

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 μ 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 ± 0.033 (Kunming), 0.015 ± 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].

References

- [1] Zhong NS, Zheng BJ, Li YM, Poon ZH, Chan KH, Li PH, Tan SY, Chang Q, Xie JP, Liu XQ, Xu J, Li DX, Yuen KY, Guan Y. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February 2003. *Lancet* 2003;362:1353–8.
- [2] Hon KL, Leung CW, Cheng WT, Chan PK, Chu WC, Kwan YW, Li AM, Fong NC, Ng PC, Chiu MC, Li CK, Tam JS, Fok TF. Clinical presentations and outcome of severe acute respiratory syndrome in children. *Lancet* 2003;361:1905.
- [3] Chiu WK, Cheung PC, Ng KL, Ip PL, Sugunan VK, Luk DC, Ma LC, Chan BH, Lo KL, Lai WM. Severe acute respiratory syndrome in children: experience in a regional hospital in Hong Kong. *Pediatr Crit Care Med* 2003;4:279–83.
- [4] Wong GW, Li AM, Ng PC, Fok TF. Severe acute respiratory syndrome in children. *Pediatr Pulmonol* 2003;36:261–6.
- [5] Capital Institute of Pediatrics, China. Younger children manifested a high positivity rate (more than 40%) of the anti-SARS antibodies. <http://www.xinhuanet> (03 July 2003 07:37:08).
- [6] Liu JH. Anti-SARS activity only existed in 2% of the children's serum samples. <http://www.people.com.cn> (22 August 2003 10:30).
- [7] Li LH, Shi YL, Li P, Xu DX, Wan GP, Gu XQ, Zhang XL, Ma QJ, Cao C. Detection and analysis of SARS coronavirus-specific antibodies in sera from non-SARS children. *Di Yi Jun Yi Da Xue Xue Bao* 2003;23:1085–7.
- [8] Jiang Q. Something in the serum capable of binding with the SARS-coronavirus in children's serum samples. <http://www.xinhuanet.com> (05 November 2003 16:34:37).

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