



## Author's response to: 'Causality between polyhexamethyleneguanidine occurrence in unrecorded alcohol and cholestatic hepatitis outbreak in Russia'

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LETTER TO THE EDITOR

**Author's response to: 'Causality between polyhexamethyleneguanidine occurrence in unrecorded alcohol and cholestatic hepatitis outbreak in Russia'**

To the Editor:

We are grateful to Lachenmeier and colleagues for their letter 'Causality between polyhexamethyleneguanidine occurrence in unrecorded alcohol and cholestatic hepatitis outbreak in Russia' and their valuable comments on our paper. We well understand the doubts on the causative relation of the antiseptic 'Extracept-1' containing polyhexamethyleneguanidine hydrochloride (PHMG) and the development of cholestatic hepatitis in persons ingesting this antiseptic. Naturally, we considered that the development of clinical hepatitis was closely connected with chronic hepatic lesions due to long-term alcohol abuse by practically all the patients in our series. Nevertheless, it is impossible to deny the association of this mass outbreak with the use of alcohol drinks including PHMG. To emphasize this, we would also highlight that this episode of mass poisoning in 2006–2007 was preceded by a similar smaller event in 2004 in the small town of Upper Salda in the Sverdlovsk region, where about 100 patients fell ill, and 4 of them died after using the alcohol containing liquid 'Helios'. This is unpublished data of coauthors of discussed article Drs KM Brusin, VG Sentsov, OV Novikova. Liquid 'Helios' contained: 83.1% of ethyl alcohol, 0.1% of diethyl phthalate (DEP) and 0.038% of PHMG. The symptoms of the disease were similar to the cases in 2006–2007. After confiscation of the liquid 'Helios' from the illegal alcohol market, the cases of the disease stopped.

In the mass poisoning in 2006–2007, which occurred in almost half the territory of Russia, it was found that the victims used the disinfecting liquid 'Extracept-1', which contained ethyl alcohol  $93 \pm 0.5\%$ , DEP 0.08–0.15% and PHMG  $0.1\text{--}0.14 \pm 0.01\%$ . In addition, we are also aware of several cases of similar poisoning after consumption of liquid for washing automobile glass ('Ldinka-Super'), and concentrates for adding to baths ('Sage' and 'Hawthorn'), with the aim of alcohol intoxication. Toxicological study of these liquids was done at the Institute of toxicology in St. Petersburg and revealed a composition similar to 'Extracept-1'. It is interesting to note that people had used similarly named bath concentrates in previous years, but at that time, this was not accompanied by the health disorders described in our article.

It should be noted that DEP is usually present as an additive in practically all manufactured alcohol containing products (cosmetic, technical) not intended for oral use. All these alcoholic products are regularly used for inducing intoxication, but without such severe consequences. We therefore do not believe DEP was a likely cause of the cholestatic hepatitis we observed.

Only a few cases similar to PHMG poisoning were reported after 2007. One of them was confirmed in Irkutsk, with PHMG being found in body tissue post mortem and in liquid found on scene (Unpublished data of coauthor of discussed article YV Zobnin).

According to standard practice in Russia, all in-patients had blood tested for the presence of hepatitis or HIV infection. Thus in Irkutsk, 163 patients were analyzed for viral hepatitis markers. Analyses were performed by polymerase chain reaction for viral DNA of hepatitis B; RNA of hepatitis C and RNA of hepatitis G. Immuno-enzymatic analysis was used for HBsAg, antibodies to HbsAg, IgM to HbcAg and antibodies to HCV. Hepatitis B was not found in any patients and hepatitis C was found in seven patients. Patients infected by viral hepatitis had more active manifestations of hepatic cell injury (higher levels of transaminases and non-conjugated bilirubin).

PHMG hepatic effects were studied in experiment by the personnel of the Institute of immunology and physiology of Ural department of Russian Academy of Sciences and Ural Medical Academy.<sup>1</sup> Rats had intraperitoneal administration of PHMG water solution in a total dosage of 50 mg/100 g, at a rate of 17 mg/100 g a day, and also carbon tetrachloride oily solution as positive control. Experimental rats were sacrificed on 3 and 7 days after toxicant administration. It was found that the microscopic effects and serum transaminases increased after PHMG with the length of experiment though it was less toxic than the positive effect.

We agree that there is a lack of published experimental data on PHMG toxicity, and we are encouraging our colleagues to publish their data.

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