Autism Spectrum Disorder, Genetics and Remedial Solutions

The recent joint announcement by the Wellcome Trust and Rett Syndrome Research Foundation on the discovery of the remedial effect of Tamoxifen on the symptoms of Rett Syndrome in a genetic mouse model raises a number of interesting points.
The discovery that administering the drug Tamoxifen to mice "switched on" the MECP2 mutated gene, and reverses the brain damage that gives rise to the symptoms of the condition known as Rett Syndrome. Rett Syndrome is recognised as one condition of many associated with Autistic Spectrum Disorder, children on this spectrum suffer lack of speech have unusual movement e.g. tip toe walking and lack fine motor control as well as associated learning delay.
The reversal experiments were carried out, using technology known as Cre-lox recombination. This reombination is a method to introduce transgenes into specific, single, defined sites within the mammalian genome to recreate a genetically reproducible environment for the study of expression of introduced transgenes.
In the virus bacteriophage P1, is an enzyme called Cre and particular DNA sequences called lox P sites. The lox P sites work in pairs and flank a segment of DNA called a target. When the Cre enzyme binds to the lox P sites, it cuts the lox P sites in half and then splices together the two halves after the target DNA has been removed and degraded.
In this study mouse models were created, in which the gene MECP2 was silenced by inserting a Stop cassette into the gene, creating the neurological deficits exhibited by Rett Syndrome. Removing the Stop cassette with the use of Tamoxifen could reverse the silencing, which stimulated the Cre enzyme to enter the cell nucleus where it could splice out the Stop cassette.

In several previously published articles in (this) www.theautismcentre.co.uk web site referring to the Etiology of the Autism Spectrum Disorder, reference has been made to the part played by various exogenous agents on the development of the fetus in utero.
The agents identified as playing a major role in events leading to early miscarriage, premature birth, and subsequent onset of conditions displaying mobility, behaviour, and learning difficulties are listed by various organisations as alcohol, nicotine, viral and bacterial infections e.g. rubella in the case of cerebral palsy.
The organisation associated with Fetal Alcohol Syndrome at their recent conference has called for a notice to be added to the labeling of alcohol containing drinks warning of the consequences of alcohol intake during pregnancy. Smoking is universally accepted as cause of neurological dysfunction, resulting from central nervous system cell damage, and many articles have been published linking bacterial and viral infections to similar outcomes.
In case of infections during pregnancy, it appears that the ease at which pregnant mothers contract the illness, may be due to reduced immunity, as a result of increased age, or possibly, as some research shows, that, one of the outcomes of neurological dysfunction, is reduced immunity. Autistic children are subject in early life to regular bouts of middle ear and upper respiratory tract infections.
It is universally recognised, that, the ingestion of products produced by smoking will lead to the cancer of the respiratory system through cellular and genetic mutations, and, on the basis a link is formulated between Stop cassettes, and the ingestion of exogenous agents described above, then we have found the link to those products and cellular and genetic mutations, which lead to the onset of Autism Spectrum Disorders.

Autistic Spectrum Disorder (ASD) is characterized by a systemic array of symptoms that has fascinated and frustrated researchers since its description over fifty years ago. The disorder has been responsible for prolific research as through the passage of time and experience the universally current view evolved from the psychological realm to the biochemical. Studies of neurochemical, neuroanatomical, immunological, genetic, neuropathological, metabolic, and pharmacological involvement, have revealed the prevalence of over fifty biochemically, genetically or metabolically associated disorders with autism.
The autistic spectrum disorders are described in the DSM-IV (Diagnostic and Statistical Manual) under "Pervasive Developmental Disorders" (FDD): Autistic Disorder (AD), Rett's Disorder (RD), Childhood

Disintegrative Disorder (CDD), Asperger's Disorder (AS) and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS).

The diagnostic criteria for the autistic spectrum disorders are extensive. The diagnostic criteria leads one to believe that autism is of psychological origin. The autistic spectrum was, in fact, originally incorrectly categorized as psychiatric and subsequently treated with therapies oriented to emotional disorder. Autism is not a constitutive disorder that is solely and statically genetic in nature, but rather may involve acquired deficits due to exposure in perinatal, prenatal or in the first few years of development to pathogens, toxins, and/or electromagnetic radiation creating systemic alterations on a cellular level mimicking a broad scope of disturbed metabolics with immune, central nervous system, gastrointestinal and endocrine involvement. Rather than the struggle of medical research focusing on the classification of a disorder when extensive overlapping of many disease states co-exist within autistic disorder, one is led towards the concept that expression of genetic disease states may be induced as is currently gaining ground in the literature. As judgment often exists that a genetic disorder is unapproachable, treatable only through gene therapy we must move beyond this limited concept.... To approach the depth of complicated disorders the blending of the sciences such as psychoneuroimmunology, neuroendocrinology, immunogenetics arose and therefore more individualized metabolic needs may be addressed. A merging of the sciences is ***paramoun****t* in grasping the complexity of autistic spectrum disorder, and should no longer be categorized or treated as a psychiatric condition.

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