

Schizophrenia: The Latex Allergy Hypothesis

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History of Schizophrenia

In his outstanding review *Schizophrenia and Civilization*, Torrey¹ makes a very strong case that this disorder is relatively new. Indeed he presents convincing evidence that a major increase in the incidence of schizophrenia paralleled the onset of the Industrial Revolution. To cite him directly:

It was as if somebody rang a bell precisely at the turn of the nineteenth century to herald the official entrance of schizophrenia. Whereas up to that point there appear to have been at best a few scattered cases in the literature, classical schizophrenia was suddenly being described by different people in different places all at about the same time. Such an entrance for a disease is rather dramatic. Almost from the first historical suggestions of schizophrenia, an accompanying theme can be heard in the background: Insanity (and schizophrenia) were rapidly increasing. The persistence of this idea throughout the nineteenth century and into the twentieth is one of the most striking facets of the short history of schizophrenia.

This dramatic increase in schizophrenia was probably first documented, in 1829, by Halliday¹ who claimed insanity had more than tripled in England during the previous 20 years. A similar increase in prevalence was obvious in France where, after an extensive analysis, Renaudin² established there had been a major increase in insanity between 1835 and 1854, especially in younger, more prone to schizophrenia, age groups. In 1861 Griesinger remarked on the growing number of insane in Germany, while six years later Belgrave¹ asserted that the same phenomenon had occurred in Denmark. Even stronger proof of an increase in schizophrenia, during the Nineteenth Century, was provided by the Australian physician, Tucker.² He visited 400 asylums, mainly located in Europe and the

United States, during the period 1882 to 1885. His report *Lunacy in Many Lands* described his three-year odyssey, concluding that the vast majority of superintendents of asylums believed that insanity had recently increased and this "must be accepted as a fact."

Statistical evidence to support the view that insanity was on the rise during the Nineteenth Century began to accumulate in 1840, in the United States, with the first census that identified the "insane and idiotic." Later censuses recorded these two categories independently. From these data, Gorwitz⁴ calculated that, in 1840, the United States prevalence rate for insanity was 50.7 per 100,000. By 1860 it had risen to 76.7, reaching 183.3 per 100,000 population by 1880. It would appear, therefore, that in the United States there was more than a three-fold increase in insanity, during a 40 year period, in the middle of the Nineteenth Century. During the same time span, the number of inmates in insane asylums rose from 2,561 to 38,047. By 1904² there were 150,151 such patients.⁵

On the basis of this evidence, Torrey¹ concluded that "schizophrenia, as we know it, is probably of recent origin, and the reasons for this have to do with the spread of civilization and its concomitants." This relationship between Western industrial civilization and schizophrenia appears to be continuing today. In India, for example, there have been several studies published since 1966 which support the view that the disease is most prevalent among the more highly educated and/or westernized castes.¹ Similarly, in northern Ghana, between 1937 and 1963, as Westernization occurred, the prevalence of schizophrenia rapidly increased.¹ In Papua and New Guinea, more than a twenty-fold difference in schizophrenia prevalence was identified among districts, those where the disease was most common having the greatest contact with Western civilization.¹

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In 1988, this author⁶ published the results of a study which involved correlating the prevalence of schizophrenia in the United States (based on the number of patients in 272 state and county mental hospitals in 1965) with 219 environmental variables. Five of the seven strongest associations were found to be between the prevalence of schizophrenia and indicators of industrialization, such as the proportion of the population employed in manufacturing ($r=0.55393$, $p=0.0001$) and industrial water withdrawals ($r=0.54871$, $p=0.0001$). While it may be true that schizophrenics tend to relocate in cities,⁷⁻⁸ the preceding description of the growth of this disorder during Nineteenth Century industrialization suggests there is more to the relationship than this.

The Bell Ringer?

The evidence, therefore, suggest that schizophrenia was rare until about 1810 and then began to spread rapidly throughout industrialized countries. There are several plausible explanations for such a phenomenon, each of which will now be briefly reviewed.

Infectious agents

In 1913, the discovery of spirochetes in the brains of patients with neurosyphilis encouraged speculation that schizophrenia might also be infectious. Since many viral diseases including influenza, measles and rubella tend to diffuse more rapidly in high density urban centres, it has been suggested that the virus causing schizophrenia might only be able to diffuse as a result of the urban growth spawned by the Industrial Revolution. There are many weaknesses in this argument, not the least of which are the global pandemics, such as the bubonic plague, and syphilis which predated industrialization.⁹⁻¹⁰ Indeed, if schizophrenia is caused by a pathogen, why does it still fail to spread rapidly in the Developing World? HIV has shown no such reticence. To date, no pathogen has been iden-

tified that can cause schizophrenia, despite repeated attempts to identify one. Kauffman and colleagues,¹¹ for example, inoculated the brain tissue from ten schizophrenics into 57 experimental animals, including chimpanzees, monkeys and guinea pigs. No behavioural or neuropathic differences were observed when compared, over six years, with control animals.

Pollutants

The Industrial Revolution brought with it an enormous range of pollutants that adversely affected air, water and soil quality. By 1977, the America Chemical Society had registered some four million chemical compounds, 32,000 of which were in commercial use.¹² It is unknown how many of these are potentially dangerous, although there are currently some 2,450 substances that are thought to cause cancer is the workplace.¹³ While attempts are generally made to establish the possible carcinogenicity of such industrial chemicals,¹⁴ their potential effects on mental health rarely appear to be considered.

Clearly, while it is possible that one of the early pollutants created by the Industrial Revolution "rang the bell heralding the official entrance of schizophrenia,"¹ it seems unlikely. Coal and associated products drove initial industrialization but petroleum is now the dominant energy source of the Developed World. A vast array of other changes have occurred to the industrial base of the Developed World without any associated major fluctuations in the incidence, or prevalence, of schizophrenia during the twentieth century. If schizophrenia is caused by a pollutant, why is this disorder most prevalent amongst India's highly educated and westernized castes,¹ who are less likely than the urban poor to be exposed to pollutants? Similarly, why is the prevalence of schizophrenia so elevated in Ireland and Scandinavia, hardly amongst the most highly polluted centres of Europe?²¹⁵

Product(s)

In the author's opinion, schizophrenia is most likely to be associated with exposure to seasonally used product or products. If this is the case, such goods must have been invented, or widely diffused in Britain in the first two decades of the Nineteenth Century¹ and must then have been rapidly accepted elsewhere in the Industrialized World. Such products must still be in demand today, especially in urban centres and must be rapidly accepted by indigenous populations exposed to westernization. Since in the United States only one out of every hundred inhabitants¹⁵ eventually develops schizophrenia, the majority of the population either do not use, or are unaffected by, the product(s). An extensive literature search identified only one substance, latex and associated rubber products, that met these criteria. The possibility that schizophrenia is fundamentally a latex allergy, therefore, will now be discussed in more detail.

Latex and the Industrial Revolution

In the Sixteenth Century, Spanish explorers discovered that the aboriginals of tropical South America used rubber. Chroniclers described their process for making balls from the milk of the tree *Havea brasiliensis* by smoking latex on a wooden paddle to evaporate its water and so cure the rubber.¹⁶ They also wrote of the use of the same substance to create waterproof coats, capes and shoes. For many years, the Spaniards tried to duplicate these waterproof native products but were unsuccessful, so that rubber remained a European museum curiosity for two centuries. However, in 1791, the English manufacturer Samuel Peal patented a method of waterproofing cloth by treating it with a solution of rubber in turpentine. By 1823 Charles Macintosh had established a plant in Glasgow, Scotland for the manufacture of macintoshes, the waterproof, rubberized garments that still carry his name.¹⁶ As a

result, therefore, rubber was in widespread use in England by 1829, when Halliday¹ commented on the recent rise in insanity in that country.

Interest in rubber grew rapidly in industrialized Europe and, in 1834, the German chemist Friedrich Ludersdorf and the American chemist Nathaniel Hayward both discovered that adding sulfur to gum rubber lessened the tackiness of finished rubber products, increasing their consumer appeal. Rubberized goods also had become very popular in the United States by the 1830s and bottles and shoes made from it were being imported, in large numbers, from South America. Other rubber articles were being brought from England. As a result, in 1832 John Haskins and Edward Chaffee established the first rubber-goods factory in the United States, at Roxburg, Massachusetts.¹⁶ Rubber use in the United States, therefore, had become widespread just before the first 1840 census which identified the "insane and idiotic." Its use continued to increase throughout the Nineteenth Century, as did the prevalence of schizophrenia. During this entire period, manufacturing processes improved and the diversity of rubber products markedly increased. After the invention of the pneumatic tire in 1877, rubber from its wear gradually became a ubiquitous air pollutant throughout the Industrialized World. From carpet backing to tennis balls, wherever "civilization" spread so to did rubber.¹⁶

Latex Allergies

Latex is the milky fluid found in the specialized lactiferous cells of many higher plants. It is characterized by the presence of colloidal particles of terpenes dispersed in water and it also contains a very complex emulsion of gums, tannins, resins, alkaloids, proteins, oils, starches and sugars.¹⁷ Most commercial gums, including rubber and chewing gum, are made from refined latex. By far the most important commercial source of latex is the rubber tree, *Havea brasiliensis*.¹⁶

Less than one per cent of the general public is allergic to latex from the rubber tree.¹⁸ However, constant exposure in health care workers and in children with spina bifida and other conditions that involve numerous surgical procedures increases susceptibility to allergies.¹⁹ To illustrate, Liss and co-workers conducted a survey of 1351 employees of a general hospital in Hamilton, Ontario. The prevalence of latex sensitization, as shown by skin prick tests with latex reagents, was 12.1 percent. It did not vary by gender, age, hospital or smoking status.²⁰

A "latex-fruit syndrome" has been identified, however, by Blanco and co-workers²¹ and allergy to bananas often occurs in patients sensitized to latex.²² In addition, the latex of papaya is also a significant inflammagen.²³ In contrast, synthetic rubber does not contain allergy-inciting plant proteins and is derived from petrochemicals.

Allergic reactions to latex can include skin rashes, itching, hives, burning eyes, swollen lips and tongue, difficulty breathing, wheezing, dizziness, abdominal pain, nausea and diarrhea. In rarer cases, a strongly allergic individual suffers shock; blood pressure drops markedly, the throat swells and airways in the lungs constrict. Without immediate treatment with epinephrine, death occurs.²⁴

There is a considerable biochemical literature that has explored exactly what happens on exposure to latex. It is known, for example, that chronic inflammatory response usually characterized by the presence of numerous polymorphonuclear leukocytes.²⁵ Matthews and co-workers have shown that when such polymorphonuclear leukocytes are activated by latex (polystyrene) beads, oxidation of adrenaline to adrenochrome is detectable within five minutes and continues for at least four hours.²⁶ Interestingly the treatment of choice for anaphylaxis, whether caused by latex,²⁷ peanuts or insect stings,²⁸ is epinephrine, a dilute solution of adrenalin.

This tends to suggest that the rapid conversion of adrenalin to adrenochrome is a common phenomenon associated with a large number of allergic reactions. Interestingly, as will now be discussed in more detail, this process also may be of major importance in schizophrenia.

The Adrenochrome Theory of Schizophrenia

Schizophrenics frequently display abnormally high levels of the hallucinogen adrenochrome in their urine. This is naturally created from adrenalin by oxidation. For decades, Hoffer²⁹ has successfully treated schizophrenics with nutrients which are designed to lower such elevated adrenochrome levels. This goal can be achieved by the use of the natural methyl acceptors thiamine (vitamin B₁), riboflavin (vitamin B₂), niacin (vitamin B₃) and ubiquinone (Coenzyme Q10). Niacin is usually the treatment of choice. The oxidation of adrenalin to adrenochrome occurs in two steps. Initially, adrenalin loses one electron to form oxidized adrenalin, a highly reactive molecule. In the presence of nicotinamide adenine dinucleotide, which is created in both oxidized (NAD) and reduced forms (NADH) from niacin, oxidized adrenalin recaptures one electron to reform adrenalin. If NAD and NADH are in short supply, however, oxidized adrenalin loses another electron and is converted to adrenochrome. This second reaction is not reversible.²⁹ Adrenochrome, therefore, cannot be converted back to adrenalin. This explains why many schizophrenics display depressed levels of noradrenalin and elevated levels of adrenochrome.²⁹

In a letter to the editor of the *Journal of Orthomolecular Medicine*, this author³⁰ has argued that schizophrenics are also typically very deficient in glutathione peroxidase because it acts as a natural defence against adrenochrome.³¹ It was further suggested that, when this seleno-enzyme is used to protect adrenalin from oxidation, its stores are likely to be depressed. In

schizophrenics this, in turn, is thought to result in excessive oxidation of the essential fatty acids and hence failure of formation and action of certain crucial prostaglandins.^{32,33} This relationship explains why schizophrenia is more prevalent in low selenium environments.^{6,34} It is possible that such essential fatty acid and associated prostaglandin deficiencies may account for the brain atrophy and increased ventricle-brain ratios, identified in chronic schizophrenics, by Buckman and co-workers.³⁴ In summary, evidence suggests that the excessive production of adrenochrome by schizophrenics creates a cascade of abnormal biochemical responses that ultimately cause physical damage to the brains of long-term, chronic patients.³⁵

Schizophrenia: The Latex Sensitivity Hypothesis

The evidence presented here does not prove that schizophrenia is a latex sensitivity disorder. Nevertheless, it cannot be denied that initial exposure to rubber in Europe occurred at exactly the same time that schizophrenia prevalence dramatically increased. It is also probable that sensitivity to latex and schizophrenia are both associated with the abnormal continuous oxidation of adrenalin to adrenochrome. The possibility exists, therefore, that schizophrenia is a consequence of latex sensitivity. If this is the case, a new avenue is opened for the treatment of this disorder.

Figure 1 (p. 88) presents a heuristic model that identifies seven major steps in the postulated development of chronic schizophrenia. This illustration also draws attention to a series of possible interventions which may slow, or halt, the process. In many ways it is similar to Fischhoff and colleagues³⁶ model of hazard causation, but is applied here to an individual, rather than to a society at risk from earthquake or flood.

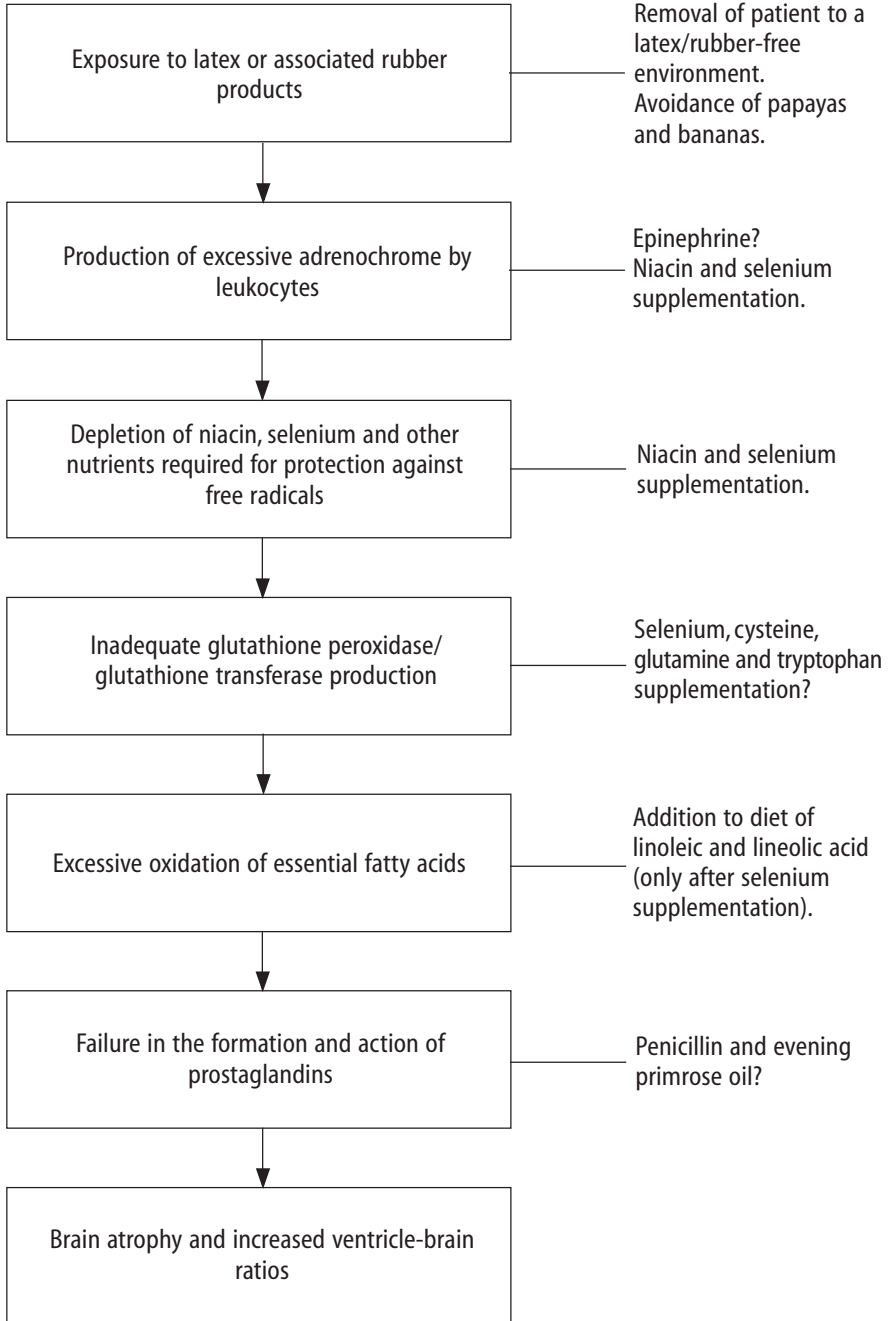
To effectively test the schizophrenia-latex hypothesis a series of direct observations are needed in order to answer the fol-

lowing basic questions. Firstly, is there any evidence that schizophrenics are abnormally allergic to latex? There are two ways to test for such allergies. In the skin-prick test, a very small amount of diluted latex, or one of its proteins, are injected beneath the skin, or applied to a small scratch on the back or arm. In allergic patients, a raised area surrounded by redness appears, at the tested site, in some 15 minutes.³⁷ This test should be performed only by a qualified physician. An alternative to the skin-prick test is a blood test for immunoglobulin E. (IgE anti-latex antibodies by RAST testing).

A second question that requires answering is "Do schizophrenics' symptoms vary as the amount of latex or rubber in the environment alters?" Certainly, Woodruff and colleagues have shown that exposure to rubber can cause inflammation of the brain.³⁸ One comment seems in order here. It is going to be extremely difficult to provide a rubber free milieu. Hospitals are full of products, ranging from gloves to enema tubing and electrode pads, that contain latex. Even rubber stoppers on medication bottles have been shown to cause allergic reactions in sensitive individuals.³⁹ Similarly, the typical home includes everything from rubber boots and running shoes to rubber filled pillows and rubber backed carpets, while the use of latex paint has been ubiquitous. Some of this rubber is natural and is derived from latex and contains allergy inciting plant proteins and some is synthetic and apparently does not.³⁹

It would also be of great interest to know whether supplements of selenium and other nutrients, designed to increase glutathione peroxidase levels and so reduce adrenochrome production and the oxidation of essential fatty acids, reduce schizophrenic symptoms. One word of warning here, although Rudin and colleagues³² have had some success in the treatment of schizophrenia with linseed oil, they argue that supplementing the diets of schizophrenics with essential fatty acids is suc-

Figure 1. A heuristic model of the possible development of schizophrenia in susceptible individuals, and the potential intervention strategies.



cessful only when selenium intake is optimum. To quote these authors directly, "If a primate is deficient in the antioxidant element selenium, providing supplemental essential fatty acids will only make the selenium deficiency worse. Whatever selenium stores are in the body will be used up that much sooner in an attempt to protect the EFA. (essential fatty acids) from oxidative damage". Interestingly, as early as 1979 Vaddadi⁴⁰ reported that a combination of penicillin and evening primrose oil (which contains both linoleic and gamma linoleic acid) had a dramatic positive effect on some schizophrenics. It would also be extremely interesting to discover whether epinephrine has any beneficial impact on schizophrenia.

Conclusion

Schizophrenia is not an old disease. Rather it is one of the costs society, as a whole, has been willing to inflict on certain susceptible individuals in order to gain the benefits of industrialization.¹ Everywhere its rise has paralleled the onset of the Industrial Revolution, as it has followed in the footsteps of "civilization." Its root cause may, or may not, be an allergy to latex and its associated rubber products. Even if not, it is hoped that this article will give a stimulus to the search for the ultimate cause of "the major mental health problem of the century."⁴¹

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