Objective: Autism is a neurodevelopmental disorder with unknown etiology. The etiology of autism is complex, and the underlying pathologic mechanisms are unknown. This study tests the autoimmune mechanisms in the pathogenesis for autism in autistic children.

Methods: The study took place in the Riyadh area of the Kingdom of Saudi Arabia between September 2003 and April 2004. Sixty-five autistic children, with a confirmed diagnosis according to E-2 diagnostic criteria for autistic spectrum disorders, participated in the study. Serological examination of antibodies to measles, mumps, rubella (MMR), and myelin basic protein (MBP) was carried out in autistic and control children.

Results: The level of MBP antibodies was significantly higher in autistic children as compared to controls ($p<0.01$). Furthermore, the level of antibodies to measles but not mumps or rubella was significantly higher in autistics compared to the control group ($p<0.05$). Moreover, 82% of autistic sera positive for measles IgG was also positive for MBP.

Conclusion: The current study supports the hypothesis that autoimmunity plays a role in the pathogenesis of autism. However, results from the current study are not enough to support that immunization by MMR is playing a role in the autoimmune process in autism.

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immune response may play a causal role in autism in the Riyadh area in Saudi Arabia. Keeping in view the literature available, we conducted the present study to determine the serological response of 3 viruses, MMR, and an antibody against the brain, myelin basic protein (MBP), exploring a possible correlation between MMR and MBP.

Methods. The study was conducted in the Department of Physiology, Faculty of Medicine, King Saud University, Riyadh, Saudi Arabia between September 2003 and April 2004. Sixty-five children, age up to 14 years old, with confirmed professional diagnoses were selected. The diagnosis was carried out either by a qualified psychologist, psychiatrist of neurologist, according to diagnostic criteria E-2.9 A written consent was obtained from their parents prior the start of the study, and then the parents were asked to fill a questionnaire regarding child’s medical and behavioral history. Healthy age and sex matched control volunteers were recruited from King Abdul-Aziz University Hospital. Blood samples were collected by venipuncture in plain tubes, and after gentle mixing were allowed to clot at room temperature, and then centrifuged at 1,500 g for 10 minutes. Then serum was collected and stored at –70°C until assay time. Samples were assayed in a single large batch, in duplicate. None of the children recruited in this study had any history of measles rash or wild type measles infection, but all have had their MMR immunization. Anti-measles, anti-rubella and anti-mumps were measured by a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Dade-Behring, Marburg, Germany). Anti-myelin basic protein (anti-MBP) was measured by a commercially available ELISA kit (Diagnostic Systems, Texas, USA). The results were analyzed using SPSS for windows and expressed as percentage. A statistical analysis for differences among the groups was assessed by t-test. P values equal to or less than 0.05 were considered significant.

Results. Sixty-five autistic children with confirmed diagnosis (61 males and 4 females) participated in the study. The mean age for the total number of autistic children participated in the study was 8.2±0.5 years, with 61 (93.8%) males and 4 females (6.2%). The male to female ratio was 17.2:1. In 40% (26) of the autistic children, the parents think that the autistic symptoms started following immunization. As Table 1 demonstrates, 32% (21) of the autistic children’s sera, and 35% (23) of the control sera were positive for mumps IgG antibody (not significant, p<0.7). Furthermore, 31% (20) of autistic children sera, and 28% (18) of control sera were positive for rubella IgG antibody (not significant, p<0.7). However, 51% (33) of autistic children’s sera, and 18% (12) of control sera were positive for measles IgG antibody (significant, p<0.0001). In addition, 54% (35) of autistics sera, and 9% (6) of control sera, were positive for MBP antibody (highly significant, p<0.0001). Moreover, 82% (27) of autistics sera positive for measles IgG were also positive for MBP (correlation r=0.71). In contrast, only 8% (1) of control sera positive for measles IgG antibodies are also positive for MBP IgG antibodies (correlation r=0.2). Highly significant results (p<0.0001) for percentages of simultaneous positive IgG for measles and MBP between autistic children and control. It is interesting to note that, 20% (13) of autistic sera were positive for mumps, measles and rubella IgG. Almost the same results were reached with control sera, 18% (12) of control sera were positive for mumps, measles and rubella IgG.

Discussion. Autism is a neurodegenerative disorder with unknown etiology. Several theories have been suggested by scientists, in an attempt to reach a causal factor in the genesis of the disease. An autoimmune reaction of the body, against brain cells, in response to infection or immunization, has been suggested. The current study demonstrates the presence of an autoimmune process in the body against the MBP, through the presence of significant levels of IgG to MBP. Moreover, the current study demonstrated a positive correlation between measles antibody and MBP antibodies in autistic children as compared to healthy control children. The result of this study is in agreement with Singh et al.3-7,10

Brain autoantibodies to MBP (anti-MBP) and neuron-axon filament protein (anti-NAFP) have been found to be significantly higher in autistic children when compared to controls.6 Singh et al.6,11 examined the association between virus serology and autoantibody by simultaneous analysis of measles virus antibody (measles IgG), human herpes virus-6 antibody (HHV-6-IgG) and anti-NAFP. They found that measles-IgG and HH-6-IgG titers were moderately higher in autistic children. In addition, they found that a vast majority of virus

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<th>Antibody</th>
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<th>Control children</th>
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<tr>
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<td>n (%)</td>
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<tr>
<td>MBP</td>
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<td>Measles</td>
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<td>Rubella</td>
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serology-positive autistic sera were also positive for brain autoantibody. Furthermore, researchers have drawn the link between the vaccines and demyelination, concluding that any vaccines can lead to inflammatory reaction involving the nervous system.12

Immunological testing of autistic children has shown certain features that are also found in patients with autoimmune disease such as systemic lupus erythematosus, thyroid disease, ankylosing spondylitis, and rheumatoid arthritis. This feature includes, genetic predisposition, autism shows a greater concordance rate in monozygotic twins than in the normal population. In addition, gender factor plays a role, autism is 4 times more common in boys than in girls. Moreover, autism might be triggered by microorganisms, rubella virus and cytomegalovirus infections have indirectly linked to autism. The parallels between autism and autoimmune disease suggest that autoimmunity may be a critical factor in the causes of autism. Since autoimmune diseases are common in our area as compared to the western world, it is likely that the ranking orders of etiological factors of autism are different in those 2 parts of the world.5,6,10,14

Accumulating evidence suggests that autoimmunity plays a key role in the pathogenesis of autism. The fact that autistic patients respond well to treatment with immune modulating drugs strengthens the idea that autism is an autoimmune disorder.15,16 Autistic children do have immune abnormalities and therefore, depending on the nature of the immune abnormality, the goal of immune modulating therapy should be to normalize or reconstitute the immune function. This will permit a more balanced immune response, avoiding major fluctuations of overt immune activity that could be risky.

Wakefield et al.17 demonstrated a possible link between MMR vaccination and autism. Then in 2004, these findings were retracted by Wakefield and his group through an article published, ruling out the possible link between vaccines and autism.18,19 Despite that, several scientists demonstrated a possible link between viral infection, vaccination and the autoimmune factor in the genesis of autism,2,6,10 which cannot be ignored from a scientific point of view.

The main outcome of this study is, first, the presence of statistically significant levels of MBP antibody in autistics as compared to controls, supporting an autoimmune basis in the development of autism in those children examined. The second result is the highly significant correlation between IgG measles antibody and IgG MBP antibody in autistics as compared to controls. From our point of view, this correlation on its own is not enough to support the hypothesis that a virus induced autoimmune response (through measles vaccine) may play a causal role in autism. Both outcomes need to be investigated further.

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References