other background variables were taken into account, there was a limited impact of bruxism on Hg in plasma. The nocturnal use of an occlusal appliance did not, however, significantly change the Hg levels. This study indicates that mechanical wear on amalgams from nocturnal bruxism may increase the Hg uptake, but the magnitude of this effect seems to be less than from the use of chewing gum.

Eur J Oral Sci 1997 Jun;105(3):251-7

Mercury release of silver amalgam fillings in vitro.

In vitro mercury release from silver amalgam fillings was analyzed by ICP (Inductively-coupled-plasma-atomic-emission-spectroscopy). Within 14 days 63.2 micrograms Hg and 41.5 micrograms Hg respectively, were released from unfinished and finished amalgam fillings (n = 5). The amounts of mercury found in this study were several times higher compared with the results from other in vitro-studies.

Dtsch Zahnarztl Z 1990 Jan;45(1):17-9

Continued on Page 4

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