

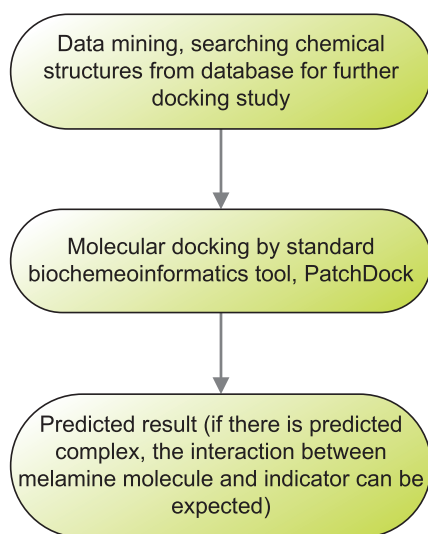
Low Rate of Proteinuria in Children After Exposure to Low-Dose Melamine

No Predicted False Positivity Due to Melamine

SIR,

Melamine nephrotoxicity as a result of consumption of tainted milk products in China has recently become an important topic in pediatric nephrology.¹ The reported cases of acute kidney failure due to the melamine intoxication is the present focus.¹ Recently, the *BMJ* published an interesting paper on the screening for proteinuria in the children after exposure to low-dose melamine and the conclusion that "Urgent and large scale renal screening in children with a history of exposure to low dose melamine may not be necessary," and 1% to 2% of proteinuria rate was reported.² By nature, melamine can mimic a protein and can cause false positivity in quantitative determination of protein level in milk.¹ This can raise the question whether melamine can cause false positive results for protein in vivo. Here, the author tried to use basic biocheminformatics principles to support the observation that there is a very low rate of proteinuria in the children after exposure to low-dose melamine.

This work was done as a theoretical bioinformatics analysis (Figure). Focusing on the basic principle of



The diagram summarizing the conceptual framework in this work.

proteinuria screening, based on the colorimetric test using the indicator, especially for tetrabromophenol blue, the change of color is due to the direct interaction between the indicator and protein in urine. Hence, if a computation simulation shows a possible reaction between "melamine molecule" and "tetrabromophenol blue", the color change, which implies false positivity, can be expected. To test the mentioned reaction, a standard molecular docking technique, using a tool named PatchDock, was utilized to assess whether there is any predicted resulted complex.³ This technique is an acceptable method to assess the possible reaction between 2 references molecules in reference database (Chemical Infobox, available from <http://en.wikipedia.org/wiki/Wikipedia:CHEMBOX>) and is already described and confirmed for reliability in a previously published paper.⁵ Since the secretion of melamine into urine is feasible and there can be 2 common kinds of melamine in urine (free melamine compound and cyanuric acid crystallized melamine), the possibilities of interaction of both kinds of melamine molecules were tested. According to the bioinformatics analysis, it appeared that there was no predicted result complex between melamine and tetrabromophenol blue and between cyanuric acid crystallized crystal and tetrabromophenol blue.

Melamine can be absorbed via the gastrointestinal tract and is then excreted largely unchanged by the kidneys. This is the rooted cause of problem of melamine intoxication. The formation of melamine crystal in urine in the kidney is the main etiology of kidney damage in the intoxicated children.⁴ Here, the author assessed whether melamine could cause false positive results for urine protein screening via a theoretical bioinformatics in silico analysis, testing for the possibility on the complex formation between studied molecules and indicators, not the laboratory test of melamine or urine. No predicted interaction implies clinical relevance that melamine cannot cause false positive results for proteinuria. This might be an explanation for low prevalence of proteinuria in children exposed to melamine. In

addition, the pathological process in the affected pediatric cases is owing to the acute obstruction from melamine crystal that is unlikely to cause proteinuria. Therefore, the rationale for screening for proteinuria in pediatric cases exposed to melamine is not supported. Some limitations of this work should be noted. First, this is a bioinformatics study that still requires further *in vitro* and *in vivo* confirmation. Second, there are some new information on uric acid crystallized melamine in urine, but it is not observed in all cases and is not studied in this work due to lack of basic information on its structure.

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Reno-renal Syndrome Cross-talk Between Kidneys

SIR,

Various pathophysiological syndromes have thronged nephrology. These include hepato-renal, pulmonary-renal, and cardio-renal syndromes. We herein describe a new syndrome characterized by injury (partial or total) to one kidney, cumulating in pathophysiological changes in the other, and we shall now call it as *reno-renal syndrome*. The notion that a single kidney enlarges to compensate for the loss of its partner has been entertained since antiquity. Aristotle (384 to 322 BC) noted that a single kidney was able to sustain life in animals, and that such kidneys were enlarged. The enlargement of the glomeruli is mainly due to increase in volume. Numerous hypotheses accounting for this renal hypertrophy include large amount of metabolic solute load, renotropic factors such as renotropin, hormones, and growth factors such as insulin-like growth factor I, vascular endothelial growth factor, etc. It appears that there is increased sensitivity of kidney cells to growth promoting factors.

Both hemodynamic and nonhemodynamic responses occur after renal mass ablation. The hemodynamic responses comprise of renin-angiotensin-aldosterone system, endothelins,

REFERENCES

1. Outbreak news. Melamine contamination, China. *Wkly Epidemiol Rec*. 2008;83:358.
2. Lam HS, Ng PC, Chu WC, et al. Renal screening in children after exposure to low dose melamine in Hong Kong: cross sectional study. *BMJ*. 2008;337:a2991.
3. Schneidman-Duhovny D, Inbar Y, Polak V, et al. Taking geometry to its edge: fast unbound rigid (and hinge-bent) docking. *Proteins*. 2003;52:107-12.
4. Aleksandrian AV. Toxicity and sanitary standardization of melamine cyanurate (experimental data). *Gig Tr Prof Zabol*. 1986;(1):44-5.
5. Wiwanitkit V. Molecular structure of BRCA1-estrogen receptor alpha-estrogen complex: relevance to breast cancer? *Asian Pac J Cancer Prev*. 2005;6:561-2.

eicosanoids, natriuretic peptides, bradykinin, and nitric oxide. Nonhemodynamic factors again include angiotensin II, aldosterone, and others such as transforming growth factor β , bone morphogenic protein-7, hepatocyte growth factor, and altered glomerular permselectivity to proteins.¹

The common clinical conditions which manifest as reno-renal syndrome include: postnephrectomy condition, unilateral renal dysplasia, unilateral renal agenesis, oligomeganephronia, segmental hypoplasia, vesicoureteric reflux, the condition following urinary diversion, accident-related reduction of renal mass, conditions associated with renovascular disease, unilateral obstruction, and cortical necrosis.² The end results of these pathologic syndromes are proteinuria, hypertension, and progression to chronic kidney disease by means of focal segmental glomerulosclerosis. Therefore, interventions aiming to control of hypertension, dyslipidemia, weight gain, anemia, calcium-phosphate metabolism, decrease protein intake, and renin-angiotensin-aldosterone system blockade may not only prevent but may also reverse reno-renal syndrome.

To summarize, reno-renal syndrome is a