A child is born, say, in the US. She immediately receives an antibiotic to protect against eye related pathogens acquired during birth. Earaches turn out to be a problem over the next couple of years and her paediatrician, under pressure to keep her mother satisfied with the level of care, repeatedly prescribes antibiotics. Earaches are mostly replaced by the sore throats, flu, colds and other respiratory problems after the early years and the fear of serious complications drives prescribing antibiotics, even if the problem is probably viral, because the antibiotics protect against secondary bacterial problems.

Her sore throats were never cultured prior to antibiotic therapy. As a teenager, she develops acne and is put on a low dose of antibiotic for an extended period. As an adult she has both frequent bladder infections and gastric problems, the latter diagnosed as H. pylori related. Both are treated with antibiotics. She also eats plenty of meat, and thus ingests residual antibiotics from the widespread practice of giving farm animals a steady diet of antibiotics to get more weight gain per pound of feed. The continuous antibiotic exposure also impacts the risk of obesity, and she is diagnosed at 40 with the metabolic syndrome. When in the hospital for observation after passing out from hypoglycaemia due to careless use of anti-glycemic drugs to control her type 2 diabetes, she contracts a C. difficile infection which is treated with antibiotics. When this gut infection and its bothersome or even serious diarrhea recur, more antibiotics are prescribed. In addition, gastric problems and bladder infections continue to recur and are treated.

Thus repeated exposure to antibiotics, in some cases unnecessary, is so common that public health authorities and medical scientists are becoming concerned. This concern is driven by the relentless increase of antibiotic resistant pathogens and the spectre of mankind returning to the pre-antibiotic era where vast numbers perished from infectious diseases curable today. But some medical scientists are also worried about what all these antibiotics are doing to the friendly bacteria we host, a crowd that in fact, in terms of cell numbers, considerably exceeds the number of cells in the human body. These bacteria do not just happen to be there because no one has gotten around to mounting a public health campaign on the scale of the anti-fat dietary campaign to eliminate them, although the use of “antibacterial” in marketing reflects a recognition that there is a widespread belief among the general public that all bacteria are bad. The bacteria to whom we offer a home in various places in our bodies and on our skin are in fact part of the grand scheme and are vital to making our biochemistry and microbiology and immunology work properly. These friendly bacteria have evolved over eons into a so-called microbiome that works very efficiently at a large number of tasks to keep us healthy and functioning properly. However, amid the hand wringing over antibiotic resistant bugs, one hears almost nothing about the effects of antibiotics on this vital asset. This subject is featured in this issue.

Also included in this issue is a discussion of the mechanism of the origin of type 2 diabetes and the implications for reversal.

Finally, this issue contains a Research Review concerning what some call the crisis in psychiatry, a topic that unfortunately should be of interest to the majority of readers.
Finally, if you need to restock your supplements, please remember that by ordering through our on-line vitamin store you will be helping to maintain the web site and publication of IHN. You can find the store at http://www.yourhealthbase.com/vitamins.htm.

Wishing you and your family good health,

William R. Ware, PhD, Editor

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**BACTERIA WE HOST, AND HOW THESE FRIENDS ARE AT RISK**

**THE HUMAN MICROBIOME**
The human microbiome is defined as the entire collection of microorganisms, not just bacteria, found in the entire body. It contains more than 100 trillion bacterial and fungal cells, exceeding by a factor of 10-100 the estimated number of cells in the adult body. They can be found on skin, in the mouth, nose and ears, in the esophagus, stomach, and in their main home, the gut. Women also normally harbour a large assortment (five major types) of bacteria in the vagina, which is a completely healthy situation. There are fifty known phyla (group of genetically related organisms) of bacteria in the world and eight to twelve have been found resident in humans. Six of these phyla account for 99.9% of the human microbiome and 90% can be found in the gut. The bacterial gut microbiome provides essential functions for its host, assisting, for example with digestion or metabolism of complex carbohydrates, the extraction of nutrients, vitamin synthesis, the metabolism of medications and even chemotherapeutic agents. In addition, some bacteria defend against dangerous pathogens, help maintain stable blood pressure, and are critically involved in our immune functions. Up to 15% of the calories obtained from food are directly or indirectly generated by our guest bacteria. The microbiome constitutes an example of a vast and highly organized ecosystem with competition and cooperation normally under control and has been termed a "super organ" with diverse roles in health and disease.

The Human Microbiome Project found that the distribution of populations of bacteria in humans is unique to each individual but it was possible to approximately characterize normal populations with regard to phyla and species. Such studies require advanced modern techniques only recently available since up to 80% of gut bacteria cannot be grown in culture. One tampers with this system, which has evolved over eons, at their own risk. One way is to expose the microbiome to both selective and broad spectrum antibiotics, although diet and other factors can also have a significant impact.

**THE ANTIBIOTIC DILEMMA**
Antibiotics clearly have had a major impact on the course of human illness. They are responsible for the transition from infectious diseases to chronic diseases, especially of aging, as being a major cause of death. Their use is universal. Patients demand them for even minor problems. But there’s a downside. They also affect the bacteria resident in humans, the human microbiome, significantly reducing some populations, changing the balance and completely killing off others. Furthermore, there is ample evidence of wholesale over-use with the concomitant development of antibiotic resistant bacteria; a problem that in the near future may expand into a true crisis.
Thus there arise three questions: (1) how serious and durable is the impact of antibiotics on the vast number of human colonies of bacteria found throughout the body, (2) is there a connection between human diseases and disorders and modifications in the populations of these bacteria and their diversity and (3) what are the implications and consequences of drastically altering these populations on childhood development and on childhood diseases and disorders? Modern medicine recognizes the existence of the microbiome but has largely ignored its importance as well as the impact of antibiotics, especially broad spectrum antibiotics, on what some call one of our vital organs. However, this appears to be changing with a flood of new research. In connection with the following discussion, a very recent book by Dr. Martin J. Blaser, MD, titled *Missing Microbe. How overuse of antibiotics is fuelling our modern plague,* provides invaluable insights and information.

A number of diseases appear to be much more prevalent than they were 50-60 years ago. These include obesity, childhood diabetes, asthma, hay fever, food allergies, esophageal reflux, esophageal cancer, celiac disease, Crohn’s disease, ulcerative colitis, autism and eczema. Dr. Blaser cites statistics that suggest dramatic increases. While there are a number of hypotheses to account for the increase for each disease, he wonders if there could be one underlying cause responsible for the parallel increases. He advances a theory which has as its central feature the several pounds of bacteria that live in our guts and elsewhere in and on our bodies, and the changes, both quantitative and qualitative in the nature of this microbiome due to antibiotics that could be partly responsible. On average, individuals between birth and age of 20 in the US will experience 17 courses of antibiotics. However, antibiotics are an essential and vital tool in modern medicine. Thus the dilemma.

**HOW BABIES ESTABLISH THEIR MICROBIOME AND WHAT CAN HAPPEN**

Before a baby is born, it is thought to be microbe free. The first inoculation occurs orally during passage through the birth canal and thus provides the start of the colonization. Included are lactobacilli which enable the digestion of the mother’s milk. The mother’s oral bacteria are also introduced very early into the baby’s system. The first milk (colostrum) contains antibodies which inhibit competing and possibly more dangerous bacteria from becoming established. This process of colonization of course has evolved over literally eons to successfully provide, for example, metabolic and immunologic functions while crowding out undesirable types. It thus would appear imminently reasonable not to intentionally or inadvertently disturb the colonization process which has been optimized by evolution. However, during pregnancy the mother’s oral and vaginal spectrum of bacterial species can undergo artificial alterations due to medications, especially antibiotics, and while most parents are not aware of it, the baby gets its first of countless exposure to antibiotics within hours after birth. If they develop normally the intestinal microbiota ultimately resemble that of a normal adult by age 3, that is, more or less stable but diverse.

After birth, the baby passes through its critical years of early development, a process which depends on everything working properly including the microbiome. But this microbiome is, for many infants and toddlers, under repeated attack from antibiotics that alter it by killing off some classes of bacteria and changing the distribution of species that remain. As will be discussed below, many species reduced by antibiotics recover, some slowly, but some do not. While no one argues with the necessity of this therapy in acute and life-threatening situations, there are certainly doctors and medical scientists who do not agree that many of the indications such as sore throat, earache, fever or cold are, when initially treated, serious enough to justify the damage rendered to the microbiome. But they are a voice crying in the wilderness since modern medicine barely recognizes the importance of properly function microbiome. In fact, this disregard continues into adulthood and by the time most of us reach a ripe old age, the number of encounters with powerful antibiotics is for most probably very large indeed.
IMPACT OF CAESAREAN SECTION BIRTH

Children born by C-section are at increased risk of allergies, asthma, autism, celiac disease, type I diabetes and gastroenteritis. Such a diversity suggests a common cause. Birth by C-section, a very recent development in the course of evolution, deprives the baby of the natural initial oral bacterial inoculation. Instead, the colonizing bacteria are derived from the mother’s skin and mouth bacteria and develop into distinctly different populations as compared to what is found with natural delivery. C-sections are common in developed countries, ranging up to 50% or more, and a significant fraction is elective. A recent Canadian study compared the microbiome of children born naturally with those born via C-section. The latter were found to have very low bacterial richness and diversity. The effect was diminished in children born by C-section that became necessary during problems with natural birth. In this case, there was some exposure to the bacteria in the birth canal prior to the surgery. This study also revealed significant differences between the microbiome when breast fed children were compared to those fed formula. The authors point out that in Canada more than 25% of children are born by C-section and less than 15% are breast fed for the recommended 6 months.

A recent study found an association between C-section delivery and child adiposity from age 6 weeks to 15 years. Infant antibiotic exposure accomplished the same end result, as might be expected since tons of antibiotics are used to fatten animals raised for meat and the earlier the treatment is started, the better the results. Childhood susceptibility to autoimmune disorders, and in particular type 1 diabetes have been associated with imbalances in the gut microbiome. A recent study reported significant increased risk of autism spectrum disorder with or without intellectual disability associated with both elective and emergency C-section delivery.

It would obviously be a simple matter to orally inoculate C-section babies with a swab sample of the mother’s vaginal bacteria, but this would require acceptance as evidence-based (randomized controlled trials) the notion that this could be beneficial.

EXTENT AND DURATION OF ANTIBIOTIC DAMAGE TO GUT MICROBIOTA

This issue is just beginning to receive the attention it deserves, mostly because the research tools needed have only recently come into use. As mentioned above, most of the gut bacteria cannot be cultured. And even a more modern approach using gel electrophoresis is inadequate when compared with studies based on sophisticated RNA sequencing. Thus there are only a very limited number of informative studies related to this critical question. Nevertheless, culture based studies had already indicated gross changes in the human microbiome at several sites due to antibiotic treatment.

These modern techniques reveal very large changes in microbial composition (dysbiosis) associated with antibiotic treatment but also found that the composition mostly reverted to approximately the pre-treatment state within around a month after the end of treatment. However, some bacterial species never recovered. Repeated antibiotic treatment generated larger short-term and long-term changes. In fact, repeated antibiotic treatment was found to result in long-term impacts on the human intestinal microbiota 2 years post treatment. Thus in addition to eliminating some species, antibiotic treatment is constantly creating time windows of opportunity of variable duration for adverse effects. There was individual variability as would be expected given the variation in the untreated microbiota populations. Given the complexity of the microbiota and the changes found, the implications regarding long-term harm or increased disease risk will require significant research to clarify the associations, especially at the level of changes in individual species or phyla with pathology. However, such results would then potentially suggest targeted therapeutic interventions. Also, the study of the variation of intestinal microbiota damage with the type of antibiotic has just begun. The above cited studies and review involved ciprofloxacin, amoxicillin and clindamycin.
Finally, the impact of antibiotics on the gut microbiota must ultimately involve an understanding of the changes in metabolic processes dependent on bacteria, the balance in metabolites, and changes in the susceptibility to increased colonization by undesirable pathogens. Research in this area is expanding rapidly and there is reason for considerable optimism. Nevertheless, the concern regarding the damage caused by antibiotics and the implications appear fully justified. In the interim, it will be important to rely mainly on evidence from clinical studies regarding the association of dysbiosis (microbial imbalance) and pathological conditions.

**DYSBIOSIS AND CANCER**

It is generally acknowledged that gene-environmental interactions underlie the susceptibility to cancer and its progression. Nevertheless, only limited knowledge exists regarding the nature of these environmental factors and their relative importance in tumor genesis. Recently, there has been growing appreciation of the potential role in this context of the microbial communities inhabiting the gastrointestinal tract and other body sites. Colorectal cancer (CRC) provides an excellent example of rapid progress.

In a study published in 2013, Ahn et al reported on a case-control study (comparison of cases and selected controls) which compared 47 CRC subjects with 94 controls. The CRC cases showed decreased overall fecal microbial community diversity and when cases were compared to controls and the prevalence of various phyla were examined, there were significant increases in two and a significant decrease in one. These observations were consistent with animal studies where again enrichment and decreases in various phyla were seen depending on the presence of colon tumors. Fecal transplantation results into gut-sterile mice suggested that in fact these imbalances were causative for the colon cancer. These animal studies were followed by a report from the same group in 2014 announcing that by examining the characteristics of the gut microbiome in CRC and pre-CRC (adenoma) patients and CRC free controls, it was possible to differentiate these three groups with remarkable accuracy, and this was suggested as an important screening tool. Incidentally, intestinal preparation for colonoscopy does not significantly alter the gut microbiome.

There are a number of animal studies providing evidence of tumor promoting effects of bacterial microbiota. In addition to CRC, gastric cancer and cancer of the liver, lung and breast have been studied. Human studies of gastric, skin and ocular cancers have been based on regression after eradication of specific bacteria.

The importance of dysbiosis in other disorders will be discussed below in the context of fecal transplantation.

**AUTISM AND THE MICROBIOME**

Autism has been frequently related to gut dysfunction. The following comments of two clinicians with extensive experience in treating autism are significant:

Dr. Natasha Campbell-McBride, MD, MMed Sci (neurology), MMedSci (nutrition) in the book *Gut and Psychology Syndrome (GAPS)*:

“I have yet to meet a child with autism, ADHD/ADD, asthma, eczema, allergies, dyspraxia or dyslexia who has not had digestive abnormalities. In many cases they are severe enough for the parents to start talking about them first.”

“Amongst all the parents of GAPS children I have met, the mother always invariably has signs of chronic Gut Dysbiosis. Most mothers have been taking contraceptive pills for years before having children. Many mothers have had numerous courses of antibiotics. Many of them have not been breastfed as babies and their mothers show typical symptoms of Gut Dysbiosis. Almost every one of them has one or more health conditions which are typically associated with abnormal gut flora. The most common health problems which mothers of
GAPS children suffer from are: digestive disorders, asthma, eczema, hay fever and other allergies, migraines, PMS, arthritis, skin problems, chronic cystitis and vaginal thrush. These conditions seem to be unrelated, but they are all children of one parent—Gut Dysbiosis.”

Dr. Jaquelyn McCandless, MD:


“Gastrointestinal Health is a Key Issue, …the majority of autistic children suffer from impaired gastrointestinal health.”

What is being seen in the clinical setting is quite probably partly the result of C-sections and multiple courses of antibiotics adversely affecting the gut microbiome of both newborns and the developing child along with a surprising preconception and prenatal maternal influence. This view is consistent with the rapid increase in autism over several decades along with the significant increase in both pediatric antibiotic use and the elective C-sections. Both of these physicians address gut problems early in their treatment protocol which is driven by a recognition of the multifactorial nature of the causes. Modern medicine mostly treats autism behavioral and cognitive symptoms, in some cases with powerful psychiatric drugs.

These clinical observations are significantly reinforced by recent studies on the difference between normal and autistic children when the species of gut flora are studied. It is found that autistic children typically have a grossly abnormal gut microbiome. The extent of the abnormalities also correlates with autism severity.

**PROBIOTICS, AN OBVIOUS SOLUTION?**

Even if medicine went back to using antibiotics only when absolutely necessary and governments banned them for non-medical use in animals there would still be a problem for many individuals. Dr. Blaser offers some suggestions, such as much more targeted antibiotics that would not raise havoc with the microbiome, and understanding disorders treated with antibiotics to the point where a non-antibiotic treatment can be devised. He is very cautious regarding the use of over-the-counter probiotics to address dysbiosis and the changes caused by antibiotics, since their use is not really evidence based and there are many potential candidates and subspecies of bacteria to consider. This may represent excessive caution since a number of probiotics, including VSL#3, have a considerable literature indicating remarkable benefit and no downside.

In 2013 a phone survey was reported in the literature which examined the probiotics stocked in 126 US academic medical centers. The most popular stocked in 27% of hospital pharmacies was Culturella which contains a particular strain of *Lactobacillus rhamnosus*. Second in 25% of pharmacies was Lactivex which contained two Lactobacillus species but not the one in Culturella. Coming in 6th at 3.5% was VSL#3, which contains eight different bacteria. This illustrates that not only are probiotics not popular therapeutic agents in modern medicine, and that a formulation containing a large number of bacterial types, VSL#3, with a quite considerable peer reviewed literature concerning efficacy, was only rarely stocked. VSL#3 has been available over the internet for years.

**A RADICAL APPROACH TO RESTORING THE NORMAL MICROBIOTA OF THE GUT**

In his book Dr. Blaser closes his discussion of probiotics with a treatment that is about ready for prime time, the so-called fecal transplant. In theory, this is very simple. One treats the highly damaged or compromised gut microbiome with a donor sample of the microbiota derived from the stool of a hopefully healthy individual or better still, from a mixture derived from several or a number of individuals. The potential for transferring pathogens is a serious issue and presents a challenge in screening donors. This probiotic is introduced either into the upper end of the small intestine via a tube put down the throat, or by endoscopic guided
introduction via the colon, or simply by a long retention enema. This approach has been highly successful in treating refractory diarrhea due to the microbe *C. difficile*, a disorder that has become common in hospitals and even among the general public, is dangerous and potentially fatal. The conventional therapy involves antibiotics which may have some initial effect, but recurrence is terribly frequent and if the problem is a damaged microbiome, then the use of more antibiotics is counterintuitive.

The *C. difficile*-associated disorder is caused by toxins released by this bacterium that attack the intestinal wall (epithelium) leading to an intense inflammatory response and diarrhea. *C. difficile* is native to part of the gut but its growth and pathogenic activity is normally held in check by other bacteria, a good example of a balance that one does not want to disturb. It is not surprising that antibiotic use is the main risk factor for *C. difficile* infection (CDI). It is thus interesting that antibiotics are the standard treatment. Also, with successive rounds of antibiotic treatment the bacteria become antibiotic resistant. Studies indicate that CDI patients have markedly decreased microbial diversity and experience significant decreases of certain types of bacteria and increases in others. Fecal transplantation appears to promptly restore the microbiome of the patients gut to correspond to that of the donor. In more than 500 cases worldwide, fecal transplantation had a cumulative efficacy of approximately 90% for the treatment of *C. difficile* with few if any adverse events. Many of the patients had experienced recurrent CDI, a very serious condition with the potential for significant patient deterioration, even death. Most had no doubt also been given a number of courses of antibiotics, obviously with no permanent benefit, probably even making the long-term outlook worse.32

Some individuals with (CDI) who have heard of fecal transplants but are unable to find a practitioner willing to try it, have taken matters into their own hands and tried it at home, having found a donor regarded as healthy and directions on the internet. This is of course highly risky, because when done by a professional, the source of the fecal matter is very carefully vetted to prevent the transfer of infectious disease. In fact, there are new FDA regulations now in place in the US regarding this therapy. In the future screening of donors may also involve an examination of the gut microbiome to make sure hidden dysbiosis is not present.

Fecal transplantation has also been tried for a number of other disorders.33

- **Inflammatory Bowel Disease.** A recent meta-analysis found over 60% of treated patients with ulcerative colitis went into remission, were able to stop medication or experienced reduced symptoms.
- **Irritable Bowel Syndrome.** Fifty published case studies indicate about a 60% success rate in treating this disorder with fecal transplantation.
- **Chronic Fatigue Syndrome.** An uncontrolled study of sixty patients found about half to experience resolution of sleep problems, lethargy or fatigue during 15-20 year follow-up after fecal transplant therapy.
- **Metabolic and Cardiovascular Disorders.** In obese men, fecal transplantation from lean donors was found to increase insulin sensitivity, consistent with the hypothesis that dysbiosis can actually cause obesity and insulin resistance. Studies are underway to examine the impact of fecal transplants on fatty liver disease and vascular inflammation.
- **Autoimmune diseases.** Some evidence exists indicating that fecal transplantation has beneficial effects on multiple sclerosis. In a disorder where antibodies were attacking platelet surface antigens, a patient treated for ulcerative colitis who also had this disorder had a significant increase in platelet level which was durable.

This list helps make the case for the importance of an abnormal gut microbiome, i.e. dysbiosis, as a potential causative factor for a variety of serious disorders, mostly unrelated.
THE FUTURE
The current focus in medicine includes the looming crisis associated with the development of antibiotic resistant bacterial species, not the damage antibiotics cause to the microbiome and the consequences. In fact, attempts to treat disorders associated with these resistant microbes will generally involve more intensive antibiotic treatment creating even greater microbiome abnormalities and damage.

Anyone familiar with the pace that medicine changes in response to research results will probably agree that the outlook as regards the above issues is not favourable. Antibiotics will continue to be over-prescribed and elective C-sections will continue to be popular. It is hard to believe that the pressure being exerted on farmers to decrease their use of antibiotics to increase weight gain will be successful and thus antibiotics will continue to be present in the food we eat. The acceptance of probiotics will be slow due to the demands for evidence and large randomized controlled clinical trials, the large number of potential species and in general the lack of patent protection necessary to bring Big Pharma money into play.

There is strong and long established resistance, especially among patients, to any suggestion that the use of antibiotics, one of the mainstays of modern medicine, be restricted to well defined and acute situations. In fact, the growing threat of antibiotic resistant bacteria appears to be the only driving force prompting caution, not the potential danger antibiotics present to the nature, diversity and functioning of the microbiome. Modern medical research is typically reductionist, i.e. there is a tendency to attempt to focus, in this context, on individual bacterial species before deciding to replace a depleted population or do something about a greatly enhanced population. It is obviously not that simple since it is clear that the huge number of species is due to how we evolved, and that the complexities of interactions and symbiotic associations are highly complex.

It is important to realize that the nature and function of the human microbiome and how it is affected by antibiotics is an area that is just now gaining significant interest, partly because it is now possible to characterize the microbiome in much greater detail with high through-put genetic profiling which has partly solved the problem presented by the inability to culture many of the bacteria. Thus one approach that is essentially a broad spectrum probiotics therapy using fecal transplants is an encouraging development, although it may some years before this approach becomes a standard of care when physicians are confronted with one or more of the many problems that appear to be associated with or caused by a permanently changed microbiome.

In the meantime, over the counter probiotics after a course of antibiotics appears to be the only remedy. The effectiveness of this approach remains to be tested with different products and tests should be based on observing changes in the impaired microbiome. Since a variety of bacteria can accomplish the same tasks in the gut, identifying and replacing species wiped out by antibiotics may not be necessary.

WHAT IS THE ETIOLOGY OF TYPE 2 DIABETES, THAT IS, HOW AND WHY DOES IT DEVELOP?

The November 2013 IHN featured a study involving a dietary approach to actually reversing (curing) diabetes. The head of the group that carried out this research has recently published a discussion of how the results of this study impacts our understanding of the mechanism by which type 2 diabetes develops. The following is a summary of the hypothesis concerning the etiology of this disease.

Diet, lifestyle and genetic factors lead to muscle insulin resistance (IR). Insulin is required for the metabolism of glucose by cells to produce energy. To maintain metabolic rates insulin
levels increase. Physiologically important muscle IR can operate over many years and in the presence of excess energy (calories) intake, concomitant increase in insulin levels will expedite the accumulation of liver fat by the stimulation of fat synthesis in the liver itself. The increase in liver fat will cause the development of resistance to insulin-mediated suppression by the liver of glucose production causing blood glucose levels to rise. Fasting glucose will increase slowly and be compensated for by increased insulin production in an attempt to maintain normal levels. This increase in insulin further increases the conversion in the liver of excess calories into fat. Thus a cycle is established characterized by increasing insulin levels and increasing glucose production from the liver, the latter due to fat induced blunted suppression of liver glucose production. The export of fatty acids such as triacylglycerol from the liver increases fat delivery to all tissues including the pancreas. This process is stimulated by elevated blood glucose levels. An excess of fatty acids in the pancreas then impairs the beta cell insulin secretion in response to dietary glucose and the results is postprandial hyperglycaemia, i.e. abnormally elevated blood glucose followed by a slower decline after eating. But this postprandial increase in blood glucose further increases insulin secretion, which further enhances liver fat production. Thus two inter connected cycles in the liver and pancreas operate to continually increase the fatty acid levels in the pancreas and thus reduce beta cell functioning until the tipping point is reached and the individual's glucose metabolism is impaired and hyperglycemia reaches the point at which the definition of type 2 diabetes is satisfied.

Each step in this process is well documented by independent studies and the above hypothesis puts the pieces together. The role of decreasing beta-cell functionality leads to the conventional view that type 2 diabetes is irreversible and an incurable disease, an observation consistent with the history of the disease where anti-hyperglycaemic drugs fail to halt the progression to insulin dependence where insulin must be given to compensate for low production from the pancreas, in a sense a merger of the clinical manifestation of the two diabetes types. The above hypothesis also explains why commonly recommended diets and exercise fail. These interventions are not severe enough to break the cycles and reverse the fatty liver condition. In fact, the hypothesis is rather like calling diabetes a form of fatty liver disease and weight loss can reverse non-alcoholic liver disease in diabetics with significant improvements in insulin resistance and hyperglycemia when a substantial reduction in the liver pool of triglycerides is achieved.36

It has been known for some time that bariatric surgery, especially the most restrictive type, in a high percentage of cases leads to a complete remission of type 2 diabetes. What is interesting is that with type 2 diabetics, normalization of glucose occurred within days after surgery and before significant weight loss. The recent trial of an 8-week approximately 600 calorie diet (from a diet drink preparation augmented with non-starchy vegetables to yield 800 calories in total) has helped explain this observation and has provided strong evidence concerning the mechanism presented above.34 This study included the repeated monitoring of liver and pancreatic fat with magnetic resonance spectroscopy, the testing of beta-cell response, liver triacylglycerol levels and the fasting blood glucose to establish the time variation of each. Comparisons were made with healthy subjects not subjected to the diet to establish benchmarks for normal.

The results are fascinating. Within 7 days, liver fat had decreased 30% to become normal. Liver insulin sensitivity normalized as did fasting blood glucose, the latter observation consistent with the results from bariatric surgery. Slower changes during the 8 weeks included normalization of beta cell function including the resolution of abnormalities in the first phase of the response. Pancreatic fat decreased to normal with two big drops, one during the first week; the other during the next 3 weeks. While these results do not prove a cause and effect relationship between raised liver and pancreatic fat and the metabolic effects observed, they are highly suggestive of such an association. Mean values for weight declined steadily from 101 to 88 kg, BMI from 33 to 29, i.e. from obese to overweight, and waist to hip ratio remained the same, although individual values dropped significantly. HbA1c dropped from
7.4% to the slightly prediabetic value of 6.0%, over 8 weeks but this is a 3 month average examined two months after the intervention. Fasting glucose dropped from 9.2 to 5.7 nmol/L and triglycerides from 3.4 to 1.3 nmol/L, both within a week, to achieve approximately normal values. The picture presented by these 8-week numbers is entirely consistent with the above mechanism for the development of diabetes simply played backwards, and as well with the claim that diabetes had been reversed, in fact cured. Furthermore, the notion that beta cell damage and dysfunction were permanent appears false. Follow-up after participants had gone back to a higher calorie diet indicated that these results were durable in the absence of large weight regain but small weight gains were not important. In simple terms, get rid of excess liver fat and then do not let it accumulate again.

Bariatric surgery and the 600 calorie diet have one significant aspect in common, the acute nature of the change. Suddenly individuals are forced to burn fat and it appears that in the diet intervention, this had a remarkable impact on liver fat, which can be viewed as breaking the cycles proposed in the above mechanism. Fasting blood glucose is determined by liver production of glucose, and the abrupt change also brought not only the liver fat but also this metabolic function to normal in 7, days which seems quite remarkable.

It is also noteworthy that in the above mechanism, the development of muscle IR and the subsequent metabolic changes were hypothesized to be associated with a positive energy intake imbalance, which would normally be associated with weight gain. Diabetes risk is strongly associated with the metabolic syndrome, the manifestations of which are also consistent with the above mechanism.

Other possible protocols might be interesting such as a 600 calorie week followed by a somewhat higher calorie period using a strongly ketogenic diet for perhaps 10-12 weeks. This would be easier to maintain. The bariatric surgery provided a low calorie shock, but diabetes reversal was dependent on the degree of weight loss achieved. See the November IHN for a comparison of the 600 calorie diet and very low carbohydrate ketogenic diets.  


Thus, to avoid becoming a type 2 diabetic, it seems clear that it is important to manage diet and weight with the view of not having a positive caloric intake, maintain normal triglyceride levels, and aggressively dealing with prediabetes with diet and exercise. In view of proposed etiology of diabetes presented above, it can be argued that avoiding excess liver fats by not taking in calories in excess of what is needed may be the key intervention, and for someone with no signs of the metabolic defects associated with prediabetes, then holding the current weight may be more important than the nature of the diet. To reverse type 2 diabetes, it appears necessary to shock the metabolism by sudden near starvation which breaks the insulin, liver fat, triglyceride and hyperglycemia feedback cycles. Other than this, only bariatric surgery appears to offer a cure. For a prediabetic, even a 1-2 week 600 calorie diet may be quite effective. For many individuals, the buildup of liver fat is slow and can occur over a period of years, but the research described above suggests that even the accumulations implicated in diabetes can be rapidly eliminated in a matter of a week or two by shocking the metabolism with near starvation. Fasting glucose is a good indicator of success since this glucose comes from the liver and continued monitoring will reveal the durability of the intervention. For someone faced with a terminal illness such as diabetes, eight weeks of a very low calorie diet appears to be a rather insignificant hardship and if one or two weeks of such a diet will eliminate prediabetes, that would be a highly significant advance in public health.

REFERENCES


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**RESEARCH REVIEW**

**THE CRISIS IN PSYCHIATRY**

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*Medical research has made such enormous advances that there are hardly any healthy people left.*  
*—Aldous Huxley*

**INTRODUCTION**

Headlines suggesting that psychiatry is in crisis are frequently seen in such places as the *New York Times* and the *Psychiatric Times*, the latter a publication for professional audiences. A bit of history will help clarify the current state of this speciality. The first “drug” used in psychiatry was lithium. Its beneficial action in treating mania was observed in 1945 and it became part of the standard treatment of this disorder. This was followed by the accidental discovery in 1952 that the antihistamine Thorazine could be used to treat schizophrenia. The first antidepressant, Tofranil (imipramine) was discovered in 1956 and shortly after the first benzodiazepines came on the market as Valium and Librium. By 1960 the major psychiatric drugs were rapidly been developed, among them mood stabilizers, stimulants like Ritalin, antipsychotics, anti-anxiety drugs and more antidepressants. At last count there are an astounding 30 antidepressants on the market. Sales of psychiatric drugs...
by the end of the first decade of the 21st century exceeded $70 billion US per year and easily financed heavy criminal fines imposed on a number of the big companies for illegal and deceptive marketing which have added up to over $5 billion, just in the last few years.

Along with the growth in use, marketing became much more sophisticated. Physicians and patients were led to believe that psychiatric drugs addressed pathological biochemical imbalances in the brain and were needed to rectify the problem. This turned out to be incorrect but the highly appealing mythology endured even as it became increasingly evident that in fact while the biochemical action of many of the drugs came to be understood, this action could not be related to brain biochemical imbalances or any other well understood biological causative mechanism for the disorders being treated. A high (or low) point was reached when the street drug crystal meth, the subject of SWAT team raids on illegal labs, was approved in the US for attention deficit hyperactivity disorder (ADHD). The popular stimulant drug Ritalin used for the same disorder is also an amphetamine in the same class as cocaine and in some cases is sold illegally after acquisition with a prescription. It is now widely used to boost performance in school and at work among individuals with no evidence of ADHD as are other ADHD stimulant drugs.

Psychiatric disorders are quite different from most medical disorders in how they are diagnosed. For many infectious and chronic diseases, biochemical markers are common. Blood tests and biopsies are highly informative and in many cases, along with the patient presentation and history allow definitive diagnosis. There are countless examples. Blood sugar markers for diabetes, troponin for evidence of a heart attack, coronary calcium for atherosclerosis, C-reactive protein and sedimentation rates for inflammation, blood iron for anemia, enzymes for liver function and positive cultures for bacterial infection. These are standard tests in the diagnostic armament of modern medicine. Imaging allows differentiating between ischemic stroke and a bleeding stroke, the detection of tumors and aneurysms, and the angiogram reveals occluded coronary arteries. The list just goes on and on. This is what makes medical diagnosis in many cases scientific and extensively validated. But for psychiatric disorders, all one has are symptoms, although an attempt is made to quantify some of them with scales. Information is gathered from observations and matched to a dictionary definition of the disorder based on the number and in some cases severity and duration of symptoms and a diagnosis achieved. The details of the definitions are decided by a democratic process (consensus) in the dictionary writing groups and actual validation that might satisfy evidence based medicine is uncommon. Over 70% of diagnoses of these disorders come not from psychiatrists but from general practitioners and internists, and in many healthcare environments, require only a few minutes between presentation and a prescription.

THE DIAGNOSTIC BIBLE AND OVERDIAGNOSIS
What is this dictionary? It is called the Diagnostic and Statistical Manual of Mental Disorders, the so-called DSM or the diagnostic bible, probably the most widely discussed and controversial publication in the history of modern medicine. The DSM is just part of a bigger set of problems, the validity of psychiatric diagnoses, over-diagnosis and what of necessity almost always follows, over-treatment with powerful drugs accompanied by serious side effects but in many cases, with little evidence that they address the fundamental or causative aspects of the problem seen at presentation.

In the early 1970s, it became evident that something had to be done about the apparent randomness and inconsistency of psychiatric diagnoses not only within the US but in worldwide comparisons. The third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) was thus designed to remedy this problem and featured definitions of mental disorders that when properly used provided reliability equivalent to most medical diagnoses. Note that reliability does not reflect validity. DSM-III was partly in response to the critical view at the time that psychiatrists were second-class medical citizens due to their flaky and arbitrary culture of diagnosis. DSM-III still resulted in some doubtful diagnoses by
defining conditions that were no more than slightly more severe versions of such everyday problems such as mild depression, generalized depression, social anxiety, simple phobias, sexual dysfunctions and sleep disorders. The next revision, DSM-IV, was published in 1994 and subsequently had minor revisions around 8 years later. The hope that this edition would hold the line against further diagnostic inflation proved unrealistic, with the director of the project, Duke University psychiatrist Allen Frances, the head of the DSM-IV project, recently admitting responsibility for inadvertently causing increased overdiagnosis of depression, pediatric bipolar disorders and autism, the latter due partly to the addition of Asperger’s disorder to the spectrum of autistic disorders.

Amid much unfavourable commentary in the peer reviewed literature and other psychiatry-related publications, DMS-5 (not a misprint, they chose to use 5 rather than “V”) was published in April of 2013. The risks of over-diagnosis were mostly ignored and several high-prevalence new disorders at the fuzzy boundary with normality were introduced. These included worry about having a medical illness now called Somatic Symptom Disorder, normal grief such as associated with bereavement potentially misidentified as Major Depressive Disorder, and forgetfulness associated with aging labelled a mental disorder, thus confusing it with the true mild neurocognitive disorder. Temper tantrums became Disruptive Mood Deregulation Disorder, overeating the Binge Eating Disorder, and the criteria for Attention Deficit Disorder were loosened such that more adults will be deemed to have this affliction. Critics have been very vocal in stating their dim view of this diagnostic inflation.

If the notion of rampant overdiagnosis is incorrect, then one is left with a number of epidemics of unknown cause or origin and ever increasing case numbers that beg for an explanation. In a recent newsletter, Dr. Julian Whitaker MD cites the following shocking statistics.

- One in 10 American adults and one in four women in their 40s and 50s take antidepressants.
- Approximately 8 million American kids are on some kind of psychiatric drug.
- Since 2000, more than a million current or former American service men have been diagnosed with post-traumatic stress disorder, adjustment disorder, depression, anxiety, substance abuse and other psychiatric problems.
- Between 2005 and 2011, there was a 700% increase in the use of antidepressants, antipsychotics, mood stabilizers, sleeping pills, stimulants and other psychiatric drugs prescribed to US troops.

Other evidence of over-diagnosis:

- Researchers from Johns Hopkins performed a study on over 5500 adults diagnosed with major depression and found two-thirds did not meet the standard diagnostic criteria. This translates into a huge 86% who were inappropriately labelled and most probably medicated.²
- When the prevalence of ADHD is examined, classroom by classroom in a number of schools where there is a strict birth date threshold for entry into grade one, it is observed that the youngest in each class have the highest rate of diagnosis, and this is reproduced from grade to grade, suggesting that the youngest, having trouble adjusting, are considered to have a mental disorder when what is being observed is mostly merely a variation from normal.³
- In November 2013 the U.S. Center for Disease Control (CDC) presented a report available from their website which has been widely discussed and described in the media. It provided an update on the statistics regarding ADHD. We have reached the amazing point where more than 20% (one in five) 14 year-old boys have been diagnosed with a problem officially deemed a mental disorder. In addition, 13.3 % of American 11-year-old boys are being medicated for ADHD. New information also indicates the
childhood mental disorders are now diagnosed on average at age 7 with about half by age 6.

The above is just the tip of the iceberg. The simplest explanation is overdiagnosis. Overdiagnosis leads to overtreatment, and this is a problem because, as will be discussed below, the drugs used are far from innocuous. Quite the contrary, the serious problems with withdrawal, including failures and occasionally disasters, highlight that these drugs are in fact far from innocuous and probably addictive. They affect dramatic changes in some individuals which are then hard to reverse. These changes can have a profound effect on the quality of life. If the therapy was unnecessary or based on misdiagnosis, then this violates the cardinal rule in medicine, first do no harm. Managing withdrawal has become a significant subspecialty of psychiatry. This points to a serious problem.

In a research report just published which involved a large number of subjects, it was found that for those between 10 and 24 years of age, high dose antidepressants significantly increased the risk of suicide attempts compared to lower doses, with the increased absolute risk equivalent to one additional event in 150 high-dose treated patients. Thus there is a high risk and if there is any true benefit, it is modest and some studies now suggest it is nil.4

It is in fact generally agreed that some of these drugs, and especially antidepressants, are related to increased suicide ideation. All antidepressants in fact carry the highest level FDA warning of suicide risk, the famous black box. In a recent newsletter, Dr. Julian Whitaker cites the current figure of 22 suicides every day among veterans and that in 2012 suicide claimed more lives than combat among active duty troops. He also points out that today one in six service members are taking at least one psychiatric drug, and many are on a dangerous polypharmacy of addictive prescription medications that dull the senses, numb the emotions, impaired cognitive function, cause mania, apathy and aggressive behavior. Read Peter Breggin's book Medical Madness for a large collection of case histories of suicide. The emphasis is on young individuals taking ADHD medications or antidepressants. Of great concern is how much of this could have been avoided by never starting psychiatric drugs or using psychotherapy in response to mild problems.

A highly acclaimed and scholarly discussion of this topic can be found in Robert Whitaker's recent book, Anatomy of an Epidemic. Magic bullets, psychiatric drugs and the astonishing rise in mental illness in America.

THE NATIONAL INSTITUTE OF MENTAL HEALTH DROPS A BOMB
Just prior to the release of the new DMS-5 at the 2013 national convention of the American Psychiatric Association which publishes the DSM series, a source of considerable revenue to the organization, the U.S. National Institute of Mental Health (NIMH) announced a major change in how in the future research into mental disease they sponsored would be structured, and in in the process, significantly downplayed the relevance of the DSM. Up until this time, the research into disorders was based on DSM definitions to identify subjects and judge outcomes. That was now mostly history for NIMH sponsored research. The NIMH announced a new research paradigm, which was designed ultimately to provide a biological basis for mental disorders modeled after the rest of medicine. Note the tacit admission that a biological basis currently does not exist. Central to the scheme was research concerning understanding and identifying disorders in mental circuits and finding biomarkers and evidence from imaging that would make psychiatry more respectable and compliant with evidence based medicine. This announcement closely followed the announcement by the Obama Administration of a similar program aimed at the general problem of understanding the human brain, a project involving the National Institutes of Health, the Defence Advanced Research Projects Agency and the National Science foundation. The principal goal of the Obama Brain Initiative was finding a cure or treatment for Alzheimer’s and Parkinson’s diseases, diseases generally considered outside the realm of psychiatry.
An essential aspect of the proposed NIMH research involved the comprehensive study of mental circuits and other biological aspects of how the brain works in the context of mental health and disease. This appears bold and perhaps overly optimistic, simply because the brain is vastly more complex than the rest of the body. The architects of the plan believe that once an understanding has been achieved, diagnosis can be based on biological observations and therapeutic interventions designed to correct observed disorders. To gain perspective, the brain contains billions of neurons which are interconnected in what must be a horrendously complicated fashion. Think of this in terms of the computer chip with its several billion transistors in a complex set of circuits designed to be the brain of your computer. A chip-failure disorder in the computer brain, if serious, becomes painfully evident and is cured by getting a new chip or motherboard or replacing the entire computer. The engineers who designed the chip of course understand exactly how it works. Only because of remarkable technology are they able to convert their ideas and understanding of what they need into such a complex and miniaturized thing as the chip. It appears that the dream of the neuroscientists that by studying the brain circuits, the interconnections and the routes from one section of the brain to another or to the spinal transmission system, they will gain sufficient understanding of not only how the brain works, but also understand and identify pathology associated with such aspects as consciousness, emotions, moods, anxiety, depression imagination, ideas, the distinction between the mind and the physical brain if it exists, etc., all at a brain circuit or biological level. When dysfunctions are observed, the hope is that this leads to an understanding of the symptoms of disorders at the biological level and therapeutic insights such as targeted drugs that can be developed by Big Pharma or government sponsored research.

The new NIMH initiative has as a major goal making brain circuits a central aspect of the bold new approach to biological psychiatry. Perspective can be gained from comments reported in the July 19-20, 2014 weekend International New York Times distributed in Ontario, Canada. The issue was the proposed funding with 4.5 billion dollars of the Obama Brain Initiative which is closely related philosophically to the NIMH proposed program. In a short article by Tom Brady, one neuroscientist was quoted as saying “We can’t simulate the 302 neurons in a nematode brain. It’s a bit premature to simulate the 100 billion neurons in a human brain.” Professor Gary Marcus from New York University was quoted as saying “The controversy over the Obama initiative serves as a reminder that we scientists are not only far from a comprehensive explanation of how the brain works, we’re also not even in agreement about the best way to study it or what questions we should be asking.” The article also calls attention to the much touted electrical stimulation experiments that raise serious, practical and ethical questions concerning such experiments.

In the July 24 issue of Psychiatric Times Allen Frances voices a similar concern. He is focusing on the $650 million donation recently given to NIMH for genetic studies aimed at solving the mystery of mental illness. He comments that vast sums have already been spent with little to show for it. He points out that very smart people with the most sophisticated equipment have been at this for 40 years but most findings either don’t replicate or turn out to be trivial or do not yield useful generalizations. Hundreds of genes have been implicated as possibly associated with schizophrenia, but for each there could be at best only a tiny effect, if any. Furthermore, there is a huge overlap across different disorders. Again, a challenge of mind boggling complexity.

These new initiatives have some similarities with the genome projects which also emphasized optimistic downstream applications to health problems and targeted therapy. However, correlations between disease states and genes produces in most cases too many indications to be immediately useful, with small size effects only made interesting by the statistical indications that they did not occur by chance, called “chasing p values,” p being a measure of results occurring by chance. No one denies the value of insights gained regarding breast cancer and Alzheimer’s disease or guidance in breast cancer therapy by the genome approach and the well justified hope for the future, but we await the advent of great
breakthroughs with targeted therapies guided by specific genetic markers that were optimistically expected from the avalanche of data from genome projects. But compared to brain circuits, genetics seems simple since the genes provide blueprints for proteins and the action of proteins is much easier to study if not already known. Compare this to associating knowledge of aspects of neuron interconnectivity with anxiety or depression or imagination or bereavement grief. Even after the observation decades ago of a strong genetic link in schizophrenia and the identification of a biomarker, the indicated therapy was not successful. Little is translating into better clinical care.

Two other issues seem important. First, the brain’s inherent and amazing plasticity, a very well researched phenomenon although far from understood, makes the NIMH initiative like shooting at a moving target, and plasticity will introduce large time dependent variations in individuals with mental disorders. The second problem is it will be necessary to study subjects, many of whom have been exposed to psychiatric drugs. As will be discussed below, these drugs affect changes in the brain and have the potential to seriously complicate studies. The problems facing the investigators under the new NIMH sponsored research guidelines appear to be much greater than those planning and executing research under the new Obama Brain Research Initiative aimed at Alzheimer’s and Parkinson’s diseases, where there should be large numbers of patients available who have not received psychiatric drugs since they have either very modest or no effectiveness.

There are also some very fundamental issues. Understanding how the brain works has been the subject of research and speculation going back to the ancient philosophers and continues to this day. Questions such as what is the location and mechanism of memory, is the mind separate from the physical brain or is it even meaningful to consider the question of its existence, how do we form visual images of objects, do objects really exist outside the brain, what is consciousness, can individuals interact at a distance without visual or other contact, etc. These are not viewed, at least by some philosophers as trivial questions, and modern science has been of little help in providing even potentially productive paths of investigation, much less explanations that satisfy the various interested parties. All that seems clear is that these questions address extremely complex issues and that many popular views, even in academic circles, are simplistic, have no evidence or are simply dogmatic. Thus the endeavour now promoted by the NIMH and it’s bold new program, while undeniably ambitious and worthwhile, may indeed have little hope of discovering how memory, emotions, perception, imagination, grief, joy, satisfaction, anxiety, addiction, etc., work at the level of how the brain is wired and functions biologically, much less translate this new knowledge into guidance for drug development or other therapeutic initiatives. After all, there are records of individuals with very little brain matter who function normally and have high IQs. Furthermore, experiments involving removing parts of the brain have failed to provide enlightenment as to where our memory resides. Many other examples could be cited which should embarrass those who regard these fundamental problems soluble in the foreseeable future by employing the tools, admittedly of great sophistication, that are currently available or by stating the common belief expressed as “it is all just physics and chemistry, so simply give us time and all will be clear.” No one can deny the merits of the proposed endeavour, but the impact on the problems currently seen in psychiatry will probably be a long time in coming to fruition. The reader is directed to a very penetrating discussion of the above fundamental issues in a book titled Science Set Free by Dr. Rupert Sheldrake, a “philosophical” biologist, currently a fellow of the Institute of Noetic Sciences in California.

Thus there are many significant challenges for the NIMH approach. In summary, the results of this newly directed research initiative should

- Accommodate the placebo effect which in psychiatric disorders can be very strong and even equal the perceived effect of drugs.
- Explain the mechanisms of benefit derived from psychotherapy.
- Accommodate spontaneous remissions, especially those that are permanent.
• Explain how rather diverse environmental toxins appear to produce the same disorder such as autism.

• Solve the problem of distinguishing normal from abnormal. Is it possible through better understanding of the biological mechanisms of mental disease to successfully draw a meaningful line? In medicine it is frequently not that simple. Biomarkers are distributed in their values (and not necessarily a normal distribution) making thresholds somewhat arbitrary. Common examples are fasting blood glucose, glycated haemoglobin, blood pressure, liver enzymes, thyroid hormone levels, ferritin levels as a measure of iron stores, etc. It is hard to believe that the new approach will not encounter shades of gray between the black and white and require judgement calls and arbitrary and debated thresholds, just as is common in the rest of medicine. Put another way, individual variability will probably vastly complicate the successful execution of the mission the NIMH is launching.

• If the disorders the new initiative focuses on are not dependent on DSM definitions, how will they be described since there will always be symptoms and clinical dysfunction and patient complaints that initiate the physician-patient interaction. There is in fact a huge so-called mapping problem here where biological aspects found to be abnormal must be associated with what is seen in the clinic, but presumably without dealing with sets of patients selected by DSM diagnosis criteria.

The rejection of the DSM as part of the blueprint for research must not be interpreted as dismissing its usefulness. The DSM will remain essential to everyday practice of psychiatry since it has been integrated and imbedded into the language of the profession, ongoing research, drug development, the coding of disorders, and the systems of reimbursement and insurance. Its faults simply exemplify what some regard as serious problems in the profession. These include diagnoses that are not validated, the risk of overdiagnosis and the confusion between normal and abnormal, and even in some cases, the missing of a serious disorder due to a poor set of diagnostic criteria. Furthermore, it seems highly unlikely that the NIMH initiative will transform anything other than basic research for probably a number of decades, and the practice of psychiatry will change only very slowly, probably driven by the recognition by the general public of failures and dysfunction rather than by extensive new knowledge of how the brain is “wired.” The NIMH initiative may be counterproductive in discouraging important research because it does not meet their funding guidelines in the new era.

The bottom line seems to be that the 300 mental disorders enumerated in the 567 pages of the DSM are fundamentally different from the disorders in “the rest of medicine,” the latter in general being well described by the term pathological and even frequently evident at autopsy. For the individual with a mental disorder, what the pathologist sees at autopsy, if anything, is confounded by extensive prolonged polypharmacy, and this may even confound MRI interpretation. However, for a pathological mental disease such as Alzheimer’s or Parkinson’s, the signs at autopsy are generally clear, again emphasizing the distinction between a truly pathological mental disease and a mental disorder as defined by the DSM and characterized only by a set of symptoms such as prolonged bereavement for the loss of a loved one or an abnormal tendency to engage in binge eating or repeated and uncontrollable anger at a boss who is a first class jerk or worse.

**DRUG TREATMENT FOR MENTAL DISORDERS**

Things get really interesting when we examine the problem of treatment. It will probably be a decade, maybe several decades before the NIMH initiative bears significant therapeutic fruit. In the meantime, life will go on with DSM-5 dictating how the psychiatry community carries out diagnosis leading to therapy.

Today psychotherapy plays a minor role in treatment and thus the main issues reside in the drugs, what they do and don’t do. Historically, drugs were used only in severe cases of psychiatric disorders, frequently in a hospital or asylum environment. Obviously this has
changed dramatically over the years with general practitioners with no in-depth training in psychiatry dispensing prescriptions for depression, sleep disorders, anxiety, etc., with little or no differential diagnosis and little or no concern for long-term side effects or even real need. It is not uncommon to have a friend or family member who has been on antidepressants for years and the prescription is automatically refilled. In fact, from the point of view of those prescribing these drugs, the view appears to be that the benefits so far outweigh the harms, if any, that taking them for life is safe. Critics regard this as reckless, thoughtless and even malpractice. The dangers of overdiagnosis in fact reside mostly in the dangers of treatment, but of course there are always the issue of being labelled as having a mental illness which can have lifelong consequences, especially in young persons who aspire to certain professions and in some cases, the label may influence eligibility for insurance.

A CONTRARY VIEW OF PSYCHIATRIC DRUGS

The notion that psychiatric drugs are relatively safe and can be widely prescribed even by those not professionally trained in psychiatry, and that the range of eligible patients extends down to toddlers and up through residents of nursing homes, has never been effectively challenged, although there are many medically and/or scientifically trained critics who are appalled at what is going on (see the bibliography). In what follows, a contrary view will be presented regarding psychiatric drugs, which indeed suggests that there is a crisis, but that patients have a bigger one than does psychiatry.

In what appears to be the most significant and serious criticism of modern psychiatry, Dr. Peter Breggin, a well-known psychiatrist who has been an active and high profile critic of modern psychiatry for a number of years, has called attention to startling research and championed a contrary view of the treatment of mental disease, summarized in a recent medical monograph *Brain-Disabling Treatments in Psychiatry* and a new book *Psychiatric Drug Withdrawal*. Breggin is called “the conscience of psychiatry” for his efforts to reform the mental health field. In the cited monograph, he describes the brain-disabling and spellbinding effects of psychiatric drugs. The latter involves the inability of a treated patient to realistically evaluate their current condition and instead confuse change with benefit. He then thoroughly documents his views with thirteen chapters of elaboration covering the entire field of mental disorder. Breggin takes exception to the view that the common mental disorders have a causal basis in biological imbalances, and he presents a diametrically different view, holding that the imbalances have never been proven and the action of psychopharmaceutical intervention involves altering and damaging the brain, sometimes permanently. The changes which occur create the impression of benefit through changes in symptoms and behavior, but real benefit is an illusion. This contrary view, which is evidence based and has staggering ramifications, will be the main subject of this section.

The following are paraphrased from Chapter 1 of Breggin’s monograph and documented in this and later chapters and in a recent journal article. The implications of these ten principles are profound and disturbing and provide an additional foundation for the view that psychiatry is in crisis.

I. All biopsychiatric treatments [psychiatric drugs] share a common mode of action: the disruption of normal brain function.

This principal implies that as soon as a toxic dose level is reached, the drug begins to have a psychoactive effect. Without toxicity, there would be no effect. All major classes of psychiatric drugs including antidepressants and stimulants can destroy neurons.

II. All biopsychiatric interventions cause generalized brain dysfunction.

The brain function is highly integrated and disabling certain mental functions will typically cause some generalized dysfunction. Breggin cites the production of emotional dullness, lethargy or fatigue and even if the effect is small, it is likely to impair attention, concentration,
alertness, self-concern or self-awareness and social sensitivity. He also points outs that shock treatment and psychosurgery always produce generalized dysfunction.

**III. Biopsychiatric treatments exert their therapeutic effect through impairment of higher human functions, including emotional responsiveness, social sensitivity, self-awareness or self-insight, autonomy, and self-determination. If the effects are drastic, they include apathy, euphoria and mania, and lobotomy-like indifference.**

Biopsychiatric interventions impair higher mental, psychological and spiritual functions, the result of generalized brain dysfunction as well as specific effects on the frontal lobe, limbic system and other brain structures. Breggin calls the lobotomy-like indifference to self and others **deactivation**, and points out that recent research confirms that these effects occur with SSRI antidepressants, stimulants, and the newer antipsychotics. Chronic use of benzodiazepines and mood stabilizers will also produce a degree of deactivation.

It is Breggin’s view that biopsychiatric treatments are deemed effective when the physician and/or patient prefer a state of diminished brain function with its narrowed or shallower range of mental capacity or emotional expression. When the drugged individual indicates feeling more effective and powerful, this is most likely due to an unrealistic appraisal, impaired judgement, or euphoria associated with what is called medication spellbinding. The inability of a patient to perceive a drug’s true impact is characteristic of spellbinding.

**IV. Each biopsychiatric treatment produces its essential or primary brain-disabling effect on all people, including normal volunteers and patients with various psychiatric diagnoses.**

This principle attacks one of the foundations of modern psychiatry, i.e. there are specific psychoactive drug treatments for specific mental disorders. All psychiatric drugs cause a generalized impairment of the brain function which reduces overall mental and emotional function in both patients diagnosed with mental disorders and normal individuals. When the treated condition goes into remission or disappears, it is probably spontaneous or a placebo effect. Placebos are in fact extraordinarily effective. Polypharmacy appears to frequently over time make the condition worse.6

Evidence for drug-induced brain damage and disablement includes PET scans that reveal changes in metabolism in various regions of the brain.9-11 MRI scans reveal atrophy associated with antipsychotic treatment in several regions of the brain,6,12,13 an observation prompting a call for limiting the use of antipsychotics for those under 18.14 Atrophy has also been observed for antidepressants and Breggin argues that age limitations should extend to all psychiatric drugs.6 In addition, there is tardive dyskinesia (Parkinson-like uncontrolled and odd movements), not an expected presentation, significant and progressive memory and cognitive impairment, and various levels of amnesia, apathy, and loss of a connection with surroundings.6,7 These are symptoms of what Breggin terms **Chronic Brain Impairment (CBI)**.

Behavioral changes attributed to CBI are traditionally attributed to the disorder being treated, and as they become more pronounced the traditional view is progression, or the treatment has unmasked a new underlying disorder. Doses are increased and medications added, potentially creating a disastrous feedback loop.6 Furthermore, CBI makes the interpretation of clinical study endpoints and judgements regarding efficacy open to serious questions. Patients are not necessarily better, they are simply different, and this may be in ways that are undesirable long-term.

Additional principles are as follows:
V. Patients respond to brain-disabling treatments with their own psychological reactions such as apathy, euphoria, compliance or resentment.

VI. To the extent that a physical disorder [e.g. Alzheimer’s disease] of the brain afflicts the patient, currently available biopsychiatric treatments will worsen or add to the disorder.

VII. Individual biopsychiatric interventions are not specific for a particular mental disorder.

VIII. The brain attempts to compensate physically for the disabling effects of biopsychiatric interventions, frequently triggering additional adverse reactions and withdrawal problems.

IX. Physicians prescribing biopsychiatric treatments often have an unrealistic appraisal of the risks and benefits.

X. Patients subjected to biopsychiatric treatments often display poor judgement about positive and negative effects of the treatment on their mental and emotional functioning, often reflecting medication induced spellbinding (intoxication anosognosia).15

Spellbound individuals fail to perceive their degree of mental or emotional impairment due to drug treatment.6,15,16 They tend to rationalize and justify their drug-induced mental distress, typically blaming negative feeling on themselves or on someone else. They often feel as if they are doing better even when in fact they are getting worse. Sometimes drug therapy leads to violence against themselves or others. Finally, extreme spellbinding produces what Breggin calls medication madness. The individual feels driven or compelled to behave totally out-of-character and in potentially disastrous ways such as murdering a family member while totally unaware of the significance of this act.17 Breggin presents a biological basis for medication spellbinding and a number of case histories.15,16

Obviously, the psychiatry establishment and Big Pharma take a very dim if not hostile view of Dr. Breggin's heretical position. While general statements about side effects of psychiatric drugs are condoned because their existence cannot be denied, it appears more or less taboo to talk about the issues he has continuously raised and documented for over a decades. Just try raising the subject of permanent brain damage while your physician is suggesting a prescription for an antidepressant or antipsychotic. Or ask your paediatrician for a list of papers describing testing the safety of psychiatric drugs being suggested for your child, and demonstrated safe by non-industry supported researchers over a the full period of development into adulthood. Adverse effects can be subtle but very serious, require years to become clinically manifest, and recognition of the connection is inhibited not only by the absence of significant, valid studies but by a strong culture of denial.

TARDIVE DYSKINESIA

Tardive dyskinesia (TD) is a movement disorder, similar that seen with Parkinson’s disease victims, that has been associated with antipsychotic drugs including older ones such as Haldol and Thorazine and new ones such as Seroquel, Abilify, Geodon, Risperdal, and Zyprexa. The newer or so-called atypical antipsychotics were promoted as having a lower rate of TD incidence, but the rate has remained significant.18,19 This connection is discussed by Peter Breggin (see peterbreggin.com). Manifestation of TD generally takes a few months after exposure to antipsychotics, but Breggin has seen TD symptoms develop after only a few doses. He claims that 15%-24% of patients taking these drugs will develop TD by the third year. When given to the elderly in nursing homes, the rates exceed 20%-30% per year with concomitant disabling effects. The muscle disorder can afflict the face, eyelids, tongue, mouth, neck, shoulders, torso, arms and legs and when severe can be disfiguring and
humiliating and strongly impact the quality of life. Since the presentation of TD to some extent mimics Parkinson’s disease, this may lead to misdiagnosis. In one malpractice suit where he acted as the psychiatric expert, an autistic child had been initially put on antidepressants and his mental and behavioral condition deteriorated a common observation according to Breggin when these drugs are used on children. He was then put on an antipsychotic and then a second psychiatrist. The defendant in the law suit put him a second antipsychotic despite the appearance of TD symptoms. The child continued to deteriorate and developing severe TD. The court awarded $1.5 million in this malpractice litigation.

The above illustrates the common scenario. The antidepressant is prescribed to treat symptoms, not the cause of the disorder. Unsatisfactory results prompt polypharmacy, eventually with powerful antipsychotic agents, which again not only did not address the underlying causes, but eventually produce permanent damage and disability. One would think that even the spellbinding effect of psychiatric drugs would not prevent a patient from realizing that TD represents a profound deterioration, rather than benefit, but evidentially any concern generated was not enough to initiate withdrawal. Unfortunately, in some cases the damage is permanent, a devastating consequence for merely treating symptoms.

**FORENSIC ISSUES**

Readers interested in the legal, ethical and forensic aspects associated with psychiatric drugs are referred to Breggin’s website (peterbreggin.com). Breggin has been practicing for 60 years and has acted as an expert witness in a number of legal cases. These are described on this website. The list of downloadable publications should be of particular interest both for parents, patients, and lawyers. For example, in the book *The Attorneys Guide to Defending Veterans in Criminal Court*, Chapter 10 by Dr. Breggin is titled TBI [Traumatic Brain Injury], PTDS and Psychiatric Drugs: A Perfect Storm for Causing Abnormal Mental States and Aberrant Behavior, and should interest lawyers, veterans and their families. Another paper titled *The Rights of Children and Parents in Regard to Children Receiving Psychiatric Diagnoses and Drugs* should be of great interest to parents with children diagnosed with ADHD or bipolar disorder and prescribed either stimulants or antipsychotics. His view is that the goal should be a prohibition against giving psychiatric drugs to children. Rather, alternative approaches should be employed to meet their needs within the family, school and society. He makes a case that it is child abuse to give children these drugs except for surgical anaesthesia, relief of physical pain and control of seizures. Since he has had a number of children as patients over the many years of his education and practice, his views are worth considering seriously.

**DISCUSSION AND CONCLUSIONS**

As mentioned above, longstanding theories regarding various mental disorders held that important neurotransmitters (e.g. serotonin and dopamine) were out of balance. Patients had a diseased brain due to too much of this neurotransmitter or too little of another. This provided a useful paradigm for drug discovery and marketing. Note the name of many antidepressants, *Selective Serotonin Reuptake Inhibitor (SSRI)*. In a recent book by a professor of psychology from the University of Hull in the UK, the author devotes an entire chapter to this theory titled “The myth of chemical imbalance.” Professor Kirsch argues that not only is the theory not proven, he regards it as about as close as a theory gets in science to be disproven by evidence. Yet the theory of chemical imbalance and later simply the notion of benefit from manipulating brain chemicals has driven drug design and promotion for several decades.

The chemical imbalance hypothesis had its origin decades ago in perceived symptomatic improvements achieved by antidepressants. It is thus significant that there is no difference between the benefits found for mild and moderate depression when one compares antidepressants to a placebo in randomized controlled trials. The strong placebo effects add an interesting dimension to the issues under discussion. This effect is also proposed to account for antidepressants appearing to provide only modest benefit in severe depression.
In this case, the disorder blunts the action of the placebo effect and may falsely indicate a small benefit. The use of an active and convincing placebo yields a null benefit even for severe depression treated with antidepressants.20 Growing evidence that antidepressants are ineffective should refocus attention on side effects, which now become indefensible.

Individuals diagnosed and given psychiatric drugs may suffer from brain damage as discussed above, and may frequently need progressively higher doses and additional drugs. The initial prescription for a single drug to treat a mild problem that histrionically would never have been treated with drugs may result in a downhill spiral to disability and a poor quality of life. Side effects reflecting brain damage may be interpreted by the prescriber and patient as worsening of the disease or unmasking an underlying disease when in fact it is caused by the treatment. Spellbinding can cause the patient to be unaware of mental deterioration, and if treatment goes on long enough, drug withdrawal, if even tried, may not result in a complete remission and may not even be a realistic option. Case histories make it clear that the end result can be the loss of a normal quality of life and in some instances an exit from the real world and total disability. Of course, not everyone reacts in this fashion, but enough do that this should be a cause for great concern. The strongest resistance to properly interpreting these abnormal and telltale changes due to psychiatric drugs seen in family members or children comes from the notion that no doctor would prescribe drugs that may do what is being described in this review and that anyway, governments protect the patient from such practices. In connection with this latter point, have individuals with faith in government regulators never heard of off-label prescriptions or the successful marketing of unapproved uses? Have they never heard of the billions of dollars in criminal fines pharmaceutical firms regularly pay for these offenses but which are simply considered the cost of doing business. They should read Bad Pharma. How Drug companies Mislead Doctors and Harm Patients by Ben Goldacre. They will never look at a prescription the same way after this introduction to the real world.

It is universally recognized in the profession that withdrawal can be dangerous, difficult to orchestrate and some attempts fail with the need to return to the full dose regime. Contrary to modern practice, withdrawal should be, according to Breggin, the first priority no matter what the stage of the disorder. For someone on psychiatric polypharmacy who is disabled, there is probably no hope unless drug therapy is withdrawn. Withdrawal requires assistance from family and a physician, psychotherapy and family therapy, and the security of 24/7 professional crisis assistance. The case histories in Breggin's latest book should give great hope to those who have been convinced, generally reluctantly and frequently by parents or a spouse or other family members, that they are on the wrong road and need help to reclaim their life before it is too late. The presence of spellbinding may make it difficult to get patient consent.

Breggin suggests with certain qualifications, that drug treatment in all cases is unnecessary. Rather, when indicated in severe cases the problem is treatment duration, which should almost never be permanent and which needs to be as short as possible. But he strongly believes that various forms of psychotherapy are the alternative to be considered at almost all initial presentations. In addition, poor diet, food allergies, micronutrient deficiencies, hormone imbalances (e.g. thyroid) and gut problems should not be ignored when considering alternative diagnoses.22,23 Unfortunately, it appears that thorough differential diagnosis is rare in those presenting with psychological disturbances and not even practical in the present culture of medical practice.

Breggin devotes Chapter 16 in his monograph to psychotherapy, and revisits this in Chapter 19 of his book on withdrawal. In the latter, he cites (p258) the approach used in a district of Finland for many years where the first response to a psychiatric crisis is from a mental health team in a home visit and involves interviewing the whole family. Psychotherapy is the preferred approach. Medication is rarely used and only for short periods. As a result of this program of considering the whole family and using psychotherapy, unemployment and
disability due to psychiatric problems has been dramatically reduced. It is also very interesting that in this area of Finland, a six months period is required to verify schizophrenia. The disorder as a diagnosis has disappeared from this region.

Finally, a significant omission from the above has been the role of the pharmaceutical industry in the writing of the diagnostic manuals and in developing and promoting the drugs used in practice. For DSM-III through DSM-5, the integrity of writing has been tarnished by the presence among the writers and experts of medical scientists with conflicts of interest associated with ties to the industry. In addition, the industry has infiltrated academia to an alarming extent and as well appears to have powerful friends in regulatory bodies. The illegal and fraudulent marketing practices of the pharmaceutical industry, especially for indications not approved for a given drug (off-label) has become so widespread that it is hard to find a major company that has not responded to criminal charges by paying huge fines but refusing to go to court. There are now two comprehensive discussions available of these problems in the form of books written by physicians, which make exceedingly depressing reading. They are Bad Pharma. How drug companies mislead doctors and harm patients, by Ben Goldacre which was mentioned above, and Deadly Medicines and Organized Crime. How Big Pharma has corrupted healthcare, by Peter Gotzsche.

There is no doubt that individuals with severe mental problems need immediate help, and that psychiatric drugs can be very useful. Psychotherapy and tapering off drugs after the initial treatment does not seem to be very popular, and in fact, if large numbers of individuals diagnosed with psychiatric disorders elected or were advised to seek psychotherapy, they would find a significant shortage of qualified therapists. However, it can be argued that for mild or moderate disorders, psychotherapy should be the first line treatment since one avoids all the problems of side effects, withdrawal, spellbinding, and if Peter Breggin is right, avoiding potentially permanent brain damage from a therapy that leaves the fundamental problem unaddressed. Psychotherapy also should not impede spontaneous recovery whereas drugs have the power to do this. Case histories which can be found in the books cited above and listed in the bibliography make it clear that there is a very significant risk of someone initially presenting with a mild disorder, quite possibly a variant of normal, who is medicated and then gets worse, spirals down to polypharmacy, is disabled and ends up in an institution. Some of these individuals can be totally salvaged by drug withdrawal, nutrition, addressing hormonal problems if they exist and psychotherapy. If this is not tried, they have, to use common phrase, had it, in fact probably for life.

A cynical but perhaps realistic view of modern psychiatry is that its greatest successes have been in orchestrating total and permanent withdrawal from the drugs, giving back to patients their lives. Furthermore, one of the biggest failures seems to be associated with interpreting the worsening of a mild or moderate disorder by viewing it as real progression or the unmasking of an underlying disorder which must now be treated, when the alternative explanation, namely that the drug therapy is making the patient worse, is almost a taboo subject. The end result of not entertaining the alternative hypothesis is that someone treated for nothing more than a variation of normal may have their life ruined and yet this is misunderstood to the point where it controls much of standard practice. The lucky ones are sometimes saved from this fate when family and friends notice that the person they knew is “not there” any longer and ask the question, could this be the drugs the person is on? Aggressively pursuing this hypothesis can save a loved one but overcoming drug induced spellbinding can be a huge challenge. What is being described is in fact, a major component of the crisis in psychiatry. Drugs do not in many cases address the causes of the problem that has been diagnosed, they merely induce changes which both the physician and the patient initially interpret as beneficial when in fact no progress has been made and significant harm is on the way. Again a view that is taboo.

It was recently reported that the pharmaceutical industry has largely abandoned drug development for mental illnesses such as schizophrenia, bipolar disorder, autism and
depression. Critics might comment that the industry has come to realize that past drug development has been based on a false paradigm. After all, as discussed above, there is now evidence that probably all 30 antidepressant drugs currently marketed are no better than a placebo for mild to moderate depression. Sooner or later, the house of cards will collapse.

Why is all of this important? Simply because we now live in a world where it is unusual, at least in developed countries, for anyone to be untouched by the revolution that is taking place in mental health, led by Big Pharma, the psychiatric profession, uncritical or misguided physicians and abetted by government regulatory bodies. It is highly unlikely that readers of this review will fail to have family or friends (or friend’s children) who have not come under the influence of this movement and succumbed to taking psychiatric prescription drugs. It is also highly unlikely that the true risks are appreciated. The medicalization of huge numbers of individuals for disorders which are not understood on a biological or mechanistic level and may, in many cases in fact be simply variations of normal, has resulted in the use of powerful drugs which appear to unfavourably alter their brain biochemistry and neurobiology. This is reason to stop and reflect on what is really going on. Quality of life is at stake and the risk of permanent impairment or even suicide real. Probably the most frightening thing of all is that antidepressants and antipsychotics are now being given even to toddlers and pregnant women. Obviously, no one has ever studied the long term effects of psychiatric drugs on the normal development processes, prenatal or postnatal, the latter over a significant period of many years, and anyone who trusts industry sponsored trials is simply naive.

Psychotherapy, which takes a number of different forms depending on the patient’s presentation, would appear to be the safest solution to non-crisis psychiatric problems, with drugs only the very last resort. Watchful waiting also has merit, allowing self-healing. Disorders such as hypothyroidism must be ruled out with an assay of the critical hormone T3, not just a TSH blood test. When possible and appropriate, the atmosphere and culture present in the patient’s family as well as the school environment must be examined. As Peter Breggin emphasized in the title of an article, treat the classroom, not the child. The ten minute office visit resulting in a prescription for a psychiatric drug should be considered malpractice.

Finally, one of the most convincing arguments made for the existence of a serious crisis in psychiatry is laid out in shocking detail in some of the case histories that conclude Dr. Allen Frances’ book Saving Normal. This chapter, titled The Worst and The Best of Psychiatry, alone is worth the expense of purchasing the book. If this is not enough, read Medical Madness by Peter Breggin. Disbelief that these case histories can actually be true illustrates the magnitude of the problem which countless individuals are facing today.

**WARNING AND DISCLAIMER**
Withdrawal from any psychiatric drug must never under any circumstances be undertaken except with the supervision and help of a trained professional and with a 24/7 back up in place in event of a crisis. This is not simply a matter of being cautious. Withdrawal reactions can lead to horrific events and even death. This review is intended only to provide information and documentation and must not be regarded as conveying medical advice. Individuals with problems related to the topic of this review are advised to seek professional help.

**BIBLIOGRAPHY**

Those wishing to read books by qualified and creditable authors which present a contrary view to that projected by the American Psychiatric Association and the pharmaceutical industry should consider the following. These represent highly significant contributions to the psychiatric literature and provide a valuable and perhaps highly disturbing perspective. Also, note that critics of modern psychiatry sometimes quote passages from Lewis Carroll’s Alice’s Adventures in Wonderland.


• Medical Madness: The role of Psychiatric Drugs in Cases of Violence, Suicide and Crime. Peter Breggin, MD. St. Martin’s Press, 2008


• For a fascinating account of the evolution of alternative medicine in psychiatry, read Adventures in Psychiatry by Abram Hoffer, MD.

All of these books are available from Amazon.com.

REFERENCES