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## Letter to Editor

### Is serum in childhood naturally protective against SARS-coronavirus?

Since the first emerging of the human severe acute respiratory syndrome (SARS) in Guangdong, China, on 16 November 2002 [1], till the leaving of the last two inpatients from the Beijing Ditan Hospital on 16 August 2003, SARS had spread in China (mainland, Taiwan and Hongkong) for about 9 months. It affected 5327 people in mainland of whom 348 died which statuted by China Center for Disease Prevention and Control. Interestingly, the morbidity of children was very low; they suffered only a mild form of the disease, none required oxygen supplementation, mechanical ventilation assistance or intensive care admission, and none of them died [2–4]. Three possible explanations were suggested: (1) children were kept relatively isolated from the outside world during the epidemic, therefore avoiding the infection; (2) the immature immune system does not cause acute lung injury; and (3) children have anti-SARS antibodies.

On 3 July 2003, the SARS research information web of Chinese Academy of Sciences delivered a retrospective study of the Capital Institute of Pediatrics. It reported that up to 40% of the children sera collected and stored before and during the SARS epidemic manifested anti-SARS antibodies, whereas the adult sera samples did not [5]. This phenomenon was presumed to be a result of multiple vaccinations in the childhood. The news intrigued all of us and we decided to verify it experimentally. We immunized two species of young mice (Balb/c and Kunming) with thirteen vaccines, namely attenuated variola, measles–mumps–rubella triple vaccine, yeast recombinant hepatitis B surface antigen, attenuated measles, diphtheria–tetanus toxoid–pertussis triple vaccine, attenuated hepatitis A, BCG, poliomyelitis and encephalitis B vaccines (all products of National Vaccine and Serum Institute, China), attenuated varicella vaccine (Changchun Institute of Biological Products, China) and influenza split inactivated vaccine (Sachsische Serumwork Co). All vaccines were diluted, 1:12 (v/v), with saline, and i.p. administrated 200  $\mu$ l per mouse, once a week for 7 successive weeks. Droplets of blood were collected from the tail veins before each inoculation and anti-SARS-coronavirus antibodies detected by indirect ELISA.

Whereas human SARS serum gave a strong positive reaction ( $A_{450} = 0.564 \pm 0.084$ ), all the sera of the inoc-

ulated mice were negative ( $A_{450}$  less than 0.06), just as negative control antisera [ $A_{450} = 0.045 \pm 0.028$  (Balb/c),  $0.049 \pm 0.033$  (Kunming),  $0.015 \pm 0.016$  (human)]. It implies that there is essentially no cross-immunoreactivity between the SARS-coronavirus and the thirteen immunogens tested.

Meanwhile it was reported that anti-SARS activity could be detected in very few if any children's serum samples [6,7]. Thus, the presence of anti-SARS antibodies in children can be apparently ruled out as the cause of the low morbidity. However, in addition to the above mentioned two reasons (low exposure and immature immune system), the existence of some other so far unknown factor(s) in the children's sera capable of interfering with the SARS-coronavirus still remains an open possibility [8].

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Qian Li  
JiaLing He  
ChengYu Wang  
ManJi Sun\*

*Beijing Institute of Pharmacology and Toxicology*  
*Beijing 100850, China*  
Corresponding author. Tel.: +86-10-66874609  
fax: +86-10-68211656  
*E-mail address:* sunmj@nic.bmi.ac.cn  
(M. Sun)

GuanFu Jin  
ZhongYuan Wang  
*309th Hospital, Beijing, China*  
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