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Serendipitous Observations and Theory

Relevant To Autism

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Autism Revisited:

Serendipitous Observations and Theory Relevant To Autism

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Introduction:

Perhaps the most divisive issue in the history of medicine has been the cause of autism. Thousands of parents continue to affirm that their children became autistic shortly after immunization with the MMR vaccine. Statistical studies however, claim to the satisfaction of the majority of the scientific community, that there is no such relationship(1). This paper, representing over 20 years of study, offers a new theory based on experimental evidence, subject observation and published scientific research. The highly controversial (and presently refuted) relationship between measles vaccine and autism, has never been experimentally testable. This research may offer the opportunity to perform reasonable medical tests to effectively confirm or deny a relationship between measles vaccine and autism.

Abstract:

It is hypothesized that the measles N protein component of the measles virus, chronically interferes with a specific homeostatic mechanism that provides balance between metabolic and immune function, resulting in autism. First, congenital metabolic diseases or risk factors, produce Primary Local and ContinuingSuppressions of enzymatic and immune

functions. Critical among these risk factors is extremely low or non-existent secretory IgA. Second, the overall cellular homeostatic environment is then severely effected by Global and Transient Metabolic and Immune Suppressions from the measles vaccination. Third, the combination of severe immune/enzymatic suppressions from the measles virus, severely reduced IgA, and other CMD's, allows opportunistic infections to flourish, which support secondary immune and enzyme suppressions. Finally, all these suppressions produce a severe intracellular messenger-metabolite flux reduction, which allows the measles N protein freedom to interact, and interfere with, the eukaryotic initiation factor eIF3P40. eIF3P40 is joined to the eukaryotic initiation factor eIF4E through an eIF4G linkage. Theoretically, this would create a severe dysregulation in the eukaryotic initiation factor eIF4E, which has been observed in autistic children, and associated with autistic behavior in animal studies. The severe repressions from reduced IgA and other CMD's, immune repression from opportunistic infections and consequent and continuing measles virus latency, results in an ongoing inability to achieve homeostasis between metabolic functions and immune functions. This manifests as autism. Three tests of this theory are possible. First, treatment with human derived measles N protein specific secretory immunoglobulin A, which is capable of neutralizing the interference. Theoretically, such a test/treatment would restore homeostasis, with a gradual improvement of the autistic condition. Second, it is proposed that if measles N protein specific IgA is properly administered concurrent to infant measles vaccination, few if any cases of autism should be observed, while still providing protection against measles. Third, immunization of the mother with MMR vaccine and subsequent immunization of the child during concurrent breastfeeding. Theoretically, children could then receive sufficient measles specific secretory IgA via breast milk with few if any cases of autism (or measles) observed. If correct, these tests could provide empirical evidence of an indirect relationship between autism and measles virus/vaccination.

Experimental Observations:

Author's disclaimer: The following observations are not A safe viable treatment for autism! No parent should attempt to use *Saccharomyces cerevisiae* and/or soy milk to treat their child's autism! You will endanger your child! You will harm your child!

Observed subject is author's son.
There are no conflicts of interest.

0.3 grams of living *Saccharomyces cerevisiae*, a common brewers yeast obtained from LALVIN(2), identification code

K1-V1116, was mixed with 150 ml of sterile water to form a suspension at room temperature. 10 -30 ml of this suspension was administered on an empty stomach, to regressive 68 kilogram male autistic teenager X, resulting in significant improvement in autistic behavior and vocalizations within 30 - 45 minutes. *S. cerevisiae* enhances phase II enzyme production, while inhibiting the Th2 component of the immune system(3). Higher suspension concentrations or doses at first offered similar improvement, but eventually produced a worsening of autistic symptoms and vocalizations. 15-40 ml of a non-diluted non-sugared basic soymilk preparation, brand name "SOY SILK"(4), was administered at the start of these worsening phases, with dramatic improvement observed within 30 minutes. Soy milk enhances the Th2 component of the immune system, while inhibiting phase II enzymes(5). On separate occasions, 15-30 ml of soy milk was administered alone, on an empty stomach, to teenager X, with similar improvement observed within 30 - 45 minutes. Higher doses of soy milk were administered with autistic improvement, then worsening, and again, corrected with 10 - 25 ml of the *S.cerevisiae* suspension.

Subtle changes in autistic behaviors, vocalizations and physical response (herein referred to as "symptom clusters"), determined treatment choice. Enhanced autistic mannerisms with wet hands and poor and reduced verbal ability, one symptom cluster, necessitated *S. cerevisiae*. Soy milk was required for enhanced autistic mannerisms with intense lip licking, dry hands and animated verbalization, another unique symptom cluster. Each particular symptom cluster was exacerbated or reduced by *S. cerevisiae* or soy milk, as stated. These observations provided evidence that two different symptom clusters could exist within the same autistic individual. Based upon the inherent and opposing properties of Soy milk and *S. Cerevisiae*, these unique symptom clusters, may provide indirect evidence for a Th2 immunity/phase II enzyme imbalance related downstream to autism, in teenager X.

note: Published research has shown that autistic children have a dysregulation of Th1 and Th2 transcription(59) with a Th1/Th2 imbalance toward Th2(95).

Discussion:

In rare instances, a temporary balance between the TH2/Th1 and phase II/phase I systems using soy milk and *S. cerevisiae* suspensions, was achieved in teenager X for 15 - 20 minutes. Only residual autistic behavioral abnormalities were observed. These residual autistic characteristics may be resultant from the long term consequences of metabolic and immunological imbalance on the autistic child's brain and blood flow to the brain(6).

Attempts to replicate these results with commercially obtained *Saccharomyces boulardii* were unsuccessful. No changes at similar dosages were observed. This raises a serious question: Why were there no immunological or enzymatic changes observed with *S. boulardii* usage? *S. boulardii* and *S. cerevisiae* are nearly identical(7). Both can alter the Th1/Th2 immune and phase I/phase II enzyme balance(8). The difference may lie in the fact that *S. cerevisiae* has greater gene copy and chromosomal numbers. Specifically, *S. cerevisiae* has far more retrotransposons(8)(9).

Retrotransposons also called Ty elements in *Saccharomyces cerevisiae*, are DNA sequences that can regulate gene expression and transpose via RNA in a host cell(10). They are similar to retroviruses. In particular, they function as enhancers or promoters by neutralizing a host cell's gene inactivation(11)(12).

The observation that only *S. cerevisiae* effected change, appears to indicate that in autism, some mechanism(s) involved with phase II enzyme production are inactivated. This inactivation, prevented *S. boulardii* from naturally enhancing phase II enzyme production, while reducing a Th2 response. Since both systems appear impaired, and they balance against each other, it is therefore reasonable to conjecture that the actual site of impairment may lie between them, at some point of homeostasis.

There are multiple interacting mechanisms involved with maintaining cellular homeostasis between the Phase II/Phase I enzyme system and the Th2/Th1 immune system(13)(14)(15) (author's note: the listed references barely touch upon the complexity and number of interactions between metabolism and the immune system.) The observations presented here offer the possibility that one of these homeostatic mechanisms may be partially compromised in teenager X, with autistic symptoms a downstream effect.

Additional observations of teenager X offer further evidence for this theory. Upon arising in the morning, with no food consumption for 8 hours, teenager X characteristically exhibited few autistic symptoms, and was at his best. As food was consumed, more autistic behaviors emerged. With larger nutritionally complex meals, autistic severity increased dramatically. Since as stated, several mechanisms contribute to cellular homeostasis, inhibition of one mechanism, during normal food consumption, may temporally overwhelm homeostasis, producing the observed effects. When small, well spaced "meal snacks" were consumed rather than regular size meals, behavior and cognition remained more stable. Behaviors also severely deteriorated after inhalation of diesel fuel oxidation products(16), or drinking plain water accidentally allowed to sit in warm commercial plastic bottles(17). The airborne oxidation byproducts as well as the "leached out" plastic bottle residues

appeared to overwhelm the normally adaptive homeostatic system(s), producing a severely autistic response.

Experimental evidence of such changes exist. Chang(2018) et al. was able to induce autistic-like behaviors in mice exposed to diesel fuel oxidation fumes(18).

Commonly observed biological responses in autistic children can also be explained using this theory. Increased autistic response from intake of high phenol content foods is one example (19). Reduced levels of the phenol sulfotransferase enzyme which processes phenolic compound foods is often found in autistic children(20). A functional reduction in these enzymes and others, would be expected under this theory. Reduction in digestive enzymes have been observed in autistic children(21). Teenager X also suffered adversely when high phenol content foods were consumed.

Reported food and other allergies in autistic children(23) may also be redefined as a failure of homeostasis. According to this theory it may occur in two ways:

The processing of endogenous or exogenous substances for assimilation, breakdown or elimination (food, hormones, smoke, etc.) requires two types of enzymes: phase I enzymes and phase II enzymes(21). Phase I enzymes (cytochrome P450 enzymes) begin the process by enzymatically activating these substances, making them more polar(22). This process however, also makes them more toxic, especially for brain and liver function and more available for immune system activation. Phase II enzymes essentially makes these substances water soluble (and significantly less toxic and less immunogenic), which allows for (as stated) their breakdown, integration into the body, or elimination(21). However, when phase II enzymes are diminished, via homeostatic failure, these activated substances can provoke a strong "innate" immune response along with their stated toxic effects(23). The end result is the increase in observed autistic behaviors.

Second, as these activated substances continue to appear in the circulation, their short term toxic and immunological effects become exacerbated by the formation of long term memory cells, and antibody production in a "specific" immune response directed at dietary proteins(23) (24)(57). This increases the "allergy-like" response, via enhanced levels of mediators of inflammation such as histamine, IgE and leukotrienes(25).

As would be expected under this theory, reduced concentrations of anti-inflammatory cytokines, as well as the increased concentrations of pro-inflammatory cytokines are observed in autistic children(25)(26). Autistic symptom severity has been associated with increased levels of pro-inflammatory cytokines(27).

This long term immunological/metabolic dysregulation can

also cause severe reduction to blood brain flow (28)(29). This blood flow reduction would limit the availability of nutrients and oxygen to the brain. It would also produce a build up of toxic metabolic byproducts in neural tissues. The consequences would be the abnormally high neural cell death, disrupted inter-neuronal connections, and enhanced levels of neural autoimmune antibodies, that is observed in autism(30)(31)(32).

Neural autoimmune antibodies are produced in the brain to assist in the removal of dead and dying neural cells. These autoimmune antibodies would be produced as a normal response to neural cell death and injury, and not as a cause of autism as has been suggested in published literature(33).

As mentioned, autistic children are often found to have reduced blood brain flow associated with immune dysregulation, resulting in neural cell death(28)(29). Simultaneous to this increased neural cell death and the related immune response, would be the enhanced neural cell growth and differentiation that occurs in the developing child's brain(34). These two competing forces could easily produce the gross and subtle morphological differences observed in the autistic child's brain(35)(36). These observations detract from the theory that autistic brain morphology has a purely genetic origin (37)(72)(91).

*A special note about autism and testosterone in boys at puberty. Male children tend to be more adversely affected by autism than females(38)(39). While testosterone is a vital part of male maturation in boys, it is also neurotoxic(40)(41). Delayed processing by phase II enzymes, as would occur in this theory, would increase testosterone metabolic half-life as well as increase its neurotoxicity(22). This may provide a partial explanation for puberty related autistic regression observed in males, and also observed in teenager X.

A Theory For Treatment A Test Of Theory:

As noted previously, any relationship between measles vaccine and autism has been statistically refuted. The following theory and test may produce results counter to that conclusion or offer further support.

Multiple interacting homeostatic mechanisms exist to balance between the Th1/Th2 and phase I/phase II systems. One such site to maintain homeostatic balance is eukaryotic initiation factor 3 (eIF3) complex, which contains the eIF3p40 eukaryotic initiation site(14)(15).

Eukaryotic initiation factors (eIF) are post-translational proteins or protein complexes that regulate the physical expression of gene directed cellular products(42)(43).*

*The process begins with the transcription of genes from the DNA template in the nucleus into RNA via the enzyme RNA polymerase. After additional processing, the formed RNA strand representing at minimum one gene, can exit the nucleus into the cytoplasm via a nuclear pore. The RNA strand (template) is translated into cell products (for example an enzyme) via ribosomes or the endoplasmic reticulum in the cytoplasm. Cell product formation as stated, is regulated by the eukaryotic initiation factors(44)(45).

The initiation site, eIF3P40 can be blocked by the N protein of the measles virus (49). Autistic children suffer from dysregulation of the local eIF4E translation initiation factor(47). The eIF4E initiation site and eIf3p40 initiation site are associated via eIF4G, which performs a bridging function(48). It is reasonable to conjecture that the blocking of one initiation factor can influence another associated adjacent initiation factor, and interfere downstream with TH2/TH1 and Phase II/Phase I homeostasis. This eIF4E dysregulation has been associated with autistic behavior in animal models(46) (see below).

This hypothesis has experimental evidence. Santini E et al in "Exaggerated Translation Causes Synaptic and Behavioral Aberrations Associated With Autism" (Nature 2013) produced autistic-like behavior in transgenic mice by altering translation levels in the eIF4E initiation site. They were then able to reverse the autistic-like behaviors:

"by reducing eIF4E/eIF4G interactions, thereby restoring homeostasis."(46)

The hypothesis that autism in humans is caused by initiation site dysregulation may be testable in humans by employing human derived secretory IgA* specific to measles N protein (87).

*Immunoglobulins or antibodies (IgA, IgG, Ig D,Ig M and Ig E) are glycoproteins produced by B cells in response to, and that combine with, foreign substances or antigens (50).

*Secretory IgA is formed when the dimeric form of IgA is bound to a secretory component, which protects it against proteolysis. It's sources include breast milk, saliva, and intestinal secretions(56). It is unique among antibodies/immunoglobulins in being able to function intracellularly(50).

Autistic children are routinely found to have subnormal secretory IgA levels, yet elevated non-IgA immunoglobulin titers(51)(52)(55). This contrasts drastically with normal

measles infection or immunization, which produces large increases in measles specific IgA in children (54). Secretory IgA can penetrate infected human cells, and directly neutralize specific viral sub-components. This is accomplished via the:

"three defense functions of immunoglobulin A (IgA)
immuno-exclusion, intracellular neutralization, and
virus excretion" - Yan et al, 2002(53)(summary quote)

Secretory Immunoglobulin A specific to measles N protein may be obtained by administering purified measles N protein, derived from standard measles vaccine type strains, to healthy human volunteers. Over an immunologically limited time period*, purified secretory IgA specific to measles N protein could be obtained, then administered to a severely autistic test subject. If this conjecture is correct, measles N protein specific secretory IgA could neutralize the interference and restore the affected homeostatic mechanism. Long term neutralization might be achievable by maintaining human derived measles N protein secretory IgA at levels equivalent to physiological norms for an unspecified time period. Empirical evidence of success could be obtained via enzyme and immune studies. Behavioral and vocalization improvement should also be demonstrable.

*"An immunologically limited time period" refers to the half-life, storage life, refrigeration needs, etc, required to maintain the efficacy of secretory IgA prior to successful administration. There are also time constraints between administration of the measles N protein to the volunteer and collection of sufficient and biologically active measles N protein specific secretory IgA(58).

Special Note:

The question arises as why not simply give secretory IgA specific to several or all measles proteins? Based on the research and observations stated, the key secretory IgA in relation to correcting the homeostatic dysregulation, is specific to the N protein. Additional secretory IgA's specific to other measles virus protein components could potentially be very helpful, but would require other technologies still in development. Research is presently being conducted on plant based production of specific secretory IgA's, which shows great promise(61). Should such technology mature sufficiently, a safe and efficacious "soup" of measles protein specific secretory IgA's may one day be possible. Admittedly, such a treatment could be potentially superior (62)(63).

Strong caution however, would need to be observed should

such testing be attempted. The possibility of a strong physiological response as the immune and enzyme systems reassert themselves after long term imbalance is a possibility. This concern is not without precedent. Autistic children treated for chronic Candida infections with antifungals or Transfer Factor, often experienced a temporary worsening of their autism during the "die off" phase before noticeably improving(60). Minimal dosage of the human derived measles N protein specific secretory IgA at start, with a gradual increase under strict medical supervision would be strongly recommended.

Measles N protein specific human derived secretory IgA could either offer a viable autism treatment option(94), or offer biological rather than the contemporary statistical evidence against the theory that measles is involved with with autism

Dicussion Addendum One:

The Combined Effects Of Non-measles Local and Continuing Suppression With measle's proteins Global and Transient Suppressions

Based on previous observations and published research, measles vaccination alone is clearly insufficient to result in autism without some other predisposing factor(s). This is reasonable in that if a measles vaccine alone could produce autism, far more immunized children would become autistic. This is clearly not the case, as referred statistical studies demonstrate(1). However, if such a relationship in any form exists, Local and Continuing Immune and Enzymatic Suppressions, may provide the theoretical predisposing factors.

These Local and Continuing Suppressions of various enzymatic mechanisms and immune systems, could be developmental, genetic, environmental, iatrogenic, microbial (viral, fungal or bacterial) or some combination. Specific combinations could reflect upon the differing severities, the incidence of autistic regression, and recovery from autism. These are commonly referred to as "risk factors" for autism(64)(3)(6)(16)(18)(37)(40)(70)(68)(67)(69)(96)(105)(106).

Examples of risk factors, include the long list of "inborn errors of metabolism", in which genes that code for certain enzymes/gene products are not functioning properly or at all(105). Also referred to as congenital metabolic diseases (CMD's), these diseases are noted for frequent co-morbidity with autism(105)(106).

Some examples of CMD's include:

severe immunoglobulin A deficiency(94)	autism assoc.
carnitine biosynthesis errors(97)	autism assoc.
phenylketoneuria(98)	autism assoc.
fragile X-syndrome(96)	autism assoc.
cerebrotendinous xanthomatosis(99)	autism assoc.
long chain fatty acid errors(100)	autism assoc.
propionic acidemia(102)	autism assoc.
adenosine deaminase deficiency(105)	autism assoc.
glucose-6-phosphatase deficiency(105)	autism assoc.

Note: While each individual CMD can be uncommon, there are hundreds known(105)(106), and an unknown number yet to be discovered. The total percentage of autistic children who have any or several CMD's is Evidence for CMD involvement in autism is demonstrated by the autistic children whose symptoms have been significantly modified by various supplements to ameliorate the particular deficiency(104).

additional risk factors include:

poor nutritional status(103)	autism assoc.
candida infection(107)	autism assoc.
environmental pollution(108)(110)	autism assoc.
viral infections(109)	autism assoc.
premature/low birth(weight)(101)	autism assoc.
fetal valproate exposure(105)	autism assoc.
hyperbilirubinemia(121)	autism assoc.

Further evidence for risk factors, and the resultant Local and ContinuingSuppressions, can be derived from the succeeding History section in regard to teenager X.

Theoretically, these deficiencies as a whole, could be represented in a biophysical sense, as reductions in the intracellular messenger-metabolite flux(see below).

Local and Continuing Suppressions as represented by risk factors or CMD's, could theoretically provide the first level of suppression of the intracellular messenger-metabolite* flux**, which occupies the intracellular fluid between the attacking measles N protein, and the eIF3P40 initiation site. This flux, when functioning normally, would theoretically prevent the measles N protein from dysregulating the eIF3p340 initiation site.

*Intracellular messengers and metabolites includes all transcriptional-translational products. These

provide continuous communication between the nucleus and organelles in the cytoplasm(43)(44)

**"Intracellular messenger-metabolite flux" refers to the millions of metabolic communications flowing back and forth within the cell in a millisecond. These communications keep the cell alive and in homeostasis. Any interference between a particular messenger or metabolite and its site of destination, is also called steric hindrance(84).

The second level of intracellular messenger-metabolite flux suppression would be conducted by the proteins of the measles virus (along with the measles N protein). The measles virus proteins, produce profound global and transient down-regulation of cellular products(113)(114)(117)(119), originating from the cell's "housekeeping genes"*.

*"Housekeeping Genes"(120) provide basic cellular maintenance that keeps the cell alive and functioning normally. They constitute the majority of genes in the nucleus. Among the many genes coded for, are those for transcription and translation factors, tRNA synthesis, ribosomal proteins, and genes of metabolism. All these genes contribute to the intracellular messenger-metabolite flux.

The measles virus as a whole consists of the Large protein(L protein), Nucleoprotein (N protein), Phosphoprotein(P protein), Matrix protein (M protein), Fusion protein(F protein), Hemagglutinin protein (H protein), V protein, C protein and RNA(49)(112)(74)(116)(115).

Specific examples of measles protein inhibitions include;

N protein - local inhibition of homeostatic regulation via the eIF3P450 initiation site and inhibition of secretory IgA(49)

V protein - interferon signaling inhibition(112), suppression of NF-kB transcription factor(65)

M protein - global (various sites) inhibition of host cell transcription(74)

P protein - Type 1 interferon inhibition, inflammatory response suppression(116)

C protein - Beta interferon transcription inhibition(115)

A third level of immune/enzyme suppression that could occur would be caused by opportunistic infections occurring as a result of suppressions by measles virus, low secretory IgA alone, and other CMD's(145)(146). These infections can exert their own repressions on immunity and/or enzyme function.

In this theory, as a result of these immune and enzymatic

product suppressions, and further suppressions from opportunistic infections, the normal levels of intracellular messenger-metabolite flux could be reduced to a critical level. This steric hindrance which stands in the way of the measles N protein, when severely reduced, allows the eIF3P40 eukaryotic initiation site to be vulnerable to attack by the measles N protein*.

*Like the archer that can't hit the target because of multiple flocks of birds rapidly flying back and forth between him and his goal, the strong reduction of the bird flux, lets the archer score a bulls eye.

This theory enables inclusivity for the extremely broad and varied risk factors associated with autism. Any risk factor which reduces intracellular messenger-metabolite flux, or reduces the immune response, increases the risk of measles virus N protein interference.

Theoretically, this sequence of events of Local and Continuing Suppressions from CMD's (especially secretory IgA deficiency), Global and Transient Suppressions by the measles virus, growth of opportunistic infections (example candida), and initiation site specific suppressions, could also set in motion the process for measles virus latency.

Published research has clearly demonstrated that the measles virus can achieve latency(75)(76)(79)(80)(81). The measles virus can establish its genome into the host cell nuclei via reverse transcriptase(77)(78). The latent measles genome then continues to produce N protein, which suppresses IgA, etc. Proof of this in autistic children, is the vastly reduced or lack of secretory IgA antibody, yet increased production of non-IgA antibodies to measles virus, years after immunization(83).

A theoretical final stage of autism may be reached by those individuals who eventually suffer from severe regressive autism. Should a latent measles infection spread to stem cells, then viral proliferation would occur along with these cells(81). Viral latency can cause immune dysfunction via long term viral reservoirs that are non-infectious.(128) Puberty with its growth and maturation spurts has been associated with severe regressions in some autistic individuals(73)(90). As previously noted, for males entering puberty, the potent addition of neurotoxic activated testosterone would only exacerbate the regression.

One last question exists: Why were there not more cases of autism prior to large scale immunization, during measles outbreaks? Natural measles infection coupled with pre-existing risk factors should have produced

occasional autistic conditions. The answer to this question may be both historic as well as diagnostic. Autism was not identified as a (rare) separate condition until 1943 by Leo Kanner(96). Prior to this, the condition was lumped in with other psychological and mental defect diagnosis. Prior to large scale immunization, infant and child mortality was high for other diseases, malnutrition and warfare associated events. Measles infection alone, historically, produced a high mortality rate(147).

Discussion Addendum Two:

The Critical Role Of Secretory Immunoglobulin A In Autism

It has been hypothesized here, that secretory IgA can be used to treat immune/enzymatic homeostatic dysregulation and resultant autism. The question thus arises, could secretory IgA deficiency in infants, be the pivotal risk factor for this condition?

Of the listed Congenital Metabolic Diseases (CMD's), or risk factors, the most commonly found in autistic children is secretory IgA deficiency(51)(52)(53). This is significant, since non-autistic children normally produce large amounts of measles specific IgA after immunization, while autistic children do not(54). Secretory IgA normally increases with age in the first 6 months of life(131).

As has been stated, congenital metabolic diseases (or risk factors) are considered individually to be rare. However, this viewpoint repeated in numerous research reports, does not accurately reflect the published data in regard to secretory IgA deficiency. As stated by Urbanas V, et al in Med Sci Monit (2016):

quote: "selective Immunoglobulin A (IgA) deficiency is the most common inherited immunodeficiency disorder worldwide"(132)

And according to Shkalim V, et al. in Clin. Immunol. (2010):

quote: "IgA deficiency appears to be a risk factor for infections, allergic diseases, autoimmune conditions, and malignancy."

(136)

It is significant that IgA deficiency in children is so common, that a diagnosis under four years of age may be considered simply transient and a result of developmental delay(122). The diagnosis itself can be misleading, since it is based on monomeric blood serum IgA, rather than the dimeric secretory IgA of the gastrointestinal mucosa(148).

Independent studies have demonstrated that on average, 25 percent of infants (premature to 1 year of age), demonstrated undetectable levels of secretory IgA:

study one:

In Infants 6 weeks to 2 1/2 years secretory IgA was detected in 72% of salivary samples.(127)

study two:

73 newborn infants (1 day old) secretory IgA was detected in 74.0% of all saliva samples (130)

In separate studies, Sudhir Gupta MD and Reed Warren PhD determined that 20 percent of autistic children had IgA deficiency. It should be noted however, that this measurement is for serum IgA not secretory IgA(140)(141).

These rates are far beyond what would be considered a "rare" condition by any acceptable standard. Dismissing the condition as "developmental" should in no way diminish it's importance to infant health.

Secretory IgA deficiency, which is considered a primary immune deficiency*, can also contribute to secondary immune deficiencies**. Thus secretory IgA deficiency as a single risk factor, can contribute to the production of additional autistic risk factors.

*Primary immune deficiencies occur when one or more components of the immune system is severely reduced or non-existent due to genetic and/or developmental causes. They can remain undiagnosed or produce re-occurring infections or other medical disorders(151).

**Secondary immune deficiencies are an indirect consequence of a primary immune deficiency. The primary deficiency can allow a microorganism to become established as a chronic infection. This chronic infection itself (whether microbial, viral or fungal) then produces an additional immune deficiency or repression(152)(153).

Severe immunoglobulin A deficiency has been indirectly linked with autism. In one study, a subset of autistic children was concurrently diagnosed with severe IgA deficiency(137). These children were susceptible to frequent viral infections. The severity of these infections was positively correlated with an increase in autistic symptoms(137). In another study, it was determined that the lower the levels of salivary secretory IgA, the greater the severity of behavioral disorders and impairment in autistic children(139)

Insufficient secretory IgA can provide an environment conducive to intestinal lymphoid tissue inflammation, similar to that observed in colitis and Crohn's disease. This has been observed in some autistic children(138). Normal levels of secretory IgA in the gastrointestinal tract can help avoid this, by providing for a homeostatic balance between essential commensal bacteria and inflammation causing pathogenic microorganisms(142).

Autistic children are often found to have dysbiosis and gastrointestinal inflammation associated with low or non-existent secretory IgA levels(162). Secretory IgA protects against this dysbiosis of the gastrointestinal tract(149). Fungal infections such as chronic *Candida albicans* is one cause of dysbiosis(82), and is commonly found in autistic children(85).

Teenager X began suffering from chronic and debilitating *Candida* infections within days of measles immunization. Chronic *Candida* infections can produce further immune suppression (118)(150), which could further enhance the dysbiosis. The severity of the dysbiosis directly correlates with autistic severity(143)(164).

As suggested, administration of secretory IgA prior to immunization may enable avoidance of such conditions. Breast milk is very high in secretory IgA(56). A recently immunized lactating mother, could administer breast milk prior to, and continuing after, measles immunization. If the infant has the previously mentioned risk factors this could be critical to preventing such conditions from occurring(93)(111). Autistic infants in general, have been shown to have a reduced amount of breast feeding then normal infants(166).

Immunoglobulin A deficiency can also interfere with the normal response to live vaccines. BCG, yellow fever, and polio vaccines are contraindicated if IgA deficiency exists (144). Logically, one should now ask whether the measles vaccine specifically, is contraindicated under conditions of IgA deficiency. Public health vaccine recommendations at this time consider it safe to immunize a child with serum IgA deficiency(165). However, this positive recommendation does not take into account the consequences of any resultant secondary immune deficiencies, and any additional

congenital metabolic diseases or risk factors. Repeated PUBLIC MEDLINE searches for the secretory IgA form as a contraindication to measles immunization, have yielded no reference results whatsoever.

Based on published research, this author believes strongly that secretory IgA deficiency in infants has been medically marginalized as to its importance both in overall infant health, and possibly as a factor in autism. Secretory IgA should, as referenced from multiple experimental studies, be reclassified as the predominant medical abnormality of newborns. Diminished levels of IgA has been associated with increased levels of viral, bacterial and fungal infections (158)(159)(160), and measles latency(161).

Restated in this context, it is theorized that the primary predisposing risk factor, or "smoking gun" of extremely low or non-existent secretory IgA, in conjunction with one or more additional congenital metabolic disorders or risk factors, and secondary opportunistic infections, enables the critical intracellular environment for measles N protein related dysregulation of homeostasis. Infants under this combination of conditions may be at greatly increased risk of autism upon measles immunization.

It is suggested here that routine testing of all newborn secretory IgA levels should be a regular part of the birth process. If subnormal secretory IgA levels are detected, immediate efforts should be taken to elevate those levels to normal ranges prior to, or coincident with immunization.

Dicussio Addendum Three:

An Alternative View

As noted, a logical sequence of events has been suggested for the genesis of autism associated with measles virus/ vaccine. However, the sharp-eyed reader may have noted two specific references cited in which autistic-like behaviors have been observed in which no measles virus was present:

(18)Prenatal and Early-Life Diesel Exhaust Exposure Causes Autism-Like Behavior Changes In Mice Chang YL, Cole TB, Costa L Part Fibre Toxicol. 2018 Apr 20;15(1):18

(46)Exaggerated Translation causes Synaptic and Behavioral Aberrations Associated With Autism. Santini E, Huynh T, et al. Nature 2013 Jan 17;493(7432):411 - 415

It may be theoretically possible that there are other causes of homeostatic dysregulation between the Th1/Th2 immune and phase1/phase2 enzyme systems. The eIf3P40 initiation site may be dysregulated by other vectors besides the measles N protein, resulting in autism. Genetic errors involving the initiation sites themselves are also possible. Theoretically, multiple errors of metabolism and risk factors together, without measles, could overwhelm homeostatic regulation via multiple initiation sites, etc. It is also important to realize that aside from vaccines, the measles virus is still in the environment available for varied human interactions. However, the theory that severe continuing intracellular homeostatic dysregulation results in autism, could still remain a viable concept.

History:

At birth, approximately 3 weeks early, Teenager X exhibited an olive green skin tone, diagnosed as hyperbilirubinemia, a condition in which large amounts of biliverdin (the oxidative product of bilirubin) build up in the skin tissue, producing a greenish skin color. This condition persisted for nearly two years. This impairment can reflect upon a developmental failure to produce the phase II enzyme(s) to clear excess bilirubin, or deficiencies in the homeostatic mechanism that controls production of these enzymes(69). As stated by Cayabyab R and Raymanathan R in *Pediatr Res* (2019):

quote: "Neonatal hyperbilirubinemia is one of the most frequent diagnoses made in neonates. A high level of unconjugated bilirubin that is unbound to albumin is neurotoxic when the level exceeds age-specific thresholds or at lower levels in neonates with neurotoxic risk factors." (123)

quote: "Severe hyperbilirubinemia in term neonates has been shown to be associated with increased risk for autism spectrum disorders." (123)

Prior to immunization, teenager X, as an infant, was exposed to large quantities of fungal elements as a result of home remodeling as well as cessation of breast feeding which normally can provide large quantities of secretory IgA(154)(155)(156).

note: At this point, we have a potential reduction in various enzyme and immune flux systems from premature birth, reduction in flux as a result of hyperbilirubinemia, and reduced maternal and intrinsic secretory IgA levels. All prior to measles immunization.

As stated by Hayes JA, Adamson-Macedo En, et al. in Neuro Endocrinol Lett. 1999:

quote: "The very young preterm neonate has multiple immune deficiencies which may increase his or her vulnerability to infection."(125)

quote: "neonates who were receiving expressed breast milk had significantly higher concentrations of SIg A (secretory IgA)"(125)

With the exception of the hyperbilirubinemia, The infant X prior to MMR immunization was normal in all respects. Healthy, alert, responsive in all ways appropriate to a five month old at the time of immunization*.

*Special note here. Infant X was immunized with MMR vaccine at 5 months of age. This NOT the presently recommended time for immunization. Initial immunization of infants with MMR is usually scheduled at 12 months of age(157).

Several hours after immunization, a moderate fever along with shrill abnormal crying patterns never heard before, continued throughout the evening. By morning, evidence of abnormality was apparent. Visual and auditory focus was severely impaired. Attentiveness to parents was diminished to the point of the appearing deaf. Facial expressions were dramatically altered. Within a week, all the classic autistic features and behaviors were manifest.

Within days of MMR immunization, The infant X began manifesting severe candida infections on the buttocks and oral candidiasis, with uncontrollable laughter, diminished pain sensation and inability to sleep. It was observed that the greater the apparent severity of the Candida infection, the greater the symptom severity. After consultation with the child's pediatrician, a topical antifungal was prescribed. This greatly reduced the behaviors, though autistic mannerisms persisted. When infant X appeared "cured" of the Candida infection and topical antifungal application ceased, a new candida infection started up again days later with resumption of behaviors. When an oral antifungal was prescribed, behaviors again improved, but again, cessation of treatment resulted in reemergence of the candida infection and behaviors. Long term control of the Candida infections during infancy and early childhood, was only achieved with the use of Transfer Factor specific to Candida(71)(86) and dosage with diphenhydramine to treat high histamine levels. This temporary stability of the autistic condition lasted until puberty.

Conclusion:

Many theories concerning the cause of autism exist. All these theories unfortunately share one thing in common: They tend to ignore well established facts about autism that lie outside the author's area of expertise. The theory presented in this paper, if correct, would hopefully enable many of the facts and observations concerning autism to be unified in a clear and reasonable manner.

The hypothesis that measles vaccination is involved in the development of autism has been disputed by numerous statistical studies. At present, any attempt to revive such a view, would elicit strong scepticism, if not outright contempt.

The evidence of teenager X presented here, the many responsible research articles cited, and the research backed theory put forth, clearly indicates that if there is an involvement between measles and autism, it is not simple or obvious.

It is a well known fact that a given pathogen does not produce the same disease state for everyone. In the age of covid-19, it is evident that a given pathogen can kill one infected individual, while leaving another an asymptomatic carrier. Predisposing conditions clearly play a significant role in the manifestation of a disease.

It is well documented, that not all children vaccinated with the same vaccine will respond in the same way(88)(89)(92). Thankfully, the vast majority of children will, but not all. It is the moral and ethical responsibility of researchers to study and weigh in on these documented exceptions with open and enquiring minds:

quote: "when live vaccines are given, significant vaccine-related adverse events can occur, including the emergence of disease from vaccine strains." summary quote, Vaccine 2014 Principi and Esposito (88)

quote: "Adverse effects of vaccines have been recognized for many years, especially the occurrence of infections caused by viable vaccine organisms in immunodeficient hosts." summary quote, Allergy Clin Immunol. 2018 Bonilla FA (92)

What is unique about the theory presented in this paper, is that it offers multiple tests of the theoretical concept. If an individual with the same characteristics as autistic Teenager X is treated successfully with human derived measles N protein specific secretory IgA, then the theory is proven.

A second related test would be that measles N protein

specific IgA be administered along with the measles vaccine to a statistically significant number of children. If this theory is correct, and the dosage regime accurate, then this addendum to the measles vaccine, should produce a significant reduction in the overall number of new autism cases. It would also allow for safe and effective immunization against measles.

A third related test of theory would require the MMR immunization of the mother prior to birth or just after. Immunization of the infant should occur coincident to breastfeeding (before, during and after immunization) The infant would theoretically receive sufficient measles specific secretory IgA via breast milk (please see quotes below). Given a statistically significant test group, there should be a reduction in autism cases.

As stated by Maertens, De Schutter, et al. in Vaccine(2014):

quote:"Vaccination during pregnancy results in an augmentation of disease specific maternal antibodies... secretory Immunoglobulin A (sIgA) is passed through breast milk."(126)

And previously stated and verified by Prentice A in Archives Of Diseases In Childhood(1987):

quote: " The concentrations and outputs of secretory IgA in urine were significantly higher in the breast fed group by a factor of three"(133)

Based upon the observations of Teenager X, published research, and pending experimental proof, it is theorized that severely subnormal secretory IgA coupled with one or more additional risk factors or CMD's, measles vaccination, and secondary opportunistic infections, results in a critical messenger-metabolite flux reduction. This flux reduction allows the opportunity for the measles N protein to interfere with immune/metabolic homeostasis via a specific eukaryotic initiation factor. Reduced secretory IgA and other suppressions, perpetuates a measles virus latency. The continuing homeostatic interference results in autism.

Experimental proof remains pending.

Immunization with MMR vaccine does not directly cause autism. Immunization with MMR vaccine saves thousands of lives every year. For the universal benefit of the public, MMR vaccination is necessary. It is the responsibility of medical science however, to identify those children for whom intrinsic risk factors (inclusive of abnormally low secretory IgA) coupled with the measles vaccine and secondary infection, could risk autism.

Lastly and sadly, should any relationship between measles and autism be established, more children may become sickened then will be restored to normality. As parents become aware, many will refuse to immunize, resulting in vast increases in measles cases. This would present a severe challenge to public health services in the necessary and critical promotion of immunization.

Special thanks to Dr. Hugh H Fudenberg whose trailblazing work involving Candida, Transfer Factor and Autism had a deep impact on me, and kept my research pointed in the right direction.

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-the author wishes to apologize in advance for any
computer related errors in regard to reference credits-

- teenager "X" is the author's son.