Geographic Correlation of Schizophrenia to Ticks and Tick-Borne Encephalitis

by James S. Brown, Jr.

Abstract

Schizophrenia prevalence in the United States is highest in urbanized Northeastern, Northwestern, and Great Lakes States. The viral theory of schizophrenia attributes this distribution to enhanced susceptibility to viral infections in crowded, urban areas. Such infections during fetal or perinatal development are hypothesized to result in the eventual onset of schizophrenia. This study attempts to identify which viral infections have a similar geographical distribution to schizophrenia. Examination of the geographical distribution of infectious diseases in the United States reveals that the spreading foci of Lyme disease and its primary vectors, Ixodid ticks, correlate significantly with high schizophrenia rate areas. Ixodid ticks are vectors in North America and throughout the world of tick-borne encephalitis (TBE). The international distribution of TBE is shown to be concentrated in countries where the highest rates of schizophrenia are found: Croatia, Norway, Finland, Germany, Ireland, and others. The geographical specificity of this correlation and the plausibility of a tick-associated or TBE theory of schizophrenia are discussed.


Various methods exist to develop testable hypotheses of the cause of disease. An infrequently used but valid technique is medical geography. Medical geography compares the geographical distribution of disease to other variables such as trace element geology, water quality, nutrient geography, and other health-associated factors.

The confirmation of an environmental cause of disease must demonstrate strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experimental confirmation, and analogy (Underwood 1971; National Research Council 1991). These nine conditions must be met to avoid errors that arise when multiple, potential causes of disease are present in the environment. These issues are extensively reviewed elsewhere and will not be reviewed here (Cannon and Hopps 1971; Hopps and Cannon 1972; Freedman 1975). Without meeting these requirements, erroneous conclusions can result in unfounded theories and even fraudulent therapies. Medical geography is valued for generating testable hypotheses based on geographic and clinical observations.

The principles of medical geography were applied previously by the author in correlating the geography of dietary selenium deficiency to the geography of schizophrenia (Brown 1994). In developing a testable hypothesis of a selenium-deficiency theory of schizophrenia, the author produced a map (figure 3; Brown 1994) depicting 14 States with historically high rates of schizophrenia based on rates reported by Torrey and Bowler (1990). As shown in figure 1 of the current article, these 14 States are located in New England, the Great Lakes region, and the Pacific Coast. For the current study, the medical geography liter-
Figure 1. Shaded States are those with highest rates of schizophrenia

Adapted from Torrey and Bowler (1990) and Brown (1994)

ature was searched for disease distributions that correlate with those regions.

Lyme disease, a zoonosis caused by the spirochete, *Borrelia burgdorferi*, was identified as having foci in New England, the Great Lakes region, and the Pacific Coast, and to a lesser degree, other regions (Barbour and Fish 1993). Using the criteria of proof described above, we tested the association of schizophrenia with Lyme disease, its vectors, hosts, and associated diseases.

Strength of the Correlation Between Lyme Disease and Schizophrenia

The 14 States with the greatest number of reported cases of Lyme disease are shown in figure 2 (Craven and Dennis 1993). Fourteen States were chosen to correlate to the 14 States with high schizophrenia rates in figure 1. Using $2 \times 2$ contingency tables, we found a significant correlation ($p < 0.05$) between these two groups of States. Contingency tables are standard tools for the analysis of categorical data. They measure Pearson’s chi-squared statistic. A $p$-value of less than 0.05 indicates the correlation is not due to random chance. In this case, the observed frequencies of high Lyme disease rates with high schizophrenia rates, and low Lyme disease rates with low schizophrenia rates are greater than the expected frequencies if the association were random.

Schizophrenic-like symptoms are associated with some cases of Lyme disease but differ from those of true schizophrenia in responsiveness to antibiotics. Unlike schizophrenia, Lyme disease-associated psychosis is reversible with antibiotics (Roelcke et al. 1992; Pass and Calev 1992).

Ixodid ticks, the primary vectors of Lyme disease, also transmit *Babesia microtia*, a protozoan, which causes babesiosis, a malaria-
like illness (Spielman et al. 1985). Organic psychoses are associated with malaria and other tropical diseases (Weiss 1985) but not specifically with babesiosis. However, the presence of either Lyme disease or babesiosis may infer the presence of Ixodid ticks. Do these vectors or their hosts correlate more significantly with schizophrenia?

Strength of the Correlation Between Ixodid Ticks and Schizophrenia

Figure 3 shows the 14 States with the greatest land areas of the ticks *Ixodes dammini* and *Ixodes pacificus*, the two primary vectors of *Borrelia burgdorferi* in the United States (Anderson 1991). Bites by these ticks account for more than 90 percent of the cases of Lyme disease (Barbour and Fish 1993). With the use of $2 \times 2$ tables, the distribution of Ixodid ticks was shown to be a stronger correlation than Lyme disease with high rates of schizophrenia ($p < 0.0001$). The primary host of these ticks in North America is the white-footed mouse, whose range encompasses most of the United States (King 1968), and does not correlate with schizophrenia rates. Given the strong geographic correlation between Ixodid ticks and schizophrenia, what further proof of an association can be demonstrated?

Coherence of a Correlation Between Ixodid Ticks and Schizophrenia

Viruses are also vectored by Ixodid ticks, and schizophrenia is hypothesized to result from a viral-induced fetal or perinatal injury (Menninger 1926; Hare 1983; Crow 1984; Delisi and Crow 1986; Torrey and Kaufmann 1986; Kaufmann and Ziegler 1988; Barr and Mednick 1991; Torrey 1991; Waltrop et al. 1991). Some theories do not espouse solely in utero viral infection, as long as latent, central nervous system (CNS) infection occurs during an individual's developmental years (Waltrop et al. 1991). Viruses such as cytomegalovirus, herpes, and influenza are suspected because they are often intrauterine or correlate with seasonal patterns of schizophrenic births. These viruses are implicated but none are confirmed (Albrecht et al. 1980; Kaufmann et al. 1983; King et al. 1985; Robert-Guroff et al. 1985; Shrikhande et al. 1985; Mednick et al. 1988; Kendell and Kemp 1989). Most viral theories owe their origin to two controversial findings: Higher rates of schizophrenia are often reported from urban rather than rural locations, and schizophrenic births have a seasonal pattern. Combined, these two characteristics suggest a seasonally active virus in heavily populated areas.

The concentration of individuals with schizophrenia in urban areas of the United States is well known (Torrey and Bowler 1990). Whereas socioeconomic "drift" is often used to explain this distribution, Torrey and Bowler (1990) found evidence of an urban factor other than drift to explain schizophrenia geography. This was confirmed by Lewis et al. (1992) and Takei et al. (1992) in Swedish and English populations, respectively.

While the possibility of zoonotic infection in rural and suburban environments is intuitively obvious, the likelihood of urban zoonoses is not. However, zoonoses are common in urban environments. Although the number of rural ticks may exceed the number of urban ticks, a small percentage of a large city population being bitten may result in a larger number of bites than a large percentage of a small
rural population being bitten.

The circumstances in which endemic zoonoses occur in urban areas are reviewed elsewhere (Rosicky and Hejny 1959; Mantovani et al. 1978). Urban populations become infected within cities and on trips to endemic, often recreational, areas. Ixodid ticks are found in urban environments on wild animals and pets, and in gardens and parks (Korenberg et al. 1984). In Russia (formerly the U.S.S.R.), Korenberg et al. (1984) found more urban than rural dwellers infected with Russian spring-summer encephalitis (RSSE), a tick-borne flavivirus. Lyme disease is transmitted to humans and animals in urban parks in the United States and the United Kingdom (Guy and Farquhar 1991; Schwartz et al. 1991). Ixodid ticks carrying both Lyme disease and Central European encephalitis (CEE), a tick-borne flavivirus, are prevalent in Berlin, Germany (Kahl and Radda 1988; Kahl et al. 1989). These examples do not rule out other viruses as potential causes of schizophrenia, but they do confirm the presence of zoonoses in urban settings.

The winter-spring seasonality of schizophrenic births is reviewed elsewhere (Katsanis et al. 1992; Sacchetti et al. 1992; Torrey et al. 1993). Seasonality is a consistent finding, but its etiology is controversial. Proposed etiologies include statistical artifact, nutritional deficiencies, perinatal complications, and viral infections (Katsanis et al. 1992). The association of viral epidemics with schizophrenia birth seasonality is reviewed by Kirch (1993). Recent studies by Sham et al. (1992) and Adams et al. (1993) correlate schizophrenic births with influenza epidemics, although these studies remain controversial (Castle and Gill 1992; Crow 1992).

Tick-borne encephalitis (TBE) has a bimodal seasonal occurrence because the biting activity of Ixodid ticks is temperature and humidity dependent (Smith 1962). In Russia and Europe, most cases occur in April/May and September/October (Smith 1962; Reid 1988). Whether this seasonality correlates with that of schizophrenia may depend on whether the injury that leads to schizophrenia is in utero or neonatal.

Shah and Murthy (1960) demonstrated that babies breast-feeding from or born to mothers with TBE in the third trimester do not contract the disease. Human milk is different from goat's and cow's milk, which produce extensive epidemics of TBE. See following sections on Powasson and CEE viruses.) No studies examine the possibility of first or second trimester transplacental infection in humans. The immunological maturity of the third trimester fetus or newborn infant may prevent transplacental or milk-borne infection. This is the case in lambs which have elevated fetal susceptibility to louping-ill, a TBE, until their immunological responses mature (Doherty et al. 1972). First trimester infection of the lamb, mouse, and hamster does occur (Doherty et al. 1972; Molnarova and Mayer 1980). First trimester human fetuses and immunologically immature second and third trimester human fetuses could possibly be at risk for contracting TBE from their mothers. Additional studies are necessary to confirm this.

If maternal transmission of TBE is questionable, then tick bites would have to occur inside the home during winter months and either inside or outside during the spring months. It is conceivable that during winter months when individuals spend more time inside, possibly in proximity to pets or rodents hosting infected ticks, bites and infection could occur.

If first trimester maternal transmission is possible, and if a woman becomes infected when she is 1 to 3 months pregnant in April/May or September/October, then her baby will be born between October-January or March-June, respectively. These months overlap the higher schizophrenic rate birth months but not precisely. A TBE-related cause of schizophrenia appears better supported by neonatal rather than prenatal infection.

Specificity of a Correlation Between Tick-Borne Flaviviruses and Schizophrenia

Ixodid ticks carry arena-, bunya-, corona-, flav-, orthomyxo-, reo-, rhabdo-, toga-, and unclassified viruses (Karabatsos 1985). Of these groups, do any demonstrate a strong geographic correlation with schizophrenia? Only the tick-borne flaviviruses are found in North America, Europe, Africa, Asia, and Australia. Numerous flaviviruses such as Dengue, Yellow Fever, and St. Louis encephalitis viruses are responsible for widespread disease but are mosquito- rather than tick-borne (Karabatsos 1985). Hantaviruses (Bunyaviridae) are also widespread but not associated with Ixodid ticks (Karabatsos 1985). Reoviruses, orthomyxo-viruses, and bunaviruses such as Colorado Tick Fever, Thogoto virus, and Crimean hemorrhagic-Congo and nairoviruses, respectively, are vectored by Ixodid ticks but are limited geographically. Other viruses including those vec-
tored by nontick arthropods or those that are geographically isolated are not ruled out as potential etiologic causes of schizophrenia by this exercise. However, of the tick-borne viruses, flaviviruses have the greatest potential for international significance.

**Tick-Borne Flaviviruses**

Flaviviruses (Family Flaviviridae, Genus Flavivirus, formerly known as Group B Arboviruses) are divided serologically by vector association: tick-borne, mosquito-borne, and vector-unassociated (Calisher and Karabatsos 1988). The tick-borne flaviviruses are subdivided in two encephalitis complexes: RSSE and Tyuleniy encephalitis. The RSSE complex includes Powassan, RSSE, CEE, Omsk hemorrhagic fever, Kyasanur Forest disease, and louping-ill viruses (Calisher and Karabatsos 1988). The Tyuleniy complex includes Tyuleniy, Saumarez Reef, and Meaban viruses (Calisher and Karabatsos 1988).

**Biological Plausibility of TBE Causing Schizophrenia**

Neurotropism, latency, and association with psychosis are features of other viruses hypothesized to be involved in schizophrenia. All strains of TBE are neurotropic, and chronic and latent forms of the disease are documented (Silber and Soloviev 1946; Albrecht 1962; Ogawa et al. 1973; Monath 1990). Meningeal, paralytic, and encephalitic forms of TBE are reported (Grinschgl 1955). Neuropsychiatric sequelae including psychosis occurs in some cases (Silber and Soloviev 1946; Grinschgl 1955; Monath 1990).

The interferon theory of schizophrenia described by Waltrip and colleagues (1990, 1991) hypothesizes that interferon induced by viral infection causes neuronal damage that results in schizophrenia during later maturation. Such viral infections can, but are not required to, occur in utero. The TBE virus could cause schizophrenia in this way because it is a stronger inducer of interferon than the herpes simplex type I virus (Libikova et al. 1977), a virus theorized to cause schizophrenia.

**Temporality of the Association Between Schizophrenia and TBE**

The criterion of proof known as temporality requires that the causative agent be present in the environment before the onset of symptoms. Some individuals do develop psychosis after the onset of TBE but less frequently than other neuropsychiatric sequelae (Silber and Soloviev 1946; Grinschgl 1955). On a historical basis, with the exception of louping-ill, most forms of TBE were formally described after schizophrenia. However, the "age" of schizophrenia is controversial, and the recognition of TBE required modern technology for diagnosis. Certainly tick vectors, although not necessarily tick viruses, were present before modern times. Temporality, therefore, cannot be demonstrated with complete confidence but is plausible.

**Biological Gradient Between TBE and Schizophrenia**

An environmental cause of disease must show biological gradient. As exposure to the cause increases, severity of the disease should also increase. For a biological gradient to exist between TBE and schizophrenia, one must demonstrate a positive correlation between TBE and schizophrenia severity. This is difficult to perform because there are no comparable measures of severity for these diseases. There is no specific biologic measure of schizophrenia, and description of its clinical severity is not internationally standardized. Furthermore, although antibody response to viral infection can be measured, its interpretation is complex (McIntosh 1990). For example, antibody responses in TBE are variable and may not occur at all (Monath 1990).

Studies of antibody titers of TBE in Russian and Czechoslovakian schizophrenia patients are summarized in table 1. In addition to those stated above, most findings are questionable for several reasons: First, TBE virus is inhibited by antipsychotics (Libikova et al. 1977; Libikova 1983). Second, some studies used random instead of geographically controlled normals. Finally, some serosurveys did not specify the viral strain used in neutralizing antibody tests. Interpretation of such studies is difficult since numerous strains of RSSE and CEE are present in the same regions. Russian strains include Tjuleny, Absettarov, and Karshi; in Czechoslovakia—Hanzalova and Hypr; in France—Meaban; and in Finland—Kumlinge (Karabatsos 1985). Omsk hemorrhagic fever, a RSSE-complex tick-borne flavivirus, is closely related to RSSE and CEE, but it is clinically and antigenically different.

**Analogy Between TBE and Schizophrenia-Related Diseases**

If analogy exists between these diseases, then TBE should cause
Table 1. Tick-borne encephalitis serosurveys in schizophrenia patients in the former U.S.S.R. and Czechoslovakia

<table>
<thead>
<tr>
<th>Study</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasiljeva et al. (1987)</td>
<td>In Tomsk (U.S.S.R.), seroprevalence is equal between schizophrenia patients and normal controls; antibody titers are higher in schizophrenia patients; in Primorsk Krai (U.S.S.R.), prevalence and titers are higher in normal controls.</td>
</tr>
<tr>
<td>Vasiljeva et al. (1991)</td>
<td>In Tomsk and Primorsk Krai (U.S.S.R.), prevalence and antibody titers are higher in schizophrenia patients than in normal controls.</td>
</tr>
<tr>
<td>Rajcani et al. (1987)</td>
<td>Prevalence is higher in Tomsk normal controls than in schizophrenia patients; prevalence is higher in Czech schizophrenia patients than in normal controls.</td>
</tr>
<tr>
<td>Libikova et al. (1979)</td>
<td>Prevalence is lower in schizophrenia patients than in patients with multiple sclerosis and certain other neurological disorders.</td>
</tr>
<tr>
<td>Libikova (1983)</td>
<td>Prevalence is higher in Czech schizophrenia patients than in normal controls.</td>
</tr>
</tbody>
</table>

Any disease that shares the etiology of schizophrenia. Multiple sclerosis (MS) is possibly a candidate. Stevens (1988) theorized that MS and schizophrenia share the same etiology. If the etiology is viral, positive seroprevalence of a mutuallty responsible virus should be similar in both diseases. Libikova et al. (1979) found positive CEE titers in 7.3 percent of 82 chronic, hospitalized schizophrenia patients compared to 17 percent of 49 patients with MS. Although fewer people with schizophrenia than with MS had positive titers, the inhibiting effect of long-term antipsychotic medication on schizophrenic titers cannot be ruled out. This finding neither confirms nor rejects an analogy between schizophrenia, MS, and TBE.

Two studies found an association between high rates of MS and a high presence of dogs and other pets (Kaufman 1990). This further supports the speculation that pets carrying ticks infected with viruses infect persons in the home. Perhaps both MS and schizophrenia are transmitted this way. If analogy does exist between MS and schizophrenia, a similar finding of a greater presence of pets in the homes of individuals with schizophrenia during their developmental years would support this notion.

Consistency of the Correlation Between Schizophrenia and TBE

To test the consistency of the theory in the absence of better serological surveys, regions with high rates of schizophrenia can be correlated with areas of TBE. The correlation of CEE in the Tribec region of Czechoslovakia (Blaskovic 1970) and schizophrenia prevalence is not possible because prevalence of schizophrenia in that country is not well-defined. However, parts of Yugoslavia, Germany, Scandinavia, and Ireland have unusually high rates of schizophrenia. These countries also have intense foci of TBE. These and other countries with high rates of either disease are discussed below and are shown in table 2. As table 2 demonstrates, this correlation is flawed because schizophrenia epidemiology outside the United States is not clearly defined geographically.

Furthermore, there is controversy surrounding the significance of geographical differences in the occurrence of schizophrenia. Folvégovic and Folvégovic-Smalc (1992) concluded that the variation in Croatia (Yugoslavia) results from selective migration and genetic loading. Their conclusions were criticized on numerous statistical points by Cooper and Eagles (1994). The impact of emigration on Irish rates is also controversial. Torrey et al. (1984) reported high Irish rates despite emigration, whereas Walsh and Walsh (1970) reported reduced rates when emigration was taken into account.

There is also no certainty that data collection methods for schizophrenia and TBE are comparable in technique or accuracy. Finally, much of the correlation relies on the use of seroprevalence studies, which pose numerous problems of interpretation discussed earlier. The remaining value of this correlation is to broaden the scope of possible, perhaps exotic, viruses involved in the pathogenesis of schizophrenia.

RSSE

Of tick-borne flaviviruses, RSSE is the most studied because it is a major health threat in Russia.
### Table 2. Locations, quality of definition, and strength of the correlation of highest rates of schizophrenia and tick-borne encephalitis (TBE) in countries reporting both diseases

<table>
<thead>
<tr>
<th>Country</th>
<th>Highest schizophrenia</th>
<th>Definition</th>
<th>Highest TBE</th>
<th>Definition</th>
<th>Strength of correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>Unknown; low rates in New South Wales</td>
<td>Poor; other areas not studied</td>
<td>New South Wales</td>
<td>Poor; other areas not studied</td>
<td>Unknown</td>
</tr>
<tr>
<td>Austria</td>
<td>Unknown</td>
<td>Poor; no surveys</td>
<td>Scattered epidemics; endemic in Graz</td>
<td>Moderate; some surveys</td>
<td>Unknown</td>
</tr>
<tr>
<td>Canada</td>
<td>Unknown</td>
<td>Poor; no surveys</td>
<td>Diverse, isolated areas</td>
<td>Moderate; some surveys</td>
<td>Unknown</td>
</tr>
<tr>
<td>Czechoslovakia</td>
<td>Unknown</td>
<td>Poor; no surveys</td>
<td>Tribec</td>
<td>Good; nationwide survey</td>
<td>Unknown</td>
</tr>
<tr>
<td>Finland</td>
<td>Selected northern and southern localities</td>
<td>Moderate; numerous surveys</td>
<td>Southern</td>
<td>Good; several surveys</td>
<td>Good correlation in south; poor in north; however, high schizophrenia areas overlap range of <em>Ixodes uirae</em>, a viral vector.</td>
</tr>
<tr>
<td>Germany</td>
<td>Southwestern</td>
<td>Good; nationwide surveys</td>
<td>Southwestern</td>
<td>Moderate; West Germany well-studied</td>
<td>Good correlation in West Germany.</td>
</tr>
<tr>
<td>India</td>
<td>Southern and Sri Lanka</td>
<td>Poor; no nationwide survey</td>
<td>Southern</td>
<td>Moderate; surveys in some areas</td>
<td>Moderate</td>
</tr>
<tr>
<td>Ireland</td>
<td>Central and southern</td>
<td>Controversial; nationwide surveys</td>
<td>Unknown</td>
<td>Poor; no human surveys</td>
<td>Moderate correlation of schizophrenia with Lyme disease and babesiosis.</td>
</tr>
<tr>
<td>Japan</td>
<td>Tokyo; Hachijo Island</td>
<td>Good; nationwide surveys</td>
<td>Unknown</td>
<td>Poor; no surveys</td>
<td>Poor correlation between schizophrenia and Lyme disease.</td>
</tr>
<tr>
<td>Malaysia</td>
<td>Unknown</td>
<td>Poor; no surveys</td>
<td>Unknown</td>
<td>Poor; no surveys</td>
<td>Unknown; both diseases present but data insufficient.</td>
</tr>
<tr>
<td>Micronesia</td>
<td>Yap and Palau</td>
<td>Good; regional survey</td>
<td>Unknown</td>
<td>Poor; no surveys</td>
<td>Unknown</td>
</tr>
<tr>
<td>Papua New Guinea</td>
<td>East coast</td>
<td>Good; nationwide survey</td>
<td>East coast</td>
<td>Good; nationwide survey</td>
<td>Good; correlation is between schizophrenia and Group B arboviruses.</td>
</tr>
<tr>
<td>Norway</td>
<td>Northern</td>
<td>Moderate; several surveys</td>
<td>Southwest</td>
<td>Good; several surveys</td>
<td>Good in south; poor in north; as in Finland, there is possible</td>
</tr>
</tbody>
</table>
Table 2. Locations, quality of definition, and strength of the correlation of highest rates of schizophrenia and tick-borne encephalitis (TBE) in countries reporting both diseases—Continued

<table>
<thead>
<tr>
<th>Country</th>
<th>Highest schizophrenia</th>
<th>Definition</th>
<th>Highest TBE</th>
<th>Definition</th>
<th>Strength of correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td>Unknown</td>
<td>Poor; isolated surveys</td>
<td>Unknown</td>
<td>Poor; no human surveys</td>
<td>Unknown; both diseases exist but data not sufficient.</td>
</tr>
<tr>
<td>Sweden</td>
<td>Northern and southern</td>
<td>Moderate; several surveys</td>
<td>Southern</td>
<td>Good; several surveys</td>
<td>Good in south; poor in north; as in Finland, there is possible correlation between schizophrenia and the tick, <em>Ixodes uriae</em>.</td>
</tr>
<tr>
<td>United States</td>
<td>Northeast, Great Lakes region and Pacific Northwest</td>
<td>Good; nationwide surveys</td>
<td>Unknown</td>
<td>Poor; few surveys</td>
<td>Strong correlation between Ixodid ticks and schizophrenia.</td>
</tr>
<tr>
<td>Russia (formerly U.S.S.R.)</td>
<td>Unknown</td>
<td>Poor; few surveys</td>
<td>Widespread</td>
<td>Poor; no formal surveys</td>
<td>Unknown</td>
</tr>
<tr>
<td>Yugoslavia</td>
<td>Slovenia and Croatia</td>
<td>Good; nationwide surveys</td>
<td>Slovenia and Croatia</td>
<td>Good; nationwide surveys</td>
<td>Good</td>
</tr>
</tbody>
</table>

Often described in conjunction with CEE, RSSE is prevalent in eastern Russia, while CEE is predominant in western Russia (Artsob 1989). Both are described in extensive reviews elsewhere (Smith 1962; Hoogstraal 1966, 1981; Korenberg 1976; Gresikova and Calisher 1989). RSSE extends from roughly 700 km east of Moscow to eastern Russia near the Sea of Japan (Vasiljeva et al. 1987; Gresikova and Calisher 1989). CEE in western Russia is found in Moscow, Leningrad, Kirov, Archangelsk, and other Baltic areas (Gresikova and Calisher 1989).

RSSE, first described in the 1930s, is vectored by the tick, *Ixodes persulcatus*, and is a severe illness with mortality up to 50 percent (Gresikova and Calisher 1989). The disease prevalence is highest in the Russian Siberian taiga (Hoogstraal 1981) where morbidity is 11.7 per 100,000 and sero-prevalence is as high as 51 percent (Gresikova and Calisher 1989). Even urban populations are at risk where morbidity is 1.8 per 100,000 (Korenberg 1976).

If high rates of schizophrenia in regions of Russia correlate with high RSSE rate areas, then the two diseases might be related. However, epidemiologic studies of schizophrenia in Russia are rare, and correlation is impossible (see table 1). Schizophrenia in Moscow is more prevalent than in northeastern Russia or the Samarkand region in southcentral Russia, but no other studies exist (Zharikov et al. 1979; Yursinova 1982; see also Jablensky 1986; Torrey 1987).

**CEE**

CEE is the primary strain of the RSSE-complex in central and western Europe where it is vectored chiefly by *Ixodes ricinus* (Hoogstraal 1981). CEE can also be acquired from infected goat’s, cow’s, and sheep’s milk (Gresikova and Calisher 1989). In such cases the disease is epidemic but with less than 5 percent mortality. CEE is called diphasic milk fever or biphasic meningoencephalitis because it has different symptoms before and after CNS infection (Grinschgl 1955; Richling 1955; Gresikova and...
Calisher 1989). Epidemic and endemic CEE is known throughout Europe (Rosicky 1959; Libikova 1962; Smith 1962; Blaskovic 1967; Wellmer and Jusatz 1981; Gresikova and Calisher 1989). Seroprevalence in Europe ranges from 0.9 to as high as 63 percent in some localities (Gresikova and Calisher 1989).

Yugoslavia

Vectored by the same Ixodes tick, Lyme disease and CEE are epidemic and endemic in Slovenia and Croatia, the northernmost republics of Yugoslavia (Kmet et al. 1955; Gresikova et al. 1975; Vesenjak-Hirjan 1976, Strle et al. 1989; Kozuch et al. 1990). Fewer cases of CEE are reported from other Yugoslavian republics (Vesenjak-Hirjan 1976).

CEE in Slovenia is concentrated in a 75-km radius around Ljubljana (Kmet et al. 1955). Other cases occur in northeastern Slovenia 50 km south of Graz, Austria, where endemic and epidemic CEE is well-known (Grinschgl 1955; Richling 1955). The regional distribution of schizophrenia in Austria is unknown and its correlation to CEE cannot be performed. More is known about schizophrenia in Yugoslavia where incidence is comparable to high-incidence regions of Germany or Norway (Folnegovic et al. 1990). Schizophrenia rates in Yugoslavia are highest in Slovenia and Croatia (Crocetti et al. 1964). In Slovenia, schizophrenia rates, like CEE, are highest near Ljubljana and around Maribor at the Austrian border near Graz (Crocetti et al. 1964).

As in Slovenia, the highest Croatian schizophrenia rates are in or near foci of Lyme disease or CEE. High schizophrenia rates in Croatia reported by Crocetti et al. (1964) were verified by later studies (Crocetti et al. 1971; Kulcar et al. 1971; Lemkau et al. 1971). Other investigations of high rates of schizophrenia in the Croatian Istrian Peninsula, the Croatian Littoral along the coast of the Adriatic Sea, and in Zagreb are reviewed by Folnegovic and Folnegovic-Smalc (1992). Lyme disease is reported from the Istrian Peninsula (Strle et al. 1989), whereas CEE is widespread but focused along the Adriatic coast and near Zagreb (Vesenjak-Hirjan 1976).

Germany

Most epidemiological studies of schizophrenia in Germany are in southwestern Germany (southern West Germany) (Dilling and Weyerer 1984). The city of Mannheim has a prevalence of 0.54 percent, which is twice the German average of 0.22–0.24 percent (Häfner and Reimann 1970; Häfner and an der Heiden 1986; Jablensky 1986). Mannheim is located on the border of two German administration districts, Rheinland-Pfalz and Baden-Württemberg. In Upper Bavaria, approximately 300 km southeast of Mannheim, Dilling and Weyerer (1984) found relatively high schizophrenia prevalence in Palling (0.7%), Traunstein (0.3%), and Traunret (0.3%). Upper Bavaria is located in the administration district, Bayern, which is east of and adjacent to Baden-Württemberg. Palling is 100 km east of Munich where the historically important King Ludwig II, who had schizophrenia, was born (Hay 1977).

These areas of high schizophrenia rates are in or near foci of Lyme disease and TBE. Although Lyme disease is present throughout western Germany, the three administration districts with the highest prevalence of antibodies to Borrelia burgdorferi (16%–30%) are Rheinland-Pfalz, Baden-Württemberg, and Bayern (Schmidt et al. 1986). The presence of CEE in Bayern and Rheinland-Pfalz is demonstrated by the seroconversion of U.S. soldiers stationed there (Clement et al. 1992). CEE is highest in Baden-Württemberg and Bayern (Rehse-Kupper et al. 1978) and concentrated east and north of Munich and south of Mannheim.

Ireland and Scotland

The reported high rates of schizophrenia in Ireland (Jablensky 1986; Torrey 1987) are controversial. Dawson (1911) described a geographical distribution of insanity in Ireland focused in central and southern counties. Studies by Walsh and Walsh (1970) and Kel- leher et al. (1974) found high rates in Counties Clare, Limerick, and Galway in the Province of Con-naught. The “three-county case register” study (Walsh et al. 1980) found high rates for Counties Carlow/South Kildare, Westmeath, and Roscommon. Torrey et al. (1984) confirm the presence of “endemic” schizophrenia in County Roscommon. Ni Nuallain et al. (1987, 1990) rejected the claims of higher schizophrenia rates throughout Ireland or in any of the Irish counties. Furthermore, Kendler et al. (1993) found no supporting evidence for an increase of schizophrenia in County Roscommon or western Ireland. Youssef et al. (1991) found average schizophrenia rates in County Cavan except for a high schizophrenia rate area in the southern portion of that county.
Eventual resolution of this controversy is necessary to correlate schizophrenia rates with the endemic TBE in Ireland known as “louping-ill.” The following correlation assumes the existence of a geographical variation of schizophrenia in Ireland.

Louping-ill, a member of the RSSE complex, is vectored by *Ixodes ricinus* (Reid 1988). The virus is found in Ireland, Scotland, and northern England (Reid 1988). The name “louping-ill” is derived from the jumping or “louping” signs of sheep when infected (Hoogstraal 1966). Clinical disease in humans is rare and usually severe (Walton 1967), but serological surveys of asymptomatic humans in Ireland are not available. In livestock, the disease is widespread in Ireland (Walton 1967). *Ixodes ricinus* also carries Lyme disease and babesiosis in Ireland. In the absence of human serosurveys of louping-ill, the distribution of Lyme disease and babesiosis will be compared to regions of presumed high occurrences of schizophrenia.

Smith et al. (1991) found a prevalence of Lyme disease in Counties Galway, Wicklow, and Meath and Dublin City. Sero-prevalence ranged from 5 percent in Dublin City to a high of 15 percent in County Galway. Gray and Harte (1985) found the highest prevalence of veterinary babesiosis in the Province of Connaught, especially in Counties Roscommon and Galway. Other areas with high rates of babesiosis are the northern portions of County Clare and an area on the border of Counties Westmeath and Cavan. The high babesiosis portion of County Cavan corresponds to the high schizophrenia portion of County Cavan reported by Youssef et al. (1991). Although the counties with high rates of Lyme disease and/or babesiosis are the same counties with presumed high schizophrenia rates, the association requires resolution of the epidemiology of schizophrenia in Ireland.

In Scotland, seroprevalence of louping-ill in humans is low (Walton 1967), but surveys were of patients with encephalitis of unknown etiology. Most European serosurveys of TBE are of the asymptomatic population because many cases of TBE are clinically undetected. Schizophrenia prevalence in rural Scotland (0.42%) is high (Mayer-Gross 1948). Rates in Salford, England, are also high (0.7%–8%) (Freeman and Alpert 1986). In Aberdeen, Scotland, prevalence is lower than in Baltimore or London (Wing et al. 1967). Louping-ill, Lyme disease, and babesiosis are present in these regions (Adam et al. 1977; Muhlemann and Wright 1987), but schizophrenia distribution is not defined well enough for correlation (Adam et al. 1977; Muhlemann and Wright 1987).

**Scandinavia**

Areas of high rates of schizophrenia in Scandinavia are numerous (Jablensky 1986; Torrey 1987). In northern Norway, Anderson (1975) found high rates in Kautokeino and Skanland, which are small communities at the 69-degree latitude. High rates are also reported from Berlevag, Norway and the Norwegian islands, Vaeroy and Rost (Bjarnar et al. 1975; Fugelli 1975). Berlevag is located on the northern coast of Norway above the 70-degree latitude. Vaeroy and Rost are small islands off the northwestern coast of Norway just below the 68-degree latitude. Overall incidence of schizophrenia in Norway, however, is average for European countries (Jablensky 1986).

Schizophrenia in Finland is high in both northern and southern regions (Jablensky 1986; Torrey 1987). Vaisanen (1975) found high rates in the Uusikaupunki and Kemijarvi regions in southern and northern Finland, respectively. Uusikaupunki is on the southern coast of Finland approximately 200 km west of Helsinki. Kemijarvi is in Lapland approximately 300 km south of Kautokeino, the high schizophrenia rate area in Norway (Anderson 1975). Kemijarvi is also 200 km southeast of the region with a high occurrence of schizophrenia described by Book (1953) and Book et al. (1978) in northern Sweden. These Swedish, Norwegian, and Finnish study areas are on or near the same latitude as Murmansk, Russia, which is 250 km east of the border between Finland and Russia.

The region with a high rate of schizophrenia in northern Sweden (Book 1953; Book et al. 1978) is well-known (Jablensky 1986; Torrey 1987). Southern Sweden is also known for high rates. In communities around Stockholm, Halldin (1984) found a prevalence of 0.6–0.7 percent. Stockholm is 250 km southwest across the Gulf of Bothnia from Uusikaupunki, the high schizophrenia rate area in southern Finland.

Lyme disease and CEE are well-known in Sweden, Norway, and Finland. In southern Sweden both diseases are concentrated around Stockholm (Gustafson et al. 1990, 1992; Holmgren and Forsgren 1990). No cases are reported as far north as the high schizophrenia rate area described by Book (1953) and Book et al. (1978). In Finland,
CEE (Kumlinge disease) is found only in the south regions, especially on the Aland Islands and the nearby Finnish coast, which includes Ususkaupunki (Brummer-Korvenkontio et al. 1973; Wahlberg et al. 1989). In Norway, CEE is found on the west coast (Traavik 1973) but not as far north as the Rost and Vaeroy Islands. Therefore, CEE is prevalent in southern, but not northern, Scandinavian areas of high schizophrenia rates. If the association of tick-borne flaviviruses with schizophrenia is valid, then why are clinical cases of CEE not present in the arctic regions?

In Norway, the tick vector of CEE, *Ixodes ricinus*, is not found in the northern latitudes (Mehl 1983). However, the tick, *Ixodes uriae*, extends to the northernmost latitudes including the Rost and Vaeroy Islands and Berlevag (Mehl 1983). Saikku et al. (1980) found over 50 arboviruses including strains of RSSE and CEE in *Ixodes uriae* on seabirds on the Rost Islands. The Rost Islands are at the same latitude as Murmansk, Russia, where Tyuleniy virus, a strain of RSSE, is found in ticks on seabirds (Lvov et al. 1979). Possibly, Arctic Circle inhabitants could become subclinically infected with strains of CEE or RSSE not present in southern latitudes.

The role of migrating seabirds is valuable in understanding the geography of viral and other infectious diseases. The distribution of Lyme disease is partially determined by migrating birds, and avian sources may be responsible for pandemics of influenza (Anderson 1991; Schafer et al. 1993). Migrating seabirds carrying ticks produce the global patterns of CEE/RSSE (Clifford 1979). For instance, *Ixodes uriae*, by migrating with polar-migrating sea and shorebirds, has a circumpolar, bipolar geographical distribution (Clifford 1979). Assuming that the flavivirus or other viral theory of schizophrenia is valid, do the flight-paths and nesting areas of migrating birds correlate to the global distribution of schizophrenia? This is speculative but valuable heuristically in the later consideration of schizophrenia distribution in Papua New Guinea.

Schizophrenia and flaviviruses coexist in numerous countries including India, Australia, Papua New Guinea, Malaysia, Micronesia, Japan, Canada, and the United States. Comparison of the two diseases in these countries will further test the theory.

**India**

Torrey (1987) reviews the consistent findings of higher schizophrenia rates in Indians of the highest castes. This finding is contrary to the notion of “downward drift” described in Western cultures. Reasons for this are unclear but would include genetic isolation. However, relative to a tick-borne theory of schizophrenia, higher castes have greater wealth and ability to travel to recreational areas with endemic TBE. Such mobility is a well-known risk factor for TBE in Russia (Korenberg et al. 1984). Schizophrenia rates in India can also be discussed on a geographical basis.

**Southern India and Sri Lanka.** Schizophrenia rates in southern India are high. Prevalence in Madras is higher than in Mannheim, Germany (Eaton 1991), and Tamil Indians from southern India and Sri Lanka (formerly Ceylon) have higher rates than northern Indians (Murphy 1968; Cooper 1978). The tick-borne flavivirus in southern India is Kyasanur Forest Disease (KFD) named for the region where it was first described. Kyasanur Forest is in the State of Mysore 700 km west of Madras (Hogstroa 1966). KFD presents as a flu-like illness, and serosurveys are necessary to determine its geographical range (Banerjee 1988). KFD extends through western India to north of Bombay (Banerjee 1988).

In Sri Lanka, human serosurveys of tick-borne flaviviruses are not available. Langat virus, a tick-borne flavivirus from Malaysia, is found in animals in Sri Lanka (Bardos et al. 1983). Although epidemiological surveys of schizophrenia and TBE in southern India and Sri Lanka are incomplete, the coexistence of high rates of schizophrenia, KFD, and Langat in southern India and Sri Lanka is consistent with the flavivirus theory.

**Northern India.** In northern India the association is less consistent. Average to high schizophrenia rates were found in the State of West Bengal near Calcutta (see Torrey 1987 for review). Only a few cases of KFD, however, are reported from Bengal (Ramanchandra 1971). KFD is not reported from Chandigarh, north of Delhi, where Sartorius et al. (1986) found high rates of schizophrenia. Schizophrenia prevalence in Uttar Pradesh, between Calcutta and Delhi, is average, but KFD is unknown there (Dube 1970). Vernacular babesiosis is present in Uttar Pradesh, but human cases are unreported (Malhotra et al. 1978). Northwest of northern India in Kabul, Afghanistan, Royal Farm virus, a tick-borne flavivirus, was
found in animals (Karabatsos 1985), but seroprevalence in India and elsewhere is unknown. Further study of these diseases in India is necessary to confirm or reject the hypothesis.

**Australia**

There are few epidemiological studies of schizophrenia in Australia. Goldstein et al. (1984) found a lower incidence of schizophrenia in New South Wales than in the United States or Europe. Yet, Lyme disease, tick-borne flaviviruses, and veterinary babesiosis are reported from New South Wales (Curnow 1973; Hawkes et al. 1985; Lawrence et al. 1986; McCrossin 1986), which is contrary to the theory linking schizophrenia with tick-borne disease. Saumarez Reef virus (SRV) is an Australian tick-borne flavivirus first identified on Saumarez Reef, part of the Great Barrier Reef off the coast of Queensland (St. George et al. 1977). Subclinical infection by SRV was found in 20 percent of 16,000 human serum samples from New South Wales (Hawkes et al. 1985). Although the presence of Lyme disease, SRV, and low schizophrenia rates in New South Wales casts doubt on the association of schizophrenia with tick-borne disease, two arguments can be made in favor of the theory. First, all individuals testing positive for SRV had higher titers of possibly cross-reacting, possibly mosquito-borne, flaviviruses. Therefore, the prevalence of SRV may be overstated. Second, more cases of Lyme disease are reported from Queensland, north of New South Wales, where the prevalence of schizophrenia is unknown (Piesman and Stone 1991). The flavivirus theory predicts higher rates of schizophrenia in Queensland than New South Wales. Epidemiological study of schizophrenia in Queensland can test this prediction.

If prevalence of schizophrenia on the Great Barrier Reef were known, it could be compared to the prevalence of Gadgets Gully virus, a tick-borne flavivirus found there in humans (Humphery-Smith and Cybinski 1987). Gadgets Gully virus was first described from Macquarie Island far south of Australia near Antarctica (St. George et al. 1985).

**Papua New Guinea**

In Papua New Guinea north of Australia, Torrey et al. (1974) found a prevalence of schizophrenia only in eastern coastal districts near Port Moresby. There are no reports of Lyme disease or babesiosis from Papua New Guinea, but arbovirus distribution is known. Group B arbovirus seroprevalence is much higher than Group A in eastern coastal districts (Wiseman et al. 1964). Above the 910–1,520 meter altitude (3,000–5,000 feet) in the western highland regions, Group A arbovirus seroprevalence prevails. Wiseman et al. (1964) did not include Group B tick-borne flaviviruses in their survey, but their findings demonstrate a vector distribution that correlates to schizophrenia incidence in Papua New Guinea.

The distribution of arboviruses in Papua New Guinea may be associated with both altitude and bird migration. Migration of birds with virus-infected ticks from New South Wales and Queensland, Australia, to eastern Papua New Guinea (Port Moresby) is a major health problem (Hoogstraal et al. 1975; Le Gonidec and Fauran 1981). This speculative association of schizophrenia distribution and bird migration was mentioned in the discussion of high schizophrenia rates in polar regions of Scandinavia.

**Malaysia**

Langat virus, a tick-borne flavivirus, is present in Malaysia (Smith 1956). Although no human cases of TBE are recorded from Malaysia (Karabatsos 1985), Pond (1963) found a 20 percent prevalence rate of RSSE in rural Malaysian villagers. Schizophrenia is present in Malaysia, but geographical prevalence is unknown.

**Micronesia**

Schizophrenia prevalence in Micronesia is highest on western Micronesian islands, especially Yap and Palau (Dale 1981). Although little is known of ticks and tick-borne diseases in Micronesia, Group B arbovirus infection is widespread on islands near Yap and Palau (Wiseman 1967). Tick-infected birds migrate from Palau and the Philippine Islands west of Palau to southern Japan (Hoogstraal et al. 1975). Yap and Palau lie just east of the known extent of the tick, *Ixodes granulatus*, from which Langat virus was recovered in Malaysia (Smith 1956, 1962). Further investigation of tick-borne diseases on Yap and Palau is needed to assess the theory.

**Japan**

Schizophrenia epidemiology in Japan is reviewed by Kato (1969). Two nationwide surveys reported average schizophrenia rates. Later surveys found higher rates in and around Tokyo (Kato 1969). Schizophrenia rates in Hachijo Island,
one of the Izu Islands 300 km south of Tokyo, are higher than Tokyo and comparable to Mannheim, Germany (Kato 1969). Hachijo Island is within the range of *Ixodes persulcatus*, the vector of Langt virus in Malaysia (Smith 1962), but no cases are reported.

The distribution of Lyme disease in Japan is high (Carlberg and Naito 1991; Miyamoto et al. 1992). Unless Lyme disease is vectored in Japan by a tick that does not carry flaviviruses, average rates of schizophrenia and high rates of Lyme disease are contrary to the flavivirus theory. Furthermore, the tick-borne flavivirus, Negishi, is present in Japan, although there are no reported human cases. Seroprevalence of Negishi is unknown (Karabatsos 1985; Venugopal et al. 1992). Japanese encephalitis, a mosquito-borne flavivirus, is also a major health threat in Southeast Asia including Japan (Burke and Leake 1988), but there are no reported cases of transmission of Japanese encephalitis by a tick vector (Karabatsos 1985). Comparison of flavivirus seroprevalence and schizophrenia in Japan is impossible until serosurveys of Negishi or other tick-borne flaviviruses are performed there.

**United States and Canada**

The distribution of Lyme disease and its vectors in the United States is discussed above. Other Ixodid ticks have the same distribution as the major Lyme vectors. *Ixodes cookei*, for instance, is concentrated in New England, the Great Lakes States, and the Northwestern States (Cooley and Kohls 1945). *Ixodes cookei* is the most common vector of Powassan virus (POW) (Artsob 1989). POW, a tick-borne flavivirus, was named after the town of Powassan, Ontario, Canada, where the virus was discovered in 1959 (Hoogstraal 1981). Most cases of POW are reported from Canada and New York, but serological surveys of ticks and vertebrates are positive for POW in California, Colorado, Connecticut, Maine, Massachusetts, South Dakota, and West Virginia (Artsob 1989). POW infection is found extensively in Russia, China (formerly People’s Republic of China), and Southeast Asia (Hoogstraal 1981). Incidence of human disease, usually severe, is extremely low but positive seroprevalence is much higher. Prevalence of positive human serology in endemic areas ranges from 0.5 to 3.3 percent (Hoogstraal 1966; Artsob 1989). Consumption of unpasteurized goat’s milk is considered a risk factor (Hoogstraal 1966; Artsob 1989). Without more extensive serological testing, the distribution of this virus cannot be correlated with the distribution of schizophrenia in the United States.

Some investigators refer to an unidentified flavivirus in U.S. serosurveys of POW (Whitney 1963; Hoogstraal 1966). This suggests that other TBE viruses exist in the United States. This notion is supported by the presence of RSSE strains in seabirds of Oregon (Clifford et al. 1971; Thomas et al. 1973). Seroprevalence of all viruses from *Ixodes cookei*, *Ixodes dammini*, and *Ixodes pacificus* in U.S. schizophrenia patients would test the association of schizophrenia with tick-borne flaviviruses.

In Canada, where seroprevalence of POW was studied in Quebec, British Columbia, and Ontario (Artsob 1989), the distribution of schizophrenia is not known. Murphy (1965) reported high rates of schizophrenia from St. Gildas and St. Xavier, Quebec, but the locations of these small villages were not provided by Murphy (1965) and are not found in modern atlases.

**Conclusion**

Definite proof of an association of TBE with schizophrenia cannot be demonstrated for several reasons. First, the epidemiology of both diseases is lacking in most countries. Second, serological surveys of TBE in individuals with schizophrenia are contradictory and flawed. Even if titers are positive in individuals with schizophrenia, this does not rule out the potential importance of other viruses in schizophrenia. However, the geographic co-occurrence of high rates of schizophrenia and TBE cannot be dismissed. How valid is the theory given the existing data?

Validity of the theory can be assessed using the previously discussed criteria for linking an environmental cause (TBE) with a disease (schizophrenia). These criteria and qualitative descriptions of their strengths of proof are shown in table 3. Although the theory is not proven, the evidence warrants serosurveys of all known Ixodid tick viruses in individuals with schizophrenia. Furthermore, since unidentified tick-borne flaviviruses probably exist in the United States and elsewhere, a rigorous search for previously unknown viruses in Ixodid ticks should be performed, and seroprevalence of antibodies to these viruses should be studied in carefully matched cohorts of schizophrenia patients and controls.

*The opinions expressed in this article are solely those of the author.*
Table 3. Criteria for confirmation of the tick-borne encephalitis theory of schizophrenia

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
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<tbody>
<tr>
<td>Strength</td>
<td>Strong</td>
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<tr>
<td>Consistency</td>
<td>Variable</td>
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<tr>
<td>Specificity</td>
<td>Moderate</td>
</tr>
<tr>
<td>Temporality</td>
<td>Plausible</td>
</tr>
<tr>
<td>Biological Gradient</td>
<td>Unknown</td>
</tr>
<tr>
<td>Plausibility</td>
<td>Good</td>
</tr>
<tr>
<td>Coherence</td>
<td>Good</td>
</tr>
<tr>
<td>Experimental confirmation</td>
<td>Unknown</td>
</tr>
<tr>
<td>Analogy</td>
<td>Unconfirmed</td>
</tr>
</tbody>
</table>

and do not represent the opinions of Walter Reed Army Medical Center, the U.S. Army, or the U.S. Government.

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Schizophrenia: Questions and Answers

What is schizophrenia? What causes it? How is it treated? How can other people help? What is the outlook? These are the questions addressed in a booklet prepared by the Schizophrenia Research Branch of the National Institute of Mental Health.

Directed to readers who may have little or no professional training in schizophrenia-related disciplines, the booklet provides answers and explanations for many commonly asked questions of the complex issues about schizophrenia. It also conveys something of the sense of unreality, fears, and loneliness that a schizophrenic individual often experiences.

The booklet describes "The World of the Schizophrenic Patient" through the use of analogy. It briefly describes what is known about causes—the influence of genetics, environment, and biochemistry. It also discusses common treatment techniques. The booklet closes with a discussion of the prospects for understanding schizophrenia in the coming decade and the outlook for individuals who are now victims of this severe and often chronic mental disorder.

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