Yeast Infection and Psychiatric disorders

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Introduction

Millions of people suffer from depression caused by multiple factors including certain infections like candidiasis every year and the cause in most cases is not known and this can be attributed to the fact that in modern medicine and CNS, there are very few knowns. It is well known that yeast like Candida albicans can penetrate any area of the body including CNS and henceforth there could be a link between Candida infection and depression. It has been observed that sign and symptoms of yeast infection include skin rash, fatigue, headache, irritability, intestinal pain, respiratory disorders, urinary problems, vaginitis and depression1. Other symptoms include digestive disorders hypoglycemia, hyperactivity, memory loss, impotence, learning difficulty, menstrual problems, premenstrual tension and short attention. As evident from the above list many symptoms are associated with nervous system which plays a role in psychiatric diseases. So we review this topic to understand and highlight the correlation between yeast infection and psychiatric disorders.

Terminology

Depression: is a universally understood condition of sadness and despondency where patient feels that life has lost its luster. People normally recover from such gloomy spells and may carry on. Some conditions of sadness may require lifestyle changes such as resolving a rocky marriage, dropping bad habits, or removing oppressive factors from one’s life. Still other situations may require the counsel of a good friend or priest or minister-someone one can trust and discuss his or her troubles with. However sometimes people don’t recover from life’s setbacks. Or they become depressed over insignificant matters for no reason at all. The feelings of sadness may simply slow them down or can debilitate them to the point where they weep continuously, cannot function in life or may consider suicide. These are the situations where an emergency psychiatric treatment is required2.

Causes of depression: When a person remains depressed despite normal efforts to treat the depression, a physical source of the depression should be considered. This is particularly true in the case of debilitating or suicidal depression2. Physiological causes of depression are very common, like endocrinal disorders in the form of hypothyroidism.

Physical causes of depression include: Nutritional deficiencies, lack of exercise, hypo-thyroidism, hyperthyroidism, fibromyalgia, candida (yeast infection), poor adrenal function, other hormonal disorders including (cushing’s disease (excessive pituitary hormone production, addison’s disease (low adrenal function), high levels of parathyroid hormone and low levels of pituitary hormones), hypoglycemia, food Allergies, heavy metals (such as mercury, lead, aluminium, cadmium, and thallium), selenium toxicity, premenstrual syndrome and sleep disturbances.

Infectious causes: AIDS, influenza, mono-nucleosis, syphilis (late stage), tuberculosis, viral hepatitis and viral pneumonia

Medical ailments/causes: Heart problems, lung disease, diabetes, multiple sclerosis, rheumatoid arthritis, chronic pain, chronic inflammation, cancer, train tumors, head injury, multiple sclerosis, parkinson’s disease, stroke, temporal lobe epilepsy, systemic lupus erythematosus and liver disease

Drugs related causes: Tranquilizers and sedatives, antipsychotic drugs, amphetamines (withdrawal from), antihistamines, beta blockers,
high blood pressure medications, birth control pills, anti inflammatory agents, corticosteroids (adrenal hormone agents, cimetidine, cycloserine (an antibiotic), indomethacin, reserpine, vinbiastine and vincristine

**Candidiasis** – Common yeast infections called candidiasis is caused by the yeast Candida albicans which thrives in the large intestines of human body. Yeast infections can manifest on skin, mouth or systemic sites. It affects people of all ages and both sexes³.

- Pre disposing factors – Moist environment supports fungal growth and that’s the reason most of fungi exist as saprophytes in soil. Whenever human body’s immune system gets compromised, fungal infections manifest as opportunistic pathogen. The prevalence of fungal infections has increased since 1980 since the emergence of HIV which causes AIDS where patient is bound to get opportunistic fungal infections when the CD4 count falls,<500. Of all the identified fungal mycosis, yeast infection account for almost 70-80% of infections⁴.

- Stages of Candidiasis – Today there are millions of people in USA and other countries who do not feel well and do not seen to get a definitive answer as to why. One potential reason which could be hypothesized is of is the overgrowth of Candida. While the human body has abundant normal flora including Candida, excess of Candida gives rise to any kind of physical problem in the form of instant fatigue, sugar craving, weight gain, lower concentration, confusion, bloating, low blood sugar, sensitivity to smells/alcohol, migraine/headache and depression. The course of Candidiasis has been divided into following 5 stages³.

**Stage One** – During the first stage of Candida infection, the mucosal lining or mucous membrane become infected leading to allergic reactions along with various types of infections such as streptococcus throat, bronchiolitis, pneumonia, tonsillitis, mononucleosis, sinusitis etc⁴.

**Stage Two** – This stage manifests in the form of headache or migraine, joint pain, fatigue, arthritis, nail infection, muscle soreness etc. due to over production of certain metabolic chemicals by Candida.

**Stage Three** – This is the stage during which patient develops behavioral and psychiatric problems. This includes decreased concentration, mood swings, depression, forgetfulness and confusion. At this stage, the patient feels out of control. Patients may land up in severe depression leading to thoughts of suicide, irrational fears, panic attacks, phobias, epilepsy and uncontrolled violence.

**Stage Four** – As Candida continues to grow and destroy the body cells, organ system within the body start reacting negatively and target towards a shutdown e.g. when Candida infections affects GIT, patient may not feel like eating and also the absorption of nutrients from GIT also get compromised. It is also hypothesized that it can affect CVS and lead to hypertension, numbness of extremities, bruising, and palpitations etc⁶. During the fourth stage, endocrine system may also get affected along with musculoskeletal system and respiratory system.

**Stage Five** – In the fifth and final stage, the person would land up with systemic spread of Candida which can prove to be fatal⁷.

**Possible Etiologies**

**Role of Tartaric acid in Autism**: Innumerable studies in past have implicated the role of abnormal organic acid produced by GIT flora in causing human diseases e.g. inborn errors of metabolism like phenylketonuria, tyrosinemia, maple syrup urine diseases etc. The same have been hypothesized as playing a role in psychiatric diseases like, autism, schizophrenia, Alzheimer’s diseases and even fibromyalgia. Urine organic testing in all these clinical conditions has shown elevated excretions of acidic products⁸.

These metabolic end products associated with Candida infection is tartaric acid. This compound forms sludge in the wine brewing process and has to be removed. Wine is sugar water fermented by yeast saccharomyces cerevisiae to alcohol and other yeast products. Humans do not produce this chemical.

**Effect of antifungal agents on Tartaric acid**: There are a lot of clinical cases where the
psychiatric symptoms in patients have been controlled by giving antifungal treatment to the patient e.g. a two year old patient was being evaluated for autism and his urine tested positive for organic acids. The child had been treated several times for ear infection with antibiotics and had developed oral thrush. Child’s behavior was badly affected and he became hyperactive with insomnia, lost his speech and eye contact with parents. Since child’s organic acids including tartaric acid was elevated in urine, a differential diagnosis of yeast infection was kept in mind and he was started on topical Nystatin (oral thrush). The child’s behavior improved within a week and elevated organic acids decreased in urine although it took over 60 days for the urine tartaric acid to return to normal range.

After 68 days of treatment the child’s mother started running out of Nystatin and began giving only half doses. During that time the tartaric acid starting increasing. When she got the Nystatin prescription refilled and restored the full dose of Nystatin, the tartaric acid decreased. Thus it was proved that Nystatin causes a marked reduction in the urine tartaric acid. The other significant finding was that even after two months of Nystatin, the biochemical abnormality can reappear within a short time of stopping the antifungal drug. Even after six months of antifungal treatment, there is often a biochemical “rebound” and loss of improvements after discontinuing antifungal therapy. This rebound also occurs after other antifungal drugs as well. Several explanations are possible for this phenomenon. One reason could be that because of one or more defects in the immune system such as IgA deficiency IgG deficiency, or severe combined immunodeficiency disease (SCID) which are found in most children with autism, the yeast, which are everywhere in our environment including the food we eat, repopulate the intestinal tract very rapidly and these yeast being very resistant may not be completely eliminated even after six months of antifungal therapy. Another theory proposed is that the yeast can genetically transform some of the human cells that line the intestinal tract and thus some of the human cells then contain yeast DNA due to transformation. These genetically transformed human cells produce both yeast and human products and are somewhat sensitive to antifungal drugs but are not killed by them and produce yeast products whenever antifungal drugs are absent. Moreover some of the yeast are embedded deep in recesses of the intestinal tract or in the deeper layers of the mucosa that lines the intestine where they are relatively safe from the drug. Although their numbers are small, they readily repopulate the intestine after antifungals are stopped. The most logical explanation given from immunology.

In addition to the immune system taking inventory of its own cells, it seems increasingly likely that the immune system also takes an inventory of bacteria and yeast cells present in the intestinal tract soon after birth. This inventory is performed by a group of cells called the CD5 +B-cells, which are among the which are among the very first immunological cells to appear in the developing embryo and appear to play a role in tolerance to intestinal microorganisms in postnatal life. These cells may play a role in regulating the secretion of IgA, the antibody class that is secreted into the intestinal tract and which may select which microorganisms are tolerated in the intestinal tract. Furthermore, the eradication of normal flora especially when antibiotics are administered repetitively during infancy may cause the CD5+cells to reject these normal organisms at a later age. Any cells that are on this early inventory may be awarded immune tolerance and will not be attacked later on by the immune system. Either antibiotic use in infancy or yeast infection of the mother during pregnancy may result in later immune tolerance to yeast.

Response of Children with Autism to Antifungal Therapy: Improvements commonly cited by parents of autistic children treated with antifungal therapy include: decreased hyperactivity, more eye contact, increased vocalization (more words and more usage), better sleep patterns, better concentration, increased imaginative play, reduced stereotypical behaviors (such as spinning objects), and better academic performance.

More than 1000 children with autism have been treated with a wide variety of antifungal agents such as Nystatin, Lamisil, Sporanox, Nizoral, Diflucan, caprylic acid, grapefruit seed extract, and garlic extract with good clinical response in perhaps 80-90%. A survey of parents of autistic children by Rimland reports that antifungal therapy is ranked...
the most effective (by a wide margin) of all drug therapies used for the reduction of autistic symptoms9.

**Molecular Basis of Tartaric Acid Toxicity in autism:** Patients with autism generally excrete tartaric acid in urine and it has been observed that many of these patients have accompanying hypotonia8. Biopsy of the muscle of autistic patients with hypotonia revealed normal structural features except for an unexplained “granularity” by electron microscopy. Electromyography, EEG’s, brain scans, and nerve conduction velocities have been found to be all normal. Literature indicates that tartaric acid is a highly toxic substance. As little as 12 gm can cause human fatality with death occurring from 12 hours to 9 days after ingestion. Gastrointestinal symptoms can be marked (violent vomiting and diarrhea, abdominal pain, thirst) followed by cardiovascular collapse and/or acute renal failure. This compound especially damages the muscles and the kidney and may even cause fatal human nephropathy (kidney damage).

A Korean study found that a patient with autism had a value of 6000 mmol/mol creatinine, a value that is about 600 times the median normal value. Assuming that the yeast in the intestine of the child were producing tartaric acid at a constant rate, this child was exposed to 4.5 grams per day of tartaric acid, (over one-third of the reported lethal dose of tartaric acid!) The child’s was given antifungal treatment for 6 weeks and his Creatinine value returned to normal within few weeks8.

**Mechanism of Tartaric acid toxicity:** Tartaric acid is an analog (a close chemical relative) of malic acid (Figure 1). Malic acid is a key intermediate in the Krebs cycle, a biochemical process used for the extraction of most of the energy from our food. Presumably tartaric acid is toxic because it inhibits the biochemical production of the normal compound, malic acid. Tartaric acid is a known inhibitor of the Krebs cycle enzyme fumarase which produces malic acid from fumaric acid.

**Role of Malic acid supplements in Fibromyalgia**

Interestingly, it has been found that tartaric acid and/or other yeast byproducts are also elevated in urine samples of adults with the disorder fibromyalgia, a debilitating disease associated with muscle and joint pain, depression, foggy thinking, and chronic fatigue8.

A large percentage of patients with fibromyalgia respond favorably to treatment with malic acid which is present in health food supplements such as Fibrocare and Supermalic. This is because supplements of malic acid are able to overcome the toxic effects of tartaric acid by supplying deficient malic acid.

Treatment with the antifungal drug Nystatin kills the yeast and values for tartaric acid steadily diminish with antifungal treatment. Fifty percent of patients with fibromyalgia often suffer from hypoglycemia even though their diet may have adequate or even excessive sugar8.

One of the reasons for the hypoglycemia may be due to the inhibition of the Krebs cycle by tartaric acid. The Krebs cycle is the main provider of raw materials such as malic acid that can be converted to blood sugar (Figure 2) by the process called gluconeogenesis when the body uses up its glucose supply.

![Fig. 1 – Composition of Malic and Tartaric Acids](Image)

![Fig. 2 - The Krebs cycle demonstrates the conversions of raw materials into Glucose, the main fuel for the brain.](Image)
If sufficient malic acid cannot be produced, the body cannot produce the sugar glucose, which is the main fuel for the brain. The person with hypoglycemia feels weak and their thinking is foggy because there is insufficient fuel for their brain. Of course, consumption of sugar may provide short-term relief but which also stimulates yeast overgrowth and within a short time symptoms are even worse.

Role of Arabinose in Autism, Alzheimer’s Disease and Schizophrenia

Arabinose is a five carbon sugar with an aldehyde function called an aldose, which is frequently elevated in autism. In some children with autism, arabinose concentrations may exceed 50 times the upper limit of normal.

The exact biochemical role of arabinose is unknown, but a closely related yeast alcohol arabitol has been used as a biochemical indicator of invasive candidiasis. None of studies have found elevated arabitol in any of the urine samples tested and arabinose has not been found in the culture media of multiple isolates of Candida albicans isolated from stool samples of autistic children.

It is assumed that arabitol produced by yeast in the intestinal tract is absorbed into the portal circulation and then converted to arabinose by the liver. Hypoglycemia occurs in inborn errors of fructose metabolism in which fructose inhibits gluconeogenesis and it is possible that children with autism might be deficient in one or more enzymes involved in the metabolism of pentoses. Elevated protein-bound arabinose has been found in the serum glycoproteins of schizophrenics and in children with conduct disorders and alteration of protein function by arabinose is another mechanism by which arabinose might effect biochemical processes.

Women with vulvovaginitis due to Candida have been found to have elevated arabinose in the urine; restriction of dietary sugar brought about a dramatic reduction in the incidence and severity of the vulvovaginitis. Thus, one of the mechanisms of action of antifungal drug therapy for autism might be to reduce the concentration of an abnormal carbohydrate produced by the yeast that can not be tolerated by the child with defective pentose metabolism. Arabinose tolerance tests should be able to rapidly determine if such biochemical defects are present in children with autism.

Molecular basis of Pentosidines toxicity in Autism and Alzheimer’s diseases:

Protein modification caused by pentosidine formation is associated with crosslink formation, decreased protein solubility, and increased protease resistance. The characteristic pathological structures associated with Alzheimer disease contain modifications typical of pentosidine formation. Specifically, antibodies against pentosidine immunocytochemically label neurofibrillary tangles and senile plaques in brain tissue from patients with Alzheimer disease.

In contrast, little or no staining with anti-pentosidine antibodies is observed in apparently healthy neurons of the same brain. The modification of protein structure and function caused by arabinose could account for the biochemical and insolubility properties of the lesions of Alzheimer disease through the formation of protein crosslinks.

Since the process of pentosidine formation is an oxidative one, the use of antioxidants as well as antifungal therapy appears to be a promising therapy for Alzheimer’s disease. Glutathione has been reported to inhibit pentosidine formation. Supplementation with the vitamins biotin, pyridoxal (B-6), and lipoic acid (whose function at protein epsilon amino groups may be blocked by pentosidines derived from arabinose) might also be beneficial because of functional deficiencies due to pentosidine formation.

Not surprisingly, neurofibrillary tangles similar to those found in the brains of Alzheimer’s victims have also been reported in the brain of an autistic person at autopsy. It has been reported that frequent urinary tract infections and high amounts of circulating immune complexes are associated with more severe Alzheimer disease. The use of antibiotics to treat urinary tract infections would of course lead to yeast overgrowth of the gastrointestinal tract.

Conclusion

Products of gastrointestinal microorganisms including yeast that have been largely ignored in the past appear to play major roles in human metabolism, development, aging, and disease.

Elevation of yeast metabolites such as tartaric...
acid and arabinose are found in many of the same disorders and are even more common in autism, SLE, Alzheimer’s disease, fibromyalgia, attention deficit hyperactivity, and chronic fatigue syndrome. The arabinose may interfere with gluconeogenesis and also may through pentosidine formation significantly alter protein structure, transport, solubility, and enzymatic activity as well as triggering autoimmune reactions to the modified proteins.

The finding of pentosidine in the neurofibrillary tangles of Alzheimer’s brains and its absence from normal areas of the brain may indicate a direct role of a yeast byproduct in accelerating the normal aging process. Tartaric acid from yeast overgrowth has a direct toxic effect on muscles and is an inhibitor of a key Krebs cycle enzyme that supplies raw materials for gluconeogenesis and offers an explanation for many of the symptoms of fibromyalgia.

Thus psychiatric disorders require not only the antipsychotic treatment but also antifungal to treat the organic cause behind such illness.

References
3. Yeast sign and symptoms by capture health.