Melamine contamination of dairy products in China – public health impact on citizens of the European Union

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On 10 September 2008, ProMED issued a request for information concerning 14 cases of kidney stones in infants hospitalised in Gansu province, China, in the previous two months [1]. On 21 September, Chinese authorities reported 39,965 cases of kidney stones in infants, including three deaths related to the consumption of melamine-contaminated powdered infant formula. On that day, 12,892 of them were hospitalised, 104 with severe illness. Most of these cases (82%) affected children under two years of age.

A large melamine contamination of milk-containing products, including infant formula, was reported from China. The level of contamination is variable but reaches high levels among certain producers. Contaminated food items include infant formula, liquid milk, frozen yoghurt dessert, coffee creamer, ice-cream, chocolate cookies and candies [2,3]. Food safety agencies in Hong Kong and Taiwan as well as in several other countries and locations have identified locally sold contaminated products originating from China, including: Singapore, New Zealand, Indonesia, South Korea, Vietnam and Canada [4]. Contaminated products were also exported to Bangladesh, Burundi, Myanmar, Gabon and Yemen. Media in the European Union (EU) have reported that milk products originating from China had been found in Spain and Portugal [5,6]. Ireland has withdrawn confectionary from sales outlets that had been identified by New Zealand health authorities as contaminated [7]. On 17 September, China recalled tons of milk powder produced by Sanlu Group Co since March 2008.

The importation in the EU of milk products from China has been prohibited under EU legislation since 2002. However, certain amounts of composite products (i.e., products which contain a processed product of animal origin and a product of non-animal origin) containing processed milk components may have reached the EU in the past, including confectionary, biscuits, chocolate, toffee or cakes.

Effects of melamine on health
Melamine, when associated with cyanuric acid [10], can cause renal failure by the formation of insoluble melamine cyanurate crystals in renal tubules and/or the formation of calculi in kidneys, ureter, urethra or the urinary bladder. These calculi are a mixture of melamine, protein, uric acid and phosphate and as such are distinct from other kidney stones. They are radiolucent and give a negative image on urinary tract X-ray. Usually both kidneys and ureters are affected. In severe cases, ultrasound investigation reveals bilateral renal enlargement (due to renal tract obstruction) with increased echogenicity. Furthermore, the urine sediment crystals may contain material with a characteristic double refraction in microscopy. Further details on differential diagnosis and ultrasound and x-ray findings can be found on the WHO webpage (http://www.who.int/csr/don/2008_09_29a/en/index.html)

Although there is evidence for the carcinogenicity of melamine under conditions that produce bladder calculi in animals, this evidence is still lacking in humans [11]. The following symptoms have been observed in infants affected by the melamine-contaminated infant formula in the current outbreak in China [12]:
• Unexplained fever arising from urinary tract infections/bacteraemia secondary to urine stasis resulting from urinary tract obstruction;
• Unexplained crying in infants, especially when urinating, possible vomiting;
• Macroscopic or microscopic haematuria;
• Acute obstructive renal failure: oliguria or anuria;
• Dysuria (pain on urinating) and passage of stones while urinating (for example, a baby boy with urethral obstruction with stones normally has dysuria);
• High blood pressure, oedema, pain over the kidneys.

Urolithiasis (kidney stones) in infants is a very uncommon disease. However, the information available in the EU indicates that although several hundred cases of urinary stones possibly occur every year in the EU in children under the age of five years, these are almost certainly unrelated to melamine exposure.

Assessment for exposure of EU citizens through food products

The European Food Safety Authority (EFSA) published a statement on 24 September [13] indicating that the estimated exposure does not raise concerns for the health of adults in Europe should they consume chocolates and biscuits containing contaminated milk powder. Children with an average consumption of biscuits, milk-toffee and chocolate made with such milk powder would generally not exceed the tolerable daily intake (TDI), either. However, in a worst case scenario, with the highest level of contamination, children with high daily consumption of milk-toffee, chocolate or biscuits containing high levels of milk powder would exceed the TDI. Children who consume both such biscuits and chocolate could potentially exceed the TDI by more than three-fold. However, EFSA noted that it is presently unknown whether such high level exposure scenarios may occur in Europe.

In the view of the European Centre for Disease Prevention and Control (ECDC), the risk would be higher for children if counterfeit or illegally imported milk products were present in the EU. The risk for humans with compromised renal function or haemo-concentration associated with absorbing “acceptable” melamine doses, i.e. at the TDI, is unclear. Such individuals would be advised to avoid consumption of suspect products.

In particular, specific groups of EU citizens may have been and/or still be at higher risk of having been exposed to contaminated products:
• Visitors to China in the recent months;
• Citizens of overseas territories, to which contaminated products have been exported;
• Children who have recently been adopted from China and were exposed to contaminated infant formula of Chinese origin provided they are still exposed to infant formula originating from China;
• Travellers to and residents in China; they should currently be aware of the possibility of contamination of dairy products still sold in China, including milk, milk products and infant formula until the extent of the contamination is fully ascertained by Chinese authorities.

Assessment of public health impact of potential exposure

Even though there were indications of potential contamination already in late 2007, the period of potential exposure can be considered to have started in March 2008, when the contaminated batches were produced which triggered the alert. The assessment of the public health impact of potential exposure of EU citizens to melamine-contaminated food products during this period should therefore focus on children under the age of 10 years (the oldest case reported in Hong Kong) even though most of the cases were younger than three years. The ECDC suggests the assessment to be done as follows:

• Retrospectively, by checking hospital discharge data (or other appropriate sources e.g. emergency consultation registers) for ICD 10 codes related to renal failure and urolithiasis, for infants under the age of 10 years, as most cases in China were in this age group. The relevant ICD codes include N17, N19, N20, N21 and N23. This review should cover the period from March 2008 onwards. Data retrieved should be compared to historical baseline data;
• Prospectively, by informing health care providers in paediatric wards of the clinical presentation of the disease. Children, under the age of 10 years, who present with symptoms or signs of urolithiasis or acute renal failure and for whom other potential causes of kidney stones have been excluded by differential diagnosis, should be tested for melamine exposure using a food exposure questionnaire and, if appropriate, by testing for melamine; confirmed cases should be notified to the health authorities.

References
