Clinical utility of the Coombs test

The article by J. Manuel Zarandona and Mark Yazer on the clinical utility of the Coombs test¹ prompts consideration of the pitfalls of a negative test result. Specifically, further evaluation will be required if a patient with clinically significant hemolysis has a negative result on Coombs testing.

A negative result on the direct antiglobulin test (DAT) may occur if there are low-affinity antibodies coating the erythrocyte surface that are removed in the washing process or by prior use of corticosteroid therapy. IgG antibodies and C3d complement are detected by the DAT; however, IgM and particularly IgA antibodies may not be detected by the polyclonal anti-human-globulin serum. Therefore, DAT using anti-IgA or anti-IgM antibodies may be required if the results of DAT with anti-IgG antibodies do not correlate with the clinical manifestations. Patients whose erythrocytes are coated with multiple immunoglobulins will have severe hemolysis and may need intensive therapy with immunosuppressive agents² or even splenectomy.³

At a major immunohematology referral centre in the United Kingdom, 124 of 5235 patients had warm-reactive elutable IgA antibodies and of these, 6 had only IgA autoantibodies coating erythrocytes.⁴ It is known that IgA complexes can activate the alternative pathway, causing complement activation. Therefore, measurement of com-

plement components C3 and C4 could prove useful in some situations. Splenic sequestration of IgA-sensitized erythrocytes may occur, and in-vitro analysis has shown that monocytes are involved in hemolysis of the sensitized erythrocytes.⁵ Naturally occurring antibodies of the IgM isotype, which bind complement and autoantibodies of this class, occur in conjunction with anti-IgG and or anti-IgA immunoglobulins. In-vivo autoagglutination of IgM antibodies can lead to multiorgan failure and is usually associated with a high mortality rate.⁶ Sokol and colleagues⁷ described 2 patients with only IgM autoantibodies who had chronic hemolysis, one of whom required splenectomy.

It is important that clinicians be aware of the limitations of biological tests and investigate further when a patient with severe hemolysis and organ involvement has a negative Coombs test result.

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REFERENCES

1. Zarandona JM, Yazer MH. The role of the Coombs test in evaluating hemolysis in adults. *CMAJ* 2006; 174(3):305-7.
2. Sokol RJ, Booker DJ, Stamps R, et al. Autoimmune hemolytic anemia due to IgA class autoantibodies. *Immunohematology* 1996;12(1):14-9.
3. Bardill B, Mengis C, Tschopp M, et al. Severe IgA-mediated auto-immune haemolytic anaemia in a 48-yr-old woman. *Eur J Haematol* 2003;70(1):60-3.
4. Sokol RJ, Booker DJ, Stamps R, et al. IgA red cell autoantibodies and autoimmune hemolysis. *Transfusion* 1997;37(2):175-81.
5. Clark DA, Dessypris EN, Jenkins DE Jr, et al. Acquired immune hemolytic anemia associated with IgA erythrocyte coating: investigation of hemolytic mechanisms. *Blood* 1984;64(5):1000-5.
6. Friedmann AM, King KE, Shirey RS, et al. Fatal autoimmune hemolytic anemia in a child due to warm-reactive immunoglobulin M antibody. *J Pediatr Hematol Oncol* 1998;20(5):502-5.
7. Sokol RJ, Booker DJ, Stamps R, et al. Autoimmune hemolytic anemia caused by warm-reacting IgM-class antibodies. *Immunohematology* 1998;14(2):53-8.

DOI:10.1503/cmaj.1060049

Promotion of traditional lifestyles

Jeff Reading discusses some of the work being done to understand and alleviate the problem of diabetes among Aboriginal people in Canada.¹ Although the risk factors associated with diabetes and hypertension within Aboriginal communities are now reasonably well understood, the prevention and control of these conditions are not straightforward. Genetic factors alone cannot explain the prevalence of these conditions; rapid changes in lifestyle leading to unhealthy diets and physical inactivity, now widespread in Aboriginal communities, are also involved.

There is a lack of trained community health workers, nutritionists and health educators who understand the cultural heritage of Aboriginal communities and their peripheral services. This must be remedied before effective diabetes programs can be developed.

Implementing proven behavioural interventions,² especially those involving weight management, requires resources that take into account Aboriginal language, customs and cultural references. Furthermore, the problems of obesity and diabetes must be addressed in the context of the lifestyle "choices" available in Aboriginal communities. The promotion of exercise (as opposed to productive physical activities) is questionable if people do not have access to and cannot afford sports and recreational facilities.

The "best evidence" approach to the prevention and control of diabetes in Aboriginal populations must be comprehensive and multidisciplinary, taking into account not only biophysiological and lifestyle influences but also the politico-economic environment and social structures. Politico-economic policies and social structures conducive to healthy lifestyles must be ranked above health promotion and pharmaco-