**Your Task:**

1. Examine all the evidence, making annotations where necessary
2. Given what you know, you are to prove that what happened to Annalise, (ALL of her symptoms need explanations), was a result of explainable biological/psychological issues.
3. Write a 1-2 page summary of your findings, including a minimum of 5 pieces of evidence, cited in APA format**.**

**Patient Name:** Annelise Michel

**Early life**

Michel was born on 21 September 1952 in [Leiblfing](http://en.wikipedia.org/wiki/Leiblfing), [Bavaria](http://en.wikipedia.org/wiki/Bavaria), [West Germany](http://en.wikipedia.org/wiki/West_Germany) to a Catholic family. She was brought up along with three sisters by her parents, Josef and Anna. She was deeply religious and went to [mass](http://en.wikipedia.org/wiki/Catholic_mass) twice a week. When she was sixteen, she suffered a severe [convulsion](http://en.wikipedia.org/wiki/Convulsion) and was diagnosed with having temporal lobe epilepsy. In 1973, Michel graduated and joined the [University of Würzburg](http://en.wikipedia.org/wiki/University_of_W%C3%BCrzburg). Her classmates later described her as "withdrawn and very religious"

**Psychiatric treatment**

In June 1970, Michel suffered a third [seizure](http://en.wikipedia.org/wiki/Seizure) at the psychiatric hospital where she had been staying. She was prescribed anti-convulsion drugs for the first time, including [Dilantin](http://en.wikipedia.org/wiki/Dilantin), which did not bring about immediate alleviation. She began talking about seeing "devil faces" at various times of the day.[[1]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Sicilia_Informatio-1) That same month, she was prescribed another drug, Aolept, which is similar to [chlorpromazine](http://en.wikipedia.org/wiki/Chlorpromazine) and is used in the treatment of various [psychoses](http://en.wikipedia.org/wiki/Psychoses) including [schizophrenia](http://en.wikipedia.org/wiki/Schizophrenia) and disturbed behavior. In depression by 1973, she began [hallucinating](http://en.wikipedia.org/wiki/Hallucinate) while [praying](http://en.wikipedia.org/wiki/Prayer_in_Christianity), and complained about hearing voices telling her that she was "damned" and would "rot in hell".[[4]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Washington_Post-4) Michel's treatment in a psychiatric hospital did not improve her health and her depression worsened. Long term treatment did not help either, and she grew increasingly frustrated with the medical intervention. Being a devout Catholic, she began to attribute it to demonic possession. Michel became intolerant of sacred places and objects, such as the [crucifix](http://en.wikipedia.org/wiki/Crucifix).[[1]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Sicilia_Informatio-1)

Michel went to [San Damiano](http://en.wikipedia.org/wiki/San_Giorgio_Piacentino) with a family friend who regularly organised such [pilgrimages](http://en.wikipedia.org/wiki/Pilgrimages) to "holy places"—not officially recognised by the church.[[5]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-cramer-5) Her escort concluded that she was suffering from demonic possession because she was unable to walk past a crucifix and refused to drink the water of a holy spring. Both she and her family became convinced and consulted several priests, asking for an exorcism.[[4]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Washington_Post-4) The priests declined, recommended the continuation of medical treatment, and informed the family that exorcisms required the bishop's permission. In the [Catholic church](http://en.wikipedia.org/wiki/Catholic_church), official approval for an exorcism is given when the person strictly meets the set criteria, then they are considered to be suffering from possession (*infestatio*) and under demonic control. Intense dislike for religious objects and "supernatural powers" are some of the first indications.[[3]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Taz-3) Michel worsened physically and displayed aggression, self-injury, drank her own urine and ate insects. In November 1973, Michel started her treatment with [Tegretol](http://en.wikipedia.org/wiki/Tegretol), an anti-seizure drug and [mood stabilizer](http://en.wikipedia.org/wiki/Mood_stabilizer). She was prescribed [anti-psychotic drugs](http://en.wikipedia.org/wiki/Antipsychotic) during the course of the religious rites and took this frequently until shortly before her death.[[2]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Neuroscience2011-2)[[6]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-hln-6)

**Exorcism and death**

The priest Ernst Alt, whom they met, on seeing her declared that "she didn't look like an epileptic" and that he did not see her having seizures.[[5]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-cramer-5) Alt believed she was suffering from demonic possession and urged the local bishop to allow an exorcism. In a letter to him in 1975, Michel wrote, "I am nothing, everything about me is vanity, what should I do, I have to improve, you pray for me" and also once told him, "I want to suffer for other people...but this is so cruel".[[3]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Taz-3) In September of the same year, Bishop [Josef Stangl](http://en.wikipedia.org/wiki/Josef_Stangl) granted the priest Arnold Renz permission to exorcise according to the [*Rituale Romanum of 1614*](http://en.wikipedia.org/wiki/Roman_Ritual), but ordered total secrecy.[[7]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-TWS-7) Renz performed the first session on 24 September.[[4]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Washington_Post-4) Her parents stopped seeking medical treatment and relied solely on the exorcism rites. 67 exorcism sessions, one or two each week, lasting up to four hours, were performed over about ten months in 1975–1976.[[3]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Taz-3) Michel began talking increasingly about "dying to atone for the wayward youth of the day and the [apostate](http://en.wikipedia.org/wiki/Apostate) priests of the modern church", and she refused to eat towards the end.[[4]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Washington_Post-4)

On 1 July 1976, Michel died in her home. The [autopsy](http://en.wikipedia.org/wiki/Autopsy) report stated the cause was malnutrition and dehydration because of being in a semi-starvation state for almost a year while the rites of exorcism were performed.[[8]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-8) She weighed 30 kilograms (68 pounds) and the previous day, she had broken knees due to the continuous [genuflections](http://en.wikipedia.org/wiki/Genuflections) and was unable to move without assistance, and was reported to have been suffering from [pneumonia](http://en.wikipedia.org/wiki/Pneumonia).[[6]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-hln-6)

**Prosecution**

After an investigation, the state prosecutor maintained that Michel's death could have been prevented even one week before she died.[[9]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Press_courier-9)

In 1976, the state charged Michel's parents and priests Ernst Alt and Arnold Renz with [negligent homicide](http://en.wikipedia.org/wiki/Negligent_homicide).[[10]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-trial-10) During the case Michel's body was [exhumed](http://en.wikipedia.org/wiki/Exhume) and tapes were played to the court of the exorcisms over the eleven months which led to her death.[[11]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-mail-11) The parents were defended by [Erich Schmidt-Leichner](http://en.wikipedia.org/wiki/Erich_Schmidt-Leichner). The state maintained that no involved parties be jailed, instead the recommended sentence for the priests was a fine, and the prosecution said that the parents be excluded from punishment as they had "suffered enough",[[10]](http://en.wikipedia.org/wiki/Anneliese_Michel" \l "cite_note-trial-10) which is a criterion in German penal law, cf. § 60 [StGB](http://en.wikipedia.org/wiki/Strafgesetzbuch).

**Trial**

The trial started on 30 March 1978 in the district court and drew intense interest. Before the court, doctors testified that Michel was not possessed, stating that this was a psychological effect because of her strict religious upbringing and her epilepsy, but Doctor Richard Roth, who was asked for medical help by Alt, allegedly told her during the exorcism, that "there is no injection against the devil, Anneliese".[[4]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Washington_Post-4) The priests were defended by lawyers retained by the Church, and Schmidt-Leichner, who defended the parents, claimed that the exorcism was legal and that the [German constitution](http://en.wikipedia.org/wiki/German_constitution) protected citizens in the unrestricted exercise of their religious beliefs. The defence played tapes recorded at the exorcism sessions, sometimes featuring what was claimed to be "demons arguing", to assert their claim that Michel was possessed. Both priests insisted on that and claimed there were six demons including [Adolf Hitler](http://en.wikipedia.org/wiki/Adolf_Hitler), [Judas Iscariot](http://en.wikipedia.org/wiki/Judas_Iscariot) and [Nero](http://en.wikipedia.org/wiki/Nero); they further said that she was finally freed because of the exorcism just before her death.[[9]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Press_courier-9)

The bishop said that he was not aware of her alarming health condition when he approved of the exorcism and did not testify. The accused were found guilty of [manslaughter](http://en.wikipedia.org/wiki/Manslaughter) resulting from negligence and were sentenced to six months in jail (which was later suspended) and three years of probation.[[9]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Press_courier-9) It was a far lighter sentence than anticipated,[[4]](http://en.wikipedia.org/wiki/Anneliese_Michel" \l "cite_note-Washington_Post-4) but it was more than requested by the prosecution, who had asked that the priests only be fined and that the parents be found guilty but not punished. The Church approving such an old fashioned exorcism rite drew public and media attention. The case has been labelled as a misidentification of mental illness, negligence, abuse, and religious [hysteria](http://en.wikipedia.org/wiki/Hysteria).[[12]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-12)

**Exhumation and aftermath**

After the trial, the parents asked the authorities for permission to exhume the remains of their daughter. The official reason presented by the parents to authorities was that Michel had been buried in undue hurry in a cheap coffin. Almost two years after the burial, on 25 February 1978, her remains were replaced in a new oak coffin lined with tin. A [Carmelite](http://en.wikipedia.org/wiki/Carmelite) nun from the district of Allgäu, southern [Bavaria](http://en.wikipedia.org/wiki/Bavaria), told the parents that she had a vision of their daughter's still-intact body which authenticated the supernatural character of the case. The official reports state that the body bore the signs of consistent deterioration. The accused exorcists were discouraged from seeing the remains of Michel. Arnold Renz later stated that he had been prevented from entering the mortuary.[[6]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-hln-6)

In 1984, the bishops made a petition to the [Vatican](http://en.wikipedia.org/wiki/Holy_See) regarding the exorcism rite and a commission passed on the decision that she was mentally ill, not possessed.[[13]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-DW-13) Her grave still became a pilgrimage centre for fringe believers. Ulrich Niemann, a [Jesuit](http://en.wikipedia.org/wiki/Jesuit) priest, doctor and psychiatrist, whom priests call in exorcism cases, told *The Washington Post*, "As a doctor, I say there is no such thing as possession... In my view, these patients are mentally ill. I pray with them, but that alone doesn't help. You have to deal with them as a psychiatrist. But at the same time, when the patient comes from Eastern Europe and believes that he's been impaired by evil, it would be a mistake to ignore his belief system." Niemann further said that he does not think he is an exorcist and does not perform the Roman ritual of 1614.[[4]](http://en.wikipedia.org/wiki/Anneliese_Michel#cite_note-Washington_Post-4) The number of officially sanctioned exorcisms has decreased in Germany due to this case, in spite of [Pope Benedict XVI](http://en.wikipedia.org/wiki/Pope_Benedict_XVI) support for wider use of it compared to [Pope John Paul II](http://en.wikipedia.org/wiki/Pope_John_Paul_II), who previously made the rules more strict involving only rare cases in 1999

**Chlorpromazine**

**Chlorpromazine** (CPZ) — marketed, as chlorpromazine [hydrochloride](http://en.wikipedia.org/wiki/Hydrochloride), in the United States as **Thorazine** and elsewhere as **Largactil** and **Megaphen** — is a [dopamine antagonist](http://en.wikipedia.org/wiki/Dopamine_antagonist) of the [typical anti-psychotic](http://en.wikipedia.org/wiki/Typical_antipsychotic) class of medications possessing additional [anti-adrenergic](http://en.wikipedia.org/wiki/Anti-adrenergic), [anti-serotonergic](http://en.wikipedia.org/wiki/Antiserotonergic), [anti-cholinergic](http://en.wikipedia.org/wiki/Anti-cholinergic) and [anti-histaminergic](http://en.wikipedia.org/wiki/Antihistaminergic) properties used to treat [schizophrenia](http://en.wikipedia.org/wiki/Schizophrenia).[[3]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-healy1-3)[[4]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-4) First synthesized on December 11, 1950, chlorpromazine was the first drug developed with specific [antipsychotic](http://en.wikipedia.org/wiki/Antipsychotic) action and would serve as the prototype for the [phenothiazine](http://en.wikipedia.org/wiki/Phenothiazine) class of drugs, which comprises several other agents. The introduction of chlorpromazine during the 1950s into clinical use has been described as the single greatest advance in the history of psychiatric care, dramatically improving as it did the prognosis of patients in psychiatric hospitals worldwide.[[5]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-5)

Chlorpromazine works on a variety of receptors in the [central nervous system](http://en.wikipedia.org/wiki/Central_nervous_system), producing potent [anticholinergic](http://en.wikipedia.org/wiki/Anticholinergic), [antidopaminergic](http://en.wikipedia.org/wiki/Antidopaminergic), [antihistaminic](http://en.wikipedia.org/wiki/Antihistaminic), and [antiadrenergic](http://en.wikipedia.org/wiki/Antiadrenergic) effects. Both the clinical indications and [side effect profile](http://en.wikipedia.org/wiki/Adverse_drug_reaction) of CPZ are determined by the broadness of its action: its anticholinergic properties cause [constipation](http://en.wikipedia.org/wiki/Constipation), [sedation](http://en.wikipedia.org/wiki/Sedation), and [hypotension](http://en.wikipedia.org/wiki/Hypotension) but also help relieve nausea. It also has [anxiolytic](http://en.wikipedia.org/wiki/Anxiolytic) (anxiety-relieving) properties. Its antidopaminergic properties can cause [extrapyramidal symptoms](http://en.wikipedia.org/wiki/Extrapyramidal_symptoms), such as [akathisia](http://en.wikipedia.org/wiki/Akathisia) (restlessness, where the patient walks almost constantly, despite having nowhere to go due to mandatory confinement) and [dystonia](http://en.wikipedia.org/wiki/Dystonia). It is known to cause [tardive dyskinesia](http://en.wikipedia.org/wiki/Tardive_dyskinesia), which can be irreversible.[[6]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-Diaz-6) In acute settings, it is often administered as a syrup, which has a faster onset of action than tablets, and it can also be given by [intramuscular injection](http://en.wikipedia.org/wiki/Intramuscular_injection). [IV](http://en.wikipedia.org/wiki/Intravenous_therapy) administration is very irritating and is not advised; its use is limited to severe hiccups, surgery, and tetanus.[[7]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-7)

Chlorpromazine is on the [World Health Organization's List of Essential Medicines](http://en.wikipedia.org/wiki/World_Health_Organization%27s_List_of_Essential_Medicines), a list of the most important medication needed in a basic [health system](http://en.wikipedia.org/wiki/Health_system).[[8]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-8)

**Medical uses**

Chlorpromazine is classified as a low-potency [typical antipsychotic](http://en.wikipedia.org/wiki/Typical_antipsychotic) and in the past was used in the treatment of both acute and chronic [psychoses](http://en.wikipedia.org/wiki/Psychosis), including [schizophrenia](http://en.wikipedia.org/wiki/Schizophrenia) and the manic phase of [bipolar disorder](http://en.wikipedia.org/wiki/Bipolar_disorder), as well as amphetamine-induced psychoses. Low-potency antipsychotics have more anticholinergic side effects, such as dry mouth, sedation, and constipation, and lower rates of extrapyramidal side effects, while high-potency antipsychotics (such as [haloperidol](http://en.wikipedia.org/wiki/Haloperidol)) have the reverse profile.[[9]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-GG-9)

Chlorpromazine has also been used in [porphyria](http://en.wikipedia.org/wiki/Porphyria) and as part of [tetanus](http://en.wikipedia.org/wiki/Tetanus) treatment. It still is recommended for short-term management of severe anxiety and psychotic aggression. Resistant and severe [hiccups](http://en.wikipedia.org/wiki/Hiccups), severe [nausea](http://en.wikipedia.org/wiki/Nausea)/[emesis](http://en.wikipedia.org/wiki/Emesis), and [preanesthetic](http://en.wikipedia.org/wiki/Preanesthetic) conditioning are other uses.[[9]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-GG-9)[[10]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-ashp-10) Symptoms of [delirium](http://en.wikipedia.org/wiki/Delirium) in medically-hospitalized [AIDS](http://en.wikipedia.org/wiki/AIDS) patients have been effectively treated with low doses of chlorpromazine.[[11]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-Breitbart-11)

**Other**

Chlorpromazine is occasionally used off-label for treatment of severe [migraine](http://en.wikipedia.org/wiki/Migraine).[[12]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-MD-12)[[13]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-13) It is often, particularly as palliation, used in small doses to reduce nausea suffered by [opioid](http://en.wikipedia.org/wiki/Opioid)-treated cancer patients and to intensify and prolong the analgesia of the opioids as well.[[12]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-MD-12)[[14]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-14)

Chlorpromazine is the most effective substance against human infection by the [brain-eating amoeba](http://en.wikipedia.org/wiki/Naegleria_fowleri). One study concluded: "Chlorpromazine had the best therapeutic activity against *Naegleria fowleri* *in vitro* and *in vivo*. Therefore, it may be a more useful therapeutic agent for the treatment of primary amoebic meningoencephalitis than [amphotericin B](http://en.wikipedia.org/wiki/Amphotericin_B)."[[15]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-15)

In Germany, chlorpromazine still carries label indications for [insomnia](http://en.wikipedia.org/wiki/Insomnia), severe [pruritus](http://en.wikipedia.org/wiki/Pruritus), and preanesthesia.[[16]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-16) It is also used during heroin withdrawal under medical supervision.

**Adverse effects**

These antipsychotics have significant effects on gonadal hormones including significantly lower levels of estradiol and progesterone in women whereas men display significantly lower levels of testosterone and [DHEA](http://en.wikipedia.org/wiki/DHEA) when undergoing antipsychotic drug treatment compared to controls.[[17]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-Raj-17)

There appears to be a dose-dependent risk for seizures with chlorpromazine treatment.[[18]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-18) [Tardive dyskinesia](http://en.wikipedia.org/wiki/Tardive_dyskinesia) and [akathisia](http://en.wikipedia.org/wiki/Akathisia) are less commonly seen with chlorpromazine than they are with high potency typical antipsychotics such as [haloperidol](http://en.wikipedia.org/wiki/Haloperidol)[[19]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-Leucht-19) or [trifluoperazine](http://en.wikipedia.org/wiki/Trifluoperazine), and some evidence suggests that, with conservative dosing, the incidence of such effects for chlorpromazine may be comparable to that of newer agents such as [risperidone](http://en.wikipedia.org/wiki/Risperidone) or [olanzapine](http://en.wikipedia.org/wiki/Olanzapine).[[20]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-fn_36-20)

Chlorpromazine may deposit in ocular tissues when taken in high dosages for long periods of time.

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| --- | --- | --- | --- |
| Comparison of chlorpromazine to placebo[[21]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-Adams-21) | | | |
| **Measured outcome** | **Findings in words** | **Findings in numbers** | **Quality of evidence** |
| **Global effects** | | | |
| Not any improvement (9 weeks - 6 months) | 30% less risk of having no improvement in mental state, behaviour and functioning | RR 0.71 CI 0.58 to 0.86 | Very low (estimate of effect uncertain) |
| Relapse (6 months - 2 years) | 35% less risk of relapse | RR 0.65 CI 0.47 to 0.90 |
| **Adverse effects** | | | |
| Weight gain | 5 times more likely to have considerable weight gain, around 40% with chlorpromazine gaining weight | RR 4.92 CI 2.32 to 10.43 | Very low (estimate of effect uncertain) |
| Sedation | 3 times more likely to cause sedation, around 30% with chlorpromazine | RR 2.79 CI 2.25 to 3.45 |
| Acute movement disorder | 3.5 times more likely to cause easily reversible but unpleasant severe stiffening of muscles, around 6% with chlorpromazine | RR 3.47 CI 1.50 to 8.03 |
| Parkinsonism | 2 times more likely to cause parkinsonism (symptoms such as tremor, hesitancy of movement, decreased facial expression), around 17% with chlorpromazine | RR 2.11 CI 1.59 to 2.80 |
| Decreased blood pressure with dizziness | 3 times more likely to cause decreased blood pressure and dizziness, around 15% with chlorpromazine | RR 2.38 CI 1.74 to 3.25 |

**Contraindications**

Absolute contraindications include:[[1]](http://en.wikipedia.org/wiki/Chlorpromazine" \l "cite_note-TGA-1)

* Circulatory
* CNS depression
* Coma
* Drug intoxication
* Bone marrow suppression
* [Phaeochromocytoma](http://en.wikipedia.org/wiki/Phaeochromocytoma)
* [Hepatic failure](http://en.wikipedia.org/wiki/Hepatic_failure)
* Active liver disease
* Previous hypersensitivity (including jaundice, agranulocytosis, etc.) to phenothiazines, especially chlorpromazine, or any of the excipients in the formulation being used.

Relative contraindications include:[[1]](http://en.wikipedia.org/wiki/Chlorpromazine" \l "cite_note-TGA-1)

* Epilepsy
* [Parkinson's disease](http://en.wikipedia.org/wiki/Parkinson%27s_disease)
* [Myasthenia gravis](http://en.wikipedia.org/wiki/Myasthenia_gravis)
* [Hypoparathyroidism](http://en.wikipedia.org/wiki/Hypoparathyroidism)
* Prostatic hypertrophy

Very rarely, elongation of the QT interval may occur, increasing the risk of potentially fatal arrhythmias.[[22]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-22)

**Interactions**

Consuming food prior to taking chlorpromazine orally limits its absorption, likewise cotreatment with [benztropine](http://en.wikipedia.org/wiki/Benztropine) can also reduce chlorpromazine absorption.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) [Alcohol](http://en.wikipedia.org/wiki/Ethanol) can also reduce chlorpromazine absorption.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) Antacids slow chlorpromazine absorption.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) [Lithium](http://en.wikipedia.org/wiki/Lithium_%28medication%29) and chronic treatment with [barbiturates](http://en.wikipedia.org/wiki/Barbiturates) can increase chlorpromazine clearance significantly.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) [Tricyclic antidepressants](http://en.wikipedia.org/wiki/Tricyclic_antidepressants) (TCAs) can decrease chlorpromazine clearance and hence increase chlorpromazine exposure.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) Cotreatment with [CYP1A2](http://en.wikipedia.org/wiki/CYP1A2) inhibitors like [ciprofloxacin](http://en.wikipedia.org/wiki/Ciprofloxacin), [fluvoxamine](http://en.wikipedia.org/wiki/Fluvoxamine) or [vemurafenib](http://en.wikipedia.org/wiki/Vemurafenib) can reduce chlorpromazine clearance and hence increase exposure and potentially also adverse effects.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) Chlorpromazine can also potentiate the CNS depressant effects of drugs like [barbiturates](http://en.wikipedia.org/wiki/Barbiturates), [benzodiazepines](http://en.wikipedia.org/wiki/Benzodiazepines), [opioids](http://en.wikipedia.org/wiki/Opioids), lithium and anaesthetics and hence increase the potential for adverse effects such as [respiratory depression](http://en.wikipedia.org/wiki/Respiratory_depression) and [sedation](http://en.wikipedia.org/wiki/Sedation).[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1)

It is also a moderate inhibitor of [CYP2D6](http://en.wikipedia.org/wiki/CYP2D6) and also a substrate for [CYP2D6](http://en.wikipedia.org/wiki/CYP2D6) and hence can inhibit its own metabolism.[[9]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-GG-9) It can also inhibit the clearance of [CYP2D6](http://en.wikipedia.org/wiki/CYP2D6) substrates such as [dextromethorphan](http://en.wikipedia.org/wiki/Dextromethorphan) and hence also potentiate their effects.[[9]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-GG-9) Other drugs like [codeine](http://en.wikipedia.org/wiki/Codeine) and [tamoxifen](http://en.wikipedia.org/wiki/Tamoxifen) which require [CYP2D6](http://en.wikipedia.org/wiki/CYP2D6)-mediated activation into their respective active metabolites may have their therapeutic effects attenuated.[[9]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-GG-9) Likewise [CYP2D6](http://en.wikipedia.org/wiki/CYP2D6) inhibitors such as [paroxetine](http://en.wikipedia.org/wiki/Paroxetine) or [fluoxetine](http://en.wikipedia.org/wiki/Fluoxetine) can reduce chlorpromazine clearance and hence increase serum levels of chlorpromazine and hence potentially also its adverse effects.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) Chlorpromazine also reduces [phenytoin](http://en.wikipedia.org/wiki/Phenytoin) levels and increases [valproic acid](http://en.wikipedia.org/wiki/Valproic_acid) levels.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) It also reduces [propanolol](http://en.wikipedia.org/wiki/Propanolol) clearance and antagonises the therapeutic effects of [antidiabetic](http://en.wikipedia.org/wiki/Antidiabetic) agents, [levodopa](http://en.wikipedia.org/wiki/Levodopa) (a [Parkinson's](http://en.wikipedia.org/wiki/Parkinson%27s) medication. This is likely due to the fact that chlorpromazine antagonises the D2 receptor which is one of the receptors dopamine, a levodopa metabolite, activates), [amfetamines](http://en.wikipedia.org/wiki/Amfetamine) and [anticoagulants](http://en.wikipedia.org/wiki/Anticoagulant).[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) It may also interact with anticholinergic drugs such as [orphenadrine](http://en.wikipedia.org/wiki/Orphenadrine) to produce [hypoglycaemia](http://en.wikipedia.org/wiki/Hypoglycaemia) (low blood sugar).[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1)

Chlorpromazine may also interact with [epinephrine](http://en.wikipedia.org/wiki/Epinephrine) (adrenaline) to produce a paradoxical fall in blood pressure.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1)[Monoamine oxidase inhibitors](http://en.wikipedia.org/wiki/Monoamine_oxidase_inhibitors) (MAOIs) and [thiazide](http://en.wikipedia.org/wiki/Thiazide) diuretics may also accentuate the orthostatic hypotension experienced by those receiving chlorpromazine treatment.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) Quinidine may interact with chlorpromazine to increase [myocardialdepression](http://en.wikipedia.org/wiki/Myocardium).[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) Likewise it may also antagonise the effects of [clonidine](http://en.wikipedia.org/wiki/Clonidine) and [guanethidine](http://en.wikipedia.org/wiki/Guanethidine).[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) It also may reduce the seizure threshold and hence a corresponding titration of anticonvulsant treatments should be considered.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1) [Prochlorperazine](http://en.wikipedia.org/wiki/Prochlorperazine) and [desferrioxamine](http://en.wikipedia.org/wiki/Desferrioxamine) may also interact with chlorpromazine to produce transient metabolic [encephalopathy](http://en.wikipedia.org/wiki/Encephalopathy).[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1)

Other drugs that prolong the QT interval such as [quinidine](http://en.wikipedia.org/wiki/Quinidine), [verapamil](http://en.wikipedia.org/wiki/Verapamil), [amiodarone](http://en.wikipedia.org/wiki/Amiodarone), [sotalol](http://en.wikipedia.org/wiki/Sotalol) and [methadone](http://en.wikipedia.org/wiki/Methadone) may also interact with chlorpromazine to produce additive [QT interval](http://en.wikipedia.org/wiki/QT_interval) prolongation.[[1]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-TGA-1)

**Tolerance and withdrawal**

The [British National Formulary](http://en.wikipedia.org/wiki/British_National_Formulary) recommends a gradual withdrawal when discontinuing antipsychotic treatment to avoid acute withdrawal syndrome or rapid relapse.[[23]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-BNF-23) While withdrawal symptoms can occur, there is no evidence that tolerance develops to the drug's antipsychotic effects. A patient can be maintained for years on a therapeutically effective dose without any decrease in effectiveness being reported. Tolerance appears to develop to the sedating effects of chlorpromazine when it is first administered. Tolerance also appears to develop to the extrapyramidal, parkinsonian and other neuroleptic effects, although this is debatable.[[24]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-Kin-24)

A failure to notice withdrawal symptoms may be due to the relatively long half life of the drug resulting in the extremely slow excretion from the body. However, there are reports of muscular discomfort, exaggeration of psychotic symptoms and movement disorders, and difficulty sleeping when the antipsychotic drug is suddenly withdrawn, but after years of normal doses these effects are not normally seen.[[24]](http://en.wikipedia.org/wiki/Chlorpromazine#cite_note-Kin-24)

**Carbamazepine**

**Carbamazepine** (**CBZ**) (Tegretol, Equetro) is an [anticonvulsant](http://en.wikipedia.org/wiki/Anticonvulsant) and [mood-stabilizing](http://en.wikipedia.org/wiki/Mood_stabilizer) drug used primarily in the treatment of [epilepsy](http://en.wikipedia.org/wiki/Epilepsy) and [bipolar disorder](http://en.wikipedia.org/wiki/Bipolar_disorder), as well as [trigeminal neuralgia](http://en.wikipedia.org/wiki/Trigeminal_neuralgia). [Off-label](http://en.wikipedia.org/wiki/Off-label_use) uses include [attention-deficit hyperactivity disorder](http://en.wikipedia.org/wiki/Attention-deficit_hyperactivity_disorder), [schizophrenia](http://en.wikipedia.org/wiki/Schizophrenia), [phantom limb](http://en.wikipedia.org/wiki/Phantom_limb) syndrome, [complex regional pain syndrome](http://en.wikipedia.org/wiki/Complex_regional_pain_syndrome), [borderline personality disorder](http://en.wikipedia.org/wiki/Borderline_personality_disorder), and [post-traumatic stress disorder](http://en.wikipedia.org/wiki/Post-traumatic_stress_disorder).

Studies on the use of carbamazepine in pregnant women have demonstrated exposure of the fetus to the drug and its metabolites to be [teratogenic](http://en.wikipedia.org/wiki/Teratology) and is associated with the development of [spina bifida](http://en.wikipedia.org/wiki/Spina_bifida),[[2]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-2) [neurodevelopmental](http://en.wikipedia.org/wiki/Neurodevelopmental) problems,[[3]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-3) craniofacial defects, cardiovascular malformations, hypospadias, and developmental delays.

It is on the [World Health Organization's List of Essential Medicines](http://en.wikipedia.org/wiki/World_Health_Organization%27s_List_of_Essential_Medicines), a list of the most important medications needed in a basic [health system](http://en.wikipedia.org/wiki/Health_system).[[4]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-4)

## Medical uses

Carbamazepine is typically used for the treatment of [seizure](http://en.wikipedia.org/wiki/Seizure) disorders and [neuropathic pain](http://en.wikipedia.org/wiki/Neuropathic_pain).[[5]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-AHFS-5) It may be used [off-label](http://en.wikipedia.org/wiki/Off-label_use) as a second-line treatment for bipolar disorder and as an adjunct, never alone, with an [antipsychotic](http://en.wikipedia.org/wiki/Antipsychotic) in some cases of [schizophrenia](http://en.wikipedia.org/wiki/Schizophrenia) when treatment with a conventional antipsychotic alone has failed.[[5]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-AHFS-5)

In the United States, the [FDA](http://en.wikipedia.org/wiki/Food_and_Drug_Administration)-approved indications are [epilepsy](http://en.wikipedia.org/wiki/Epilepsy) (including [partial seizures](http://en.wikipedia.org/wiki/Partial_seizure), generalized [tonic-clonic seizures](http://en.wikipedia.org/wiki/Tonic-clonic_seizure) and [mixed seizures](http://en.wikipedia.org/wiki/Mixed_seizure)), [trigeminal neuralgia](http://en.wikipedia.org/wiki/Trigeminal_neuralgia), and [manic](http://en.wikipedia.org/wiki/Mania) and [mixed episodes](http://en.wikipedia.org/wiki/Mixed_state_%28psychiatry%29) of [bipolar I disorder](http://en.wikipedia.org/wiki/Bipolar_I_disorder).[[6]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Lexi-Comp-6) Although data are still lacking, carbamazepine appears to be as effective and safe as [lithium](http://en.wikipedia.org/wiki/Lithium_pharmacology) for the treatment of bipolar disorder, both in the acute and maintenance phases.[[7]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Ceron-Litvoc-7)

## Adverse effects

Common [adverse effects](http://en.wikipedia.org/wiki/Adverse_drug_reaction) may include drowsiness, dizziness, headaches and migraines, [motor coordination](http://en.wikipedia.org/wiki/Motor_coordination) impairment, nausea, vomiting and/or constipation. Alcohol use while taking carbamazepine may lead to enhanced depression of the [central nervous system](http://en.wikipedia.org/wiki/Central_nervous_system).

Less common side effects may include cardiac arrhythmias, blurry or double vision, and/or the temporary loss of [blood cells](http://en.wikipedia.org/wiki/Blood_cell) or [platelets](http://en.wikipedia.org/wiki/Platelet) and in rare cases can cause [aplastic anemia](http://en.wikipedia.org/wiki/Aplastic_anemia) or [agranulocytosis](http://en.wikipedia.org/wiki/Agranulocytosis). With normal use, small reductions in white cell count and serum [sodium](http://en.wikipedia.org/wiki/Hyponatremia) levels are common; however, in rare cases, the loss of platelets may become life-threatening. In this case, a doctor may recommend frequent blood tests during the first few months of use, followed by three to four tests per year for established patients. Additionally, carbamazepine may possibly exacerbate pre-existing cases of [hypothyroidism](http://en.wikipedia.org/wiki/Hypothyroidism), so yearly thyroid function tests are advisable for persons taking the drug.

Also, rare reports of an auditory side effect for carbamazepine use have been made, whereby patients perceive sounds about a [semitone](http://en.wikipedia.org/wiki/Semitone) lower than previously.[[8]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-pmid12581810-8)[[9]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-pmid14518681-9)[[10]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-pmid9804087-10) Thus, [middle C](http://en.wikipedia.org/wiki/Middle_C) would be heard as the note [B3](http://en.wikipedia.org/wiki/Scientific_pitch_notation) just below it, and so on. The inverse effect (that is, notes sounding higher) has also been recorded.[[11]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-pmid11020128-11)[[12]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-pmid15446396-12) This unusual side effect is usually not noticed by most people, and quickly disappears after the person stops taking carbamazepine.

[Oxcarbazepine](http://en.wikipedia.org/wiki/Oxcarbazepine), a derivative of carbamazepine, reportedly has fewer and less serious side effects.

Carbamazepine may cause [syndrome of inappropriate antidiuretic hormone](http://en.wikipedia.org/wiki/Syndrome_of_inappropriate_antidiuretic_hormone), since it both increases the release and potentiates the action of ADH ([vasopressin](http://en.wikipedia.org/wiki/Vasopressin)).

Carbamazepine may aggravate [juvenile myoclonic epilepsy](http://en.wikipedia.org/wiki/Juvenile_myoclonic_epilepsy), so it is important to uncover any history of jerking, especially in the morning, before starting the drug. It may also aggravate other types of generalized seizure disorders, particularly [absence seizures](http://en.wikipedia.org/wiki/Absence_seizures).[[13]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-13)

In addition, carbamazepine has been linked to serious adverse cognitive anomalies, including [EEG](http://en.wikipedia.org/wiki/Electroencephalography) slowing[[14]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-pmid12027908-14) and [apoptosis](http://en.wikipedia.org/wiki/Apoptosis) of [cultured](http://en.wikipedia.org/wiki/Cell_culture) [cerebellar](http://en.wikipedia.org/wiki/Cerebellum) [neurons](http://en.wikipedia.org/wiki/Neurons).[[15]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-pmid8719616-15)

The FDA informed health-care professionals that dangerous or even fatal skin reactions ([Stevens–Johnson syndrome](http://en.wikipedia.org/wiki/Stevens%E2%80%93Johnson_syndrome) and [toxic epidermal necrolysis](http://en.wikipedia.org/wiki/Toxic_epidermal_necrolysis)), that can be caused by carbamazepine therapy, are significantly more common in patients with a particular [human leukocyte antigen](http://en.wikipedia.org/wiki/Human_leukocyte_antigen) allele, [*HLA-B\*1502*](http://en.wikipedia.org/wiki/HLA-B75). This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including South Asian Indians.[[16]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-16) In Europeans, a large proportion of sensitivity is associated with [*HLA-B58*](http://en.wikipedia.org/wiki/HLA-B58). Researchers have also identified another genetic variant, *HLA-A\*3101*, which has been shown to be a strong predictor of both mild and severe adverse reactions to carbamazepine among Japanese[[17]](http://en.wikipedia.org/wiki/Carbamazepine" \l "cite_note-17) and Europeans.[[18]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Epilepsy_Society-18)

### Associated birth defects

If taken during pregnancy, carbamazepine can cause birth defects that include cardiovascular and urinary tract anomalies, craniofacial defects such as cleft palate,[[19]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Matalon-19) fingernail hypoplasia, [microcephaly](http://en.wikipedia.org/wiki/Microcephaly), developmental delays, and [intrauterine growth restrictions](http://en.wikipedia.org/wiki/Intrauterine_growth_restriction).[[20]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-FAstep2-20)

### Interactions

Carbamazepine has a potential for [drug interactions](http://en.wikipedia.org/wiki/Drug_interaction); caution should be used in combining other medicines with it, including other antiepileptics and mood stabilizers.[[6]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Lexi-Comp-6) Lower levels of carbamazepine are seen when administrated with [phenobarbital](http://en.wikipedia.org/wiki/Phenobarbital), [phenytoin](http://en.wikipedia.org/wiki/Phenytoin) (Dilantin), or [primidone](http://en.wikipedia.org/wiki/Primidone) (Mysoline), which can result in breakthrough seizure activity. Carbamazepine, as a [CYP450](http://en.wikipedia.org/wiki/CYP450) inducer, may increase clearance of many drugs, decreasing their concentration in the blood to subtherapeutic levels and reducing their desired effects.[[21]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-urleMedicine-_Toxicity.2C_Carbamazepine-21) Drugs that are more rapidly metabolized with carbamazepine include [warfarin](http://en.wikipedia.org/wiki/Warfarin) (Coumadin), lamotrigine (Lamictal), phenytoin (Dilantin), [theophylline](http://en.wikipedia.org/wiki/Theophylline), and [valproic acid](http://en.wikipedia.org/wiki/Valproic_acid) (Depakote, Depakote ER, Depakene, Depacon).[[6]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Lexi-Comp-6) Drugs that decrease the metabolism of carbamazepine or otherwise increase its levels include [erythromycin](http://en.wikipedia.org/wiki/Erythromycin),[[22]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Stafstrom-22) [cimetidine](http://en.wikipedia.org/wiki/Cimetidine) (Tagamet), [propoxyphene](http://en.wikipedia.org/wiki/Propoxyphene) (Darvon), and [calcium channel blockers](http://en.wikipedia.org/wiki/Calcium_channel_blocker).[[6]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Lexi-Comp-6) Carbamazepine also increases the metabolism of the hormones in [birth control pills](http://en.wikipedia.org/wiki/Birth_control_pill) and can reduce their effectiveness, potentially leading to unexpected pregnancies.[[6]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-Lexi-Comp-6) As a drug that induces cytochrome P450 enzymes, it accelerates elimination of many benzodiazepines and decreases their action.[[23]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-isbn1-58829-211-8-23)

Valproic acid and [valnoctamide](http://en.wikipedia.org/wiki/Valnoctamide) both inhibit [microsomal epoxide hydrolase](http://en.wikipedia.org/wiki/Epoxide_hydrolase) (MEH), the enzyme responsible for the breakdown of carbamazepine-10,11 epoxide into inactive metabolites.[[24]](http://en.wikipedia.org/wiki/Carbamazepine#cite_note-24) By inhibiting MEH, valproic acid and valnoctamide cause a build-up of the active metabolite, prolonging the effects of carbamazepine and delaying its excretion.

Grapefruit juice raises the [bioavailability](http://en.wikipedia.org/wiki/Bioavailability) of carbamazepine by inhibiting CYP3A4 enzymes in the gut wall and in the liver.

**Schizophrenia**

**Schizophrenia** ([/](http://en.wikipedia.org/wiki/Help:IPA_for_English)[ˌskɪtsɵˈfrɛniə](http://en.wikipedia.org/wiki/Help:IPA_for_English#Key)[/](http://en.wikipedia.org/wiki/Help:IPA_for_English) or [/](http://en.wikipedia.org/wiki/Help:IPA_for_English)[ˌskɪtsɵˈfriːniə](http://en.wikipedia.org/wiki/Help:IPA_for_English#Key)[/](http://en.wikipedia.org/wiki/Help:IPA_for_English)) is a [mental disorder](http://en.wikipedia.org/wiki/Mental_disorder) often characterized by abnormal social behavior and failure to recognize what is [real](http://en.wikipedia.org/wiki/Reality). Common symptoms include [false beliefs](http://en.wikipedia.org/wiki/Delusion), [unclear or confused thinking](http://en.wikipedia.org/wiki/Thought_disorder), [auditory hallucinations](http://en.wikipedia.org/wiki/Auditory_hallucination), reduced social engagement and emotional expression, and [inactivity](http://en.wikipedia.org/wiki/Avolition). Diagnosis is based on observed behavior and the person's reported experiences.

[Genetics](http://en.wikipedia.org/wiki/Genetics) and early environment, as well as [psychological](http://en.wikipedia.org/wiki/Psychology) and social processes, appear to be important contributory factors. Some recreational and prescription drugs appear to cause or worsen symptoms. The many possible combinations of symptoms have triggered debate about whether the diagnosis represents a single disorder or a number of separate syndromes. Despite the [origin](http://en.wikipedia.org/wiki/Etymology) of the term from the [Greek](http://en.wikipedia.org/wiki/Ancient_Greek) roots *skhizein* ("to split") and *phrēn* ("mind"), schizophrenia does not imply a "split personality", or "[multiple personality disorder](http://en.wikipedia.org/wiki/Dissociative_identity_disorder)"—a condition with which it is often confused in public perception.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1) Rather, the term means a "splitting of mental functions", reflecting the presentation of the illness.[[2]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-2)

The mainstay of treatment is [antipsychotic](http://en.wikipedia.org/wiki/Antipsychotic) medication, which primarily suppresses [dopamine](http://en.wikipedia.org/wiki/Dopamine) [receptor](http://en.wikipedia.org/wiki/Receptor_%28biochemistry%29) activity. [Counseling](http://en.wikipedia.org/wiki/Psychotherapy), job training and social rehabilitation are also important in treatment. In more serious cases—where there is risk to self or others—[involuntary hospitalization](http://en.wikipedia.org/wiki/Emergency_psychiatry) may be necessary, although hospital stays are now shorter and less frequent than they once were.[[3]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BeckerKilian2006-3)

Symptoms begin typically in young adulthood, and about 0.3–0.7% of people are affected during their lifetime.[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) The disorder is thought to mainly affect the ability to [think](http://en.wikipedia.org/wiki/Cognition), but it also usually contributes to chronic problems with behavior and emotion. People with schizophrenia are likely to have additional conditions, including [major depression](http://en.wikipedia.org/wiki/Major_depressive_disorder) and [anxiety disorders](http://en.wikipedia.org/wiki/Anxiety_disorder); the lifetime occurrence of [substance use disorder](http://en.wikipedia.org/wiki/Substance_use_disorder) is almost 50%.[[5]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Sim_et_al_2006-5) Social problems, such as long-term unemployment, poverty, and homelessness are common. The average [life expectancy](http://en.wikipedia.org/wiki/Life_expectancy) of people with the disorder is ten to twenty five years less than the average life expectancy.[[6]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lauren2012-6) This is the result of increased physical health problems and a higher [suicide](http://en.wikipedia.org/wiki/Suicide) rate (about 5%).[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4)[[7]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Jop2010-7)

**Symptoms**

Individuals with schizophrenia may experience [hallucinations](http://en.wikipedia.org/wiki/Hallucination) (most reported are [hearing voices](http://en.wikipedia.org/wiki/Auditory_hallucination)), [delusions](http://en.wikipedia.org/wiki/Delusion) (often bizarre or [persecutory](http://en.wikipedia.org/wiki/Persecutory_delusions) in nature), and [disorganized thinking and speech](http://en.wikipedia.org/wiki/Thought_disorder). The last may range from loss of train of thought, to sentences only loosely connected in meaning, to speech that is not understandable known as [word salad](http://en.wikipedia.org/wiki/Schizophasia) in severe cases. Social withdrawal, sloppiness of dress and hygiene, and loss of motivation and judgment are all common in schizophrenia.[[8]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-CarsonNursing-8) There is often an observable pattern of emotional difficulty, for example lack of responsiveness.[[9]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-HirschWeinberger2003p21-9) Impairment in [social cognition](http://en.wikipedia.org/wiki/Social_cognition) is associated with schizophrenia,[[10]](http://en.wikipedia.org/wiki/Schizophrenia" \l "cite_note-10) as are symptoms of [paranoia](http://en.wikipedia.org/wiki/Paranoia). [Social isolation](http://en.wikipedia.org/wiki/Social_isolation) commonly occurs.[[11]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-HirschWeinberger2003p481-11) Difficulties in [working](http://en.wikipedia.org/wiki/Working_memory) and [long-term memory](http://en.wikipedia.org/wiki/Long-term_memory), [attention](http://en.wikipedia.org/wiki/Attention), [executive functioning](http://en.wikipedia.org/wiki/Executive_functions), and speed of [processing](http://en.wikipedia.org/wiki/Information_processing) also commonly occur.[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) In one uncommon subtype, the person may be largely mute, remain motionless in bizarre postures, or exhibit purposeless agitation, all signs of [catatonia](http://en.wikipedia.org/wiki/Catatonia).[[12]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-12) About 30 to 50% of people with schizophrenia fail to accept that they have an illness or their recommended treatment.[[13]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-13) Treatment may have some effect on insight.[[14]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-14) People with schizophrenia often find facial emotion perception to be difficult.[[15]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-15)

**Positive and negative**

Schizophrenia is often described in terms of [positive and negative (or deficit) symptoms](http://en.wikipedia.org/wiki/Symptom#Positive_and_negative).[[16]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Sims_2002-16) Positive symptoms are those that most individuals do not normally experience but are present in people with schizophrenia. They can include delusions, disordered thoughts and speech, and [tactile](http://en.wikipedia.org/wiki/Tactile), [auditory](http://en.wikipedia.org/wiki/Auditory_hallucination), [visual](http://en.wikipedia.org/wiki/Visual), [olfactory](http://en.wikipedia.org/wiki/Olfactory) and [gustatory](http://en.wikipedia.org/wiki/Gustatory) hallucinations, typically regarded as manifestations of [psychosis](http://en.wikipedia.org/wiki/Psychosis).[[17]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-17) Hallucinations are also typically related to the content of the delusional theme.[[18]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM299-18) Positive symptoms generally respond well to medication.[[18]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM299-18)

Negative symptoms are deficits of normal emotional responses or of other thought processes, and respond less well to medication.[[8]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-CarsonNursing-8) They commonly include flat expressions or [little emotion](http://en.wikipedia.org/wiki/Blunted_affect), [poverty of speech](http://en.wikipedia.org/wiki/Alogia), [inability to experience pleasure](http://en.wikipedia.org/wiki/Anhedonia), [lack of desire to form relationships](http://en.wikipedia.org/wiki/Asociality), and [lack of motivation](http://en.wikipedia.org/wiki/Avolition). Negative symptoms appear to contribute more to poor quality of life, functional ability, and the burden on others than do positive symptoms.[[19]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-19) People with greater negative symptoms often have a history of poor adjustment before the onset of illness, and response to medication is often limited.[[8]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-CarsonNursing-8)[[20]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-AFP10-20)

**Onset**

Late adolescence and early adulthood are peak periods for the onset of schizophrenia,[[4]](http://en.wikipedia.org/wiki/Schizophrenia" \l "cite_note-Lancet09-4) critical years in a young adult's social and vocational development.[[21]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Addington_et_al_2007-21) In 40% of men and 23% of women diagnosed with schizophrenia, the condition manifested itself before the age of 19.[[22]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Cullen-22) To minimize the developmental disruption associated with schizophrenia, much work has recently been done to identify and treat the [prodromal (pre-onset)](http://en.wikipedia.org/wiki/Prodrome) phase of the illness, which has been detected up to 30 months before the onset of symptoms.[[21]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Addington_et_al_2007-21) Those who go on to develop schizophrenia may experience transient or self-limiting psychotic symptoms[[23]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Amminger_et_al_2006-23) and the non-specific symptoms of social withdrawal, irritability, [dysphoria](http://en.wikipedia.org/wiki/Dysphoria),[[24]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-ParnasJorgensen1989-24) and clumsiness[[25]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Coyle-25) during the prodromal phase.

**Causes**

A combination of genetic and [environmental factors](http://en.wikipedia.org/wiki/Environmental_factor) play a role in the development of schizophrenia.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1)[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) People with a family history of schizophrenia who have a transient psychosis have a 20–40% chance of being diagnosed one year later.[[26]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Drake_Lewis_2005-26)

**Genetic**

Estimates of [heritability](http://en.wikipedia.org/wiki/Heritability) vary because of the difficulty in separating the effects of genetics and the environment;[[27]](http://en.wikipedia.org/wiki/Schizophrenia" \l "cite_note-ODonovan_et_al_2003-27) averages of 0.80 have been given.[[28]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Her2011-28) The greatest risk for developing schizophrenia is having a [first-degree relative](http://en.wikipedia.org/wiki/First-degree_relative) with the disease (risk is 6.5%); more than 40% of [monozygotic twins](http://en.wikipedia.org/wiki/Monozygotic_twins) of those with schizophrenia are also affected.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1) If one parent is affected the risk is about 13% and if both are affected the risk is nearly 50%.[[28]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Her2011-28)

It is likely that many [genes](http://en.wikipedia.org/wiki/Genes) are involved, each of small effect and unknown transmission and expression.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1) Many possible candidates have been proposed, including specific [copy number variations](http://en.wikipedia.org/wiki/Copy-number_variation), [NOTCH4](http://en.wikipedia.org/wiki/NOTCH4), and histone protein loci.[[29]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Genes10-29) A number of [genome-wide associations](http://en.wikipedia.org/wiki/Genome-wide_association_study) such as [zinc finger protein 804A](http://en.wikipedia.org/wiki/Zinc_finger_protein_804A) have also been linked.[[30]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-30) There appears to be overlap in the genetics of schizophrenia and [bipolar disorder](http://en.wikipedia.org/wiki/Bipolar_disorder).[[31]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-31) Evidence is emerging that the genetic architecture of schizophrenia involved both common and rare risk variation.[[32]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-32)

Assuming a hereditary basis, one question from [evolutionary psychology](http://en.wikipedia.org/wiki/Evolutionary_psychology) is why genes that increase the likelihood of psychosis evolved, assuming the condition would have been [maladaptive](http://en.wikipedia.org/wiki/Maladaptive) from an evolutionary point of view. One idea is that genes are involved in the evolution of language and [human nature](http://en.wikipedia.org/wiki/Human_nature), but to date such ideas remain little more than hypothetical in nature.[[33]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-pmid18502103-33)[[34]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-34)

**Environment**

Environmental factors associated with the development of schizophrenia include the living environment, drug use and prenatal stressors.[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) Parenting style seems to have no major effect, although people with supportive parents do better than those with critical or hostile parents.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1) Childhood trauma, separation from ones families, and being bullied or abused increase the risk of psychosis.[[35]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-35) Living in an urban environment during childhood or as an adult has consistently been found to increase the risk of schizophrenia by a factor of two,[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1)[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) even after taking into account [drug use](http://en.wikipedia.org/wiki/Recreational_drug_use), [ethnic group](http://en.wikipedia.org/wiki/Ethnic_group), and size of [social group](http://en.wikipedia.org/wiki/Social_group).[[36]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-fn_19-36) Other factors that play an important role include [social isolation](http://en.wikipedia.org/wiki/Social_isolation) and immigration related to social adversity, racial discrimination, family dysfunction, unemployment, and poor housing conditions.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1)[[37]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Selten_et_al_2007-37)

**Substance use**

About half of those with schizophrenia use drugs or alcohol excessively.[[38]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Gregg2007-38) Amphetamine, cocaine, and to a lesser extent alcohol, can result in psychosis that presents very similarly to schizophrenia.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1)[[39]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-alcohol-39) Although it is not generally believed to be a cause of the illness, people with schizophrenia use [nicotine](http://en.wikipedia.org/wiki/Nicotine) at much greater rates than the general population.[[40]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-40)

[Alcohol abuse](http://en.wikipedia.org/wiki/Alcohol_abuse) can occasionally cause the development of a chronic substance-induced psychotic disorder via a [kindling mechanism](http://en.wikipedia.org/wiki/Kindling_%28sedative-hypnotic_withdrawal%29).[[41]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-emedicine-41) Alcohol use is not associated with an earlier onset of psychosis.[[42]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Large2011-42)

A significant proportion of people with schizophrenia use [cannabis](http://en.wikipedia.org/wiki/Cannabis_%28drug%29) to help cope with its symptoms.[[38]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Gregg2007-38) Cannabis can be a contributory factor in schizophrenia,[[43]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Chadwick2013-43)[[44]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Niesink2013-44)[[45]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Parakh2013-45) but cannot cause it alone;[[45]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Parakh2013-45) its use is neither necessary nor sufficient for development of any form of psychosis.[[45]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Parakh2013-45) Early exposure of the developing brain to cannabis increases the risk of schizophrenia,[[43]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Chadwick2013-43) although the size of the increased risk is difficult to quantify;[[43]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Chadwick2013-43)[[44]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Niesink2013-44) only a small proportion of early cannabis recreational users go on to develop any schizoaffective disorder in adult life,[[44]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Niesink2013-44) and the increased risk may require the presence of certain genes within an individual[[45]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Parakh2013-45) or may be related to preexisting psychopathology.[[43]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Chadwick2013-43) Higher dosage and greater frequency of use are indicators of increased risk of chronic psychoses.[[44]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Niesink2013-44) [Tetrahydrocannabinol](http://en.wikipedia.org/wiki/Tetrahydrocannabinol) (THC) and [cannabidiol](http://en.wikipedia.org/wiki/Cannabidiol) (CBD) produce opposing effects; CBD has antipsychotic and neuroprotective properties and counteracts negative effects of THC.[[44]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Niesink2013-44)

Other drugs may be used only as coping mechanisms by individuals who have schizophrenia to deal with depression, anxiety, boredom, and loneliness.[[38]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Gregg2007-38)[[46]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Leweke08-46)

**Developmental factors**

Factors such as hypoxia and infection, or stress and malnutrition in the mother during [fetal development](http://en.wikipedia.org/wiki/Fetal_development), may result in a slight increase in the risk of schizophrenia later in life.[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) People diagnosed with schizophrenia are more likely to have been born in winter or spring (at least in the [northern hemisphere](http://en.wikipedia.org/wiki/Northern_hemisphere)), which may be a result of increased rates of viral exposures [in utero](http://en.wikipedia.org/wiki/In_utero).[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1) The increased risk is about 5 to 8%.[[47]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-yolken-47)

**Mechanisms**

A number of attempts have been made to explain the link between altered brain function and schizophrenia.[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) One of the most common is the [dopamine hypothesis](http://en.wikipedia.org/wiki/Dopamine_hypothesis_of_schizophrenia), which attributes psychosis to the mind's faulty interpretation of the misfiring of [dopaminergic neurons](http://en.wikipedia.org/wiki/Dopamine).[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4)

**Psychological**

Many psychological mechanisms have been implicated in the development and maintenance of schizophrenia. [Cognitive biases](http://en.wikipedia.org/wiki/Cognitive_bias) have been identified in those with the diagnosis or those at risk, especially when under stress or in confusing situations.[[48]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-48) Some cognitive features may reflect global [neurocognitive deficits](http://en.wikipedia.org/wiki/Neurocognitive_deficit) such as memory loss, while others may be related to particular issues and experiences.[[49]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Bentall_et_al_2007-49)[[50]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Kurtz_2005-50)

Despite a demonstrated appearance of blunted effect, recent findings indicate that many individuals diagnosed with schizophrenia are emotionally responsive, particularly to stressful or negative stimuli, and that such sensitivity may cause vulnerability to symptoms or to the disorder.[[51]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-schizophrenia1-51)[[52]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-52) Some evidence suggests that the content of delusional beliefs and psychotic experiences can reflect emotional causes of the disorder, and that how a person interprets such experiences can influence symptomatology.[[53]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-53)[[54]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-54)[[55]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-55) The use of "[safety behaviors](http://en.wikipedia.org/wiki/Safety)" to avoid imagined threats may contribute to the [chronicity](http://en.wikipedia.org/wiki/Chronic_%28medicine%29) of delusions.[[56]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Freeman_BRT_2007-56) Further evidence for the role of psychological mechanisms comes from the effects of [psychotherapies](http://en.wikipedia.org/wiki/Psychotherapies) on symptoms of schizophrenia.[[57]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-57)

**Neurological**

[](http://en.wikipedia.org/wiki/File:Schizophrenia_fMRI_working_memory.jpg)

[Functional magnetic resonance imaging](http://en.wikipedia.org/wiki/Functional_magnetic_resonance_imaging) (fMRI) and other [brain imaging](http://en.wikipedia.org/wiki/Brain_imaging) technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory.

Schizophrenia is associated with subtle differences in brain structures, found in 40 to 50% of cases, and in brain chemistry during acute psychotic states.[[4]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Lancet09-4) Studies using [neuropsychological tests](http://en.wikipedia.org/wiki/Neuropsychological_test) and [brain imaging](http://en.wikipedia.org/wiki/Brain_imaging) technologies such as [fMRI](http://en.wikipedia.org/wiki/Functional_magnetic_resonance_imaging) and [PET](http://en.wikipedia.org/wiki/Positron_emission_tomography) to examine functional differences in brain activity have shown that differences seem to most commonly occur in the [frontal lobes](http://en.wikipedia.org/wiki/Frontal_lobe), [hippocampus](http://en.wikipedia.org/wiki/Hippocampus) and [temporal lobes](http://en.wikipedia.org/wiki/Temporal_lobe).[[58]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-58) Reductions in brain volume, smaller than those found in [Alzheimer's disease](http://en.wikipedia.org/wiki/Alzheimer%27s_disease), have been reported in areas of the frontal cortex and temporal lobes. It is uncertain whether these volumetric changes are progressive or preexist prior to the onset of the disease.[[25]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Coyle-25) These differences have been linked to the [neurocognitive deficits](http://en.wikipedia.org/wiki/Neurocognitive_deficit) often associated with schizophrenia.[[59]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Green2006-59) Because neural circuits are altered, it has alternatively been suggested that schizophrenia should be thought of as a collection of neurodevelopmental disorders.[[60]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Insel_2010-60) There has been debate on whether treatment with antipsychotics can itself cause reduction of brain volume.[[61]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-61)

Particular attention has been paid to the function of dopamine in the [mesolimbic pathway](http://en.wikipedia.org/wiki/Mesolimbic_pathway) of the brain. This focus largely resulted from the accidental finding that [phenothiazine](http://en.wikipedia.org/wiki/Phenothiazine) drugs, which block dopamine function, could reduce psychotic symptoms. It is also supported by the fact that amphetamines, which trigger the release of dopamine, may exacerbate the psychotic symptoms in schizophrenia.[[62]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Laruelle_et_al_1996-62) The influential dopamine hypothesis of schizophrenia proposed that excessive activation of [D2 receptors](http://en.wikipedia.org/wiki/Dopamine_receptor_D2) was the cause of (the positive symptoms of) schizophrenia. Although postulated for about 20 years based on the D2 blockade effect common to all antipsychotics, it was not until the mid-1990s that [PET](http://en.wikipedia.org/wiki/Positron_emission_tomography) and [SPET](http://en.wikipedia.org/wiki/SPET) imaging studies provided supporting evidence. The dopamine hypothesis is now thought to be simplistic, partly because newer antipsychotic medication ([atypical antipsychotic](http://en.wikipedia.org/wiki/Atypical_antipsychotic) medication) can be just as effective as older medication ([typical antipsychotic](http://en.wikipedia.org/wiki/Typical_antipsychotic) medication), but also affects [serotonin](http://en.wikipedia.org/wiki/Serotonin) function and may have slightly less of a dopamine blocking effect.[[63]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-JonesPilowsky2002-63)

Interest has also focused on the neurotransmitter [glutamate](http://en.wikipedia.org/wiki/Glutamate) and the reduced function of the [NMDA glutamate receptor](http://en.wikipedia.org/wiki/NMDA_receptor) in schizophrenia, largely because of the abnormally low levels of [glutamate receptors](http://en.wikipedia.org/wiki/Glutamate_receptor) found in the postmortem brains of those diagnosed with schizophrenia,[[64]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-fn_27-64) and the discovery that glutamate-blocking drugs such as [phencyclidine](http://en.wikipedia.org/wiki/Phencyclidine) and [ketamine](http://en.wikipedia.org/wiki/Ketamine) can mimic the symptoms and cognitive problems associated with the condition.[[65]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-fn_59-65) Reduced glutamate function is linked to poor performance on tests requiring frontal lobe and hippocampal function, and glutamate can affect dopamine function, both of which have been implicated in schizophrenia, have suggested an important mediating (and possibly causal) role of glutamate pathways in the condition.[[66]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-fn_28-66) But positive symptoms fail to respond to glutamatergic medication.[[67]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-fn_60-67)

**Diagnosis**

based on criteria in either the [American Psychiatric Association](http://en.wikipedia.org/wiki/American_Psychiatric_Association)'s fifth edition of the [*Diagnostic and Statistical Manual of Mental Disorders*](http://en.wikipedia.org/wiki/Diagnostic_and_Statistical_Manual_of_Mental_Disorders) (DSM 5), or the [World Health Organization](http://en.wikipedia.org/wiki/World_Health_Organization)'s [International Statistical Classification of Diseases and Related Health Problems](http://en.wikipedia.org/wiki/ICD) (ICD-10). These criteria use the self-reported experiences of the person and reported abnormalities in behavior, followed by a clinical assessment by a [mental health professional](http://en.wikipedia.org/wiki/Mental_health_professional). Symptoms associated with schizophrenia occur along a continuum in the population and must reach a certain severity before a diagnosis is made.[[1]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-BMJ07-1) As of 2013 there is no objective test.[[68]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM5pg101-68)

**Criteria**

In 2013, the American Psychiatric Association released the fifth edition of the DSM ([DSM-5](http://en.wikipedia.org/wiki/DSM-5)). To be diagnosed with schizophrenia, two diagnostic criteria have to be met over much of the time of a period of at least one month, with a significant impact on social or occupational functioning for at least six months. The person had to be suffering from delusions, hallucinations or disorganized speech. A second symptom could be negative symptoms or severely disorganized or catatonic behaviour.[[69]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM5pgxx-69) The definition of schizophrenia remained essentially the same as that specified by the 2000 version of DSM (DSM-IV-TR), but DSM-5 makes a number of changes.

* Subtype classifications – such as catatonic and [paranoid schizophrenia](http://en.wikipedia.org/wiki/Paranoid_schizophrenia)  – are removed. These were retained in previous revisions largely for reasons of tradition, but had subsequently proved to be of little worth.[[70]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-tandon-70)
* [Catatonia](http://en.wikipedia.org/wiki/Catatonia) is no longer so strongly associated with schizophrenia.[[71]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-cataonia-dsm-71)
* In describing a person's schizophrenia, it is recommended that a better distinction be made between the current state of the condition and its historical progress, to achieve a clearer overall characterization.[[70]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-tandon-70)
* Special treatment of [Schneider's first-rank symptoms](http://en.wikipedia.org/wiki/Schneider%27s_first-rank_symptoms) is no longer recommended.[[70]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-tandon-70)
* [Schizoaffective disorder](http://en.wikipedia.org/wiki/Schizoaffective_disorder) is better defined to demarcate it more cleanly from schizophrenia.[[70]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-tandon-70)
* An assessment covering eight domains of [psychopathology](http://en.wikipedia.org/wiki/Psychopathology) – such as whether hallucination or mania is experienced – is recommended to help clinical decision-making.[[72]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-dimensions-72)

The ICD-10 criteria are typically used in European countries, while the DSM criteria are used in the United States and to varying degrees around the world, and are prevailing in research studies. The ICD-10 criteria put more emphasis on Schneiderian first-rank symptoms. In practice, agreement between the two systems is high.[[73]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-Jakobsen_et_al_2005-73)

If signs of disturbance are present for more than a month but less than six months, the diagnosis of [schizophreniform disorder](http://en.wikipedia.org/wiki/Schizophreniform_disorder) is applied. Psychotic symptoms lasting less than a month may be diagnosed as [brief psychotic disorder](http://en.wikipedia.org/wiki/Brief_psychotic_disorder), and various conditions may be classed as [psychotic disorder not otherwise specified](http://en.wikipedia.org/wiki/Psychotic_disorder_not_otherwise_specified), while [schizoaffective disorder](http://en.wikipedia.org/wiki/Schizoaffective_disorder) is diagnosed if symptoms of [mood disorder](http://en.wikipedia.org/wiki/Mood_disorder) are substantially present alongside psychotic symptoms. If the psychotic symptoms are the direct physiological result of a general medical condition or a substance, then the diagnosis is one of a psychosis secondary to that condition.[[69]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM5pgxx-69) Schizophrenia is not diagnosed if symptoms of [pervasive developmental disorder](http://en.wikipedia.org/wiki/Pervasive_developmental_disorder) are present unless prominent delusions or hallucinations are also present.[[69]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM5pgxx-69)

**Subtypes**

The DSM-5 work group proposed dropping the five sub-classifications of schizophrenia included in DSM-IV-TR:[[74]](http://en.wikipedia.org/wiki/Schizophrenia" \l "cite_note-74)[[75]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-WHOICD-75)

* [Paranoid type](http://en.wikipedia.org/wiki/Paranoid_schizophrenia): Delusions or auditory hallucinations are present, but thought disorder, disorganized behavior, or affective flattening are not. Delusions are persecutory and/or grandiose, but in addition to these, other themes such as jealousy, religiosity, or [somatization](http://en.wikipedia.org/wiki/Somatization) may also be present. (DSM code 295.3/ICD code F20.0)
* [Disorganized type](http://en.wikipedia.org/wiki/Disorganized_schizophrenia): Named *hebephrenic schizophrenia* in the ICD. Where thought disorder and flat affect are present together. (DSM code 295.1/ICD code F20.1)
* [Catatonic type](http://en.wikipedia.org/wiki/Catatonia): The subject may be almost immobile or exhibit agitated, purposeless movement. Symptoms can include catatonic stupor and [waxy flexibility](http://en.wikipedia.org/wiki/Waxy_flexibility). (DSM code 295.2/ICD code F20.2)
* Undifferentiated type: Psychotic symptoms are present but the criteria for paranoid, disorganized, or catatonic types have not been met. (DSM code 295.9/ICD code F20.3)
* Residual type: Where positive symptoms are present at a low intensity only. (DSM code 295.6/ICD code F20.5)

The ICD-10 defines two additional subtypes:[[75]](http://en.wikipedia.org/wiki/Schizophrenia" \l "cite_note-WHOICD-75)

* Post-schizophrenic depression: A depressive episode arising in the aftermath of a schizophrenic illness where some low-level schizophrenic symptoms may still be present. (ICD code F20.4)
* [Simple schizophrenia](http://en.wikipedia.org/wiki/Simple-type_schizophrenia): Insidious and progressive development of prominent negative symptoms with no history of psychotic episodes. (ICD code F20.6)

[Sluggish schizophrenia](http://en.wikipedia.org/wiki/Sluggish_schizophrenia) is in the Russian version of the ICD-10. "Sluggish schizophrenia" is in the category of "schizotypal" disorder in section F21 of chapter V.[[76]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-76)

**Differential Diagnosis**

See also: [Dual diagnosis](http://en.wikipedia.org/wiki/Dual_diagnosis) and [Comparison of bipolar disorder and schizophrenia](http://en.wikipedia.org/wiki/Comparison_of_bipolar_disorder_and_schizophrenia)

Psychotic symptoms may be present in several other mental disorders, including [bipolar disorder](http://en.wikipedia.org/wiki/Bipolar_disorder),[[77]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-77) [borderline personality disorder](http://en.wikipedia.org/wiki/Borderline_personality_disorder),[[78]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-78) drug intoxication and [drug-induced psychosis](http://en.wikipedia.org/wiki/Substance-induced_psychosis). Delusions ("non-bizarre") are also present in [delusional disorder](http://en.wikipedia.org/wiki/Delusional_disorder), and social withdrawal in [social anxiety disorder](http://en.wikipedia.org/wiki/Social_anxiety_disorder), [avoidant personality disorder](http://en.wikipedia.org/wiki/Avoidant_personality_disorder) and [schizotypal personality disorder](http://en.wikipedia.org/wiki/Schizotypal_personality_disorder). Schizotypal personality disorder has symptoms that are similar but less severe than those of schizophrenia.[[68]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM5pg101-68) Schizophrenia occurs along with [obsessive-compulsive disorder](http://en.wikipedia.org/wiki/Obsessive-compulsive_disorder) (OCD) considerably more often than could be explained by chance, although it can be difficult to distinguish obsessions that occur in OCD from the delusions of schizophrenia.[[79]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-79) A small number of people withdrawing from benzodiazepines experience a severe withdrawal syndrome which may last a long time. It can resemble schizophrenia and be misdiagnosed as such.[[80]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-gabbards-80)

A more general medical and neurological examination may be needed to rule out medical illnesses which may rarely produce psychotic schizophrenia-like symptoms, such as [metabolic disturbance](http://en.wikipedia.org/wiki/Metabolic_disorder), [systemic infection](http://en.wikipedia.org/wiki/Systemic_infection), [syphilis](http://en.wikipedia.org/wiki/Syphilis), [HIV](http://en.wikipedia.org/wiki/HIV) infection, [epilepsy](http://en.wikipedia.org/wiki/Epilepsy), and brain lesions. [Stroke](http://en.wikipedia.org/wiki/Stroke), [multiple sclerosis](http://en.wikipedia.org/wiki/Multiple_sclerosis), [hyperthyroidism](http://en.wikipedia.org/wiki/Hyperthyroidism), [hypothyroidism](http://en.wikipedia.org/wiki/Hypothyroidism) and [dementias](http://en.wikipedia.org/wiki/Dementia) such as [Alzheimer's disease](http://en.wikipedia.org/wiki/Alzheimer%27s_disease), [Huntington's disease](http://en.wikipedia.org/wiki/Huntington%27s_disease), [frontotemporal dementia](http://en.wikipedia.org/wiki/Frontotemporal_dementia) and [Lewy Body dementia](http://en.wikipedia.org/wiki/Lewy_Body_dementia) may also be associated with schizophrenia-like psychotic symptoms.[[81]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-81) It may be necessary to rule out a [delirium](http://en.wikipedia.org/wiki/Delirium), which can be distinguished by visual hallucinations, acute onset and fluctuating [level of consciousness](http://en.wikipedia.org/wiki/Level_of_consciousness), and indicates an underlying medical illness. Investigations are not generally repeated for relapse unless there is a specific *medical* indication or possible [adverse effects](http://en.wikipedia.org/wiki/Adverse_effects) from [antipsychotic medication](http://en.wikipedia.org/wiki/Antipsychotic_medication). In children hallucinations must be separated from normal childhood fantasies.[[68]](http://en.wikipedia.org/wiki/Schizophrenia#cite_note-DSM5pg101-68)

**Genuflection** (or **genuflexion**), bending at least one knee to the ground, was from early times a gesture of deep respect for a superior. In 328 BC, [Alexander the Great](http://en.wikipedia.org/wiki/Alexander_the_Great) introduced into his court-etiquette some form of genuflection already in use in [Persia](http://en.wikipedia.org/wiki/Persia).[[1]](http://en.wikipedia.org/wiki/Genuflection#cite_note-1) In the [Byzantine Empire](http://en.wikipedia.org/wiki/Byzantine_Empire) even senators were required to genuflect to the emperor.[[2]](http://en.wikipedia.org/wiki/Genuflection#cite_note-2) In medieval Europe, one demonstrated respect for a king or noble by going down on one knee,[[3]](http://en.wikipedia.org/wiki/Genuflection" \l "cite_note-3) often remaining there until told to rise. It is traditionally often performed in western cultures by a male making a [proposal of marriage](http://en.wikipedia.org/wiki/Proposal_of_marriage). More recently, the gesture is largely restricted to Catholic religious practices.

The [Latin](http://en.wikipedia.org/wiki/Latin) word *genuflectio*, from which the English word is derived, originally meant [kneeling](http://en.wikipedia.org/wiki/Kneeling) rather than the rapid dropping to one knee and immediately rising that became customary in Western Europe in the [Middle Ages](http://en.wikipedia.org/wiki/Middle_Ages).[[4]](http://en.wikipedia.org/wiki/Genuflection#cite_note-4)

## What is temporal lobe epilepsy?

The features of seizures beginning in the temporal lobe can be extremely varied, but certain patterns are common. There may be a mixture of different feelings, emotions, thoughts, and experiences, which may be familiar or completely foreign. In some cases, a series of old memories resurfaces. In others, the person may feel as if everything—including home and family—appears strange. Hallucinations of voices, music, people, smells, or tastes may occur. These features are called “auras” or “warnings.” They may last for just a few seconds, or may continue as long as a minute or two.

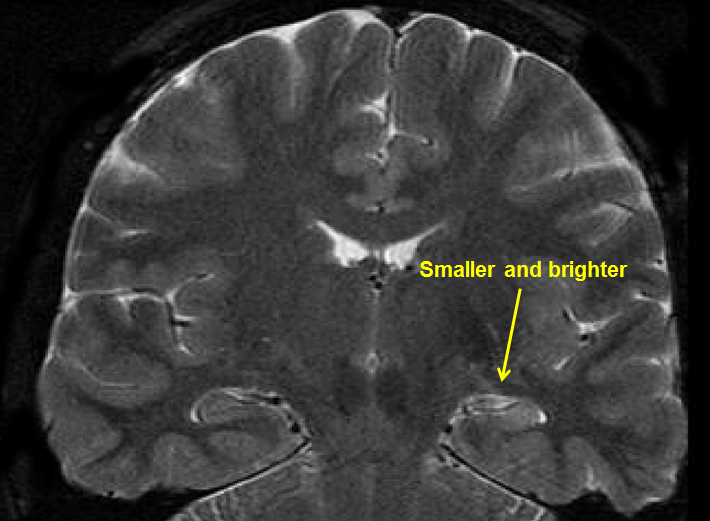
Experiences during temporal lobe seizures vary in intensity and quality. Sometimes the seizures are so mild that the person barely notices. In other cases, the person may be consumed with fright, intellectual fascination, or even pleasure.

The experiences and sensations that accompany these seizures are often impossible to describe, even for the most eloquent adult. And of course it is even more difficult to get an accurate picture of what people are feeling.

**What are the types of temporal lobe epilepsy?**

Temporal lobe epilepsy is the most common form of partial or localization related epilepsy. It accounts for approximately 60% of all patients with epilepsy. There are two types of temporal lobe epilepsy; one involves the medial or internal structures of the temporal lobe, while the second, called neocortical temporal lobe epilepsy, involves the outer portion of the temporal lobe. The most common version of these two is medial temporal lobe epilepsy.

* Medial temporal lobe epilepsy often begins within a structure of the brain called the hippocampus or its surrounding structures. It accounts for almost 80% of all temporal lobe seizures.
* Medial temporal lobe epilepsy is also considered a syndrome, which means that a lot of different conditions can result in medial temporal lobe epilepsy. Individuals who have medial temporal lobe epilepsy have seizures by definition of temporal lobe origin.
* There are a lot of different older names for the seizures that occur in temporal lobe epilepsy, including, “psychomotor seizures”, “limbic seizures”, and “temporal lobe seizures.” The modern name for these seizures is “complex partial,” if there is loss of awareness or “simple partial” if awareness is retained.
* While medial temporal lobe epilepsy is a very common form of epilepsy, it is also frequently resistant to medications and associated with a particular finding on an MRI. This finding is called hippocampal sclerosis (sclerosis means hardening) and it makes this a challenge to treat both medically and oftentimes surgical therapy is the best option for these individuals (See arrow in figure)



**What is the outlook?**

The overall prognosis for patients with drug resistant medial temporal lobe epilepsy includes a higher risk for memory and mood difficulties. This in turn leads to impairments in quality of life and an increased risk for death, as observed in patients who have frequent seizures failing to respond to treatment.

**What are some risk factors for temporal lobe epilepsy?**

Usually, the birth, labor, delivery and development of individuals with medial temporal lobe epilepsy is normal. However, there are some common risk factors:

* Conditions often associated with temporal lobe epilepsy include head trauma with loss of consciousness, injuries during early childhood and birth, brain malformations, infections such as encephalitis or meningitis, and even some tumors within the temporal lobe.
* The most common risk factor is having had a seizure associated with fever. Approximately two-thirds of patients with temporal lobe epilepsy have had a febrile seizure without an infection before the onset of complex partial seizures. Nearly 75% of these febrile seizures were considered to be either prolonged or have complex features. For example, the febrile seizures may be longer than usual, lasting 15 minutes or longer or have a very clear neurological abnormality, such as weakness in an arm or a funny posturing that suggests an abnormality in the brain.
  + Despite the fact that febrile seizures are a common risk factor for people with medial temporal lobe epilepsy, it is important to know that simply having had a seizure during a fever does not significantly increase the risk of epilepsy above that of the general population.

**When does temporal lobe epilepsy usually develop?**

Medial temporal lobe epilepsy usually begins at the end of a first or second decade in most people, following either a seizure with fever or an early injury to the brain. In women, hormonal influences during their menstrual cycle and ovulation may lead to reports of increased seizures during their menstrual cycle.

**What type of seizures are seen?**

* Seizures in temporal lobe epilepsy include simple partial seizures, such as auras, and focal seizures with complex impairment in consciousness, otherwise known as complex partial seizures.
* The most common auras are déjà-vu experiences or some gastrointestinal upset. Feelings of fear, panic, anxiety or a feeling of a rising epigastric sensation or butterflies with nausea are also other ways in which auras present in medial temporal lobe epilepsy. Some people also report a sense of unusual smell; this may raise a possibility of a hippocampal abnormality or a tumor in that area.
* Complex partial seizures can be associated with a fixed stare, impaired consciousness, fumbling with their fingers or lip-smacking movements that last 30 to 60 seconds. There can be a posture change in an arm that also can help to delineate the location of these seizures. Some people also note problems where they speak gibberish or lose their ability to speak in a sensible manner. Some individuals report difficulty with the language, particularly if the seizures are coming from the dominant temporal lobe. Some people may have a generalized tonic-clonic jerking and this can lead to weakness after the seizure has stopped.
* Some individuals can also have prolonged seizures and in some rare situations, status epilepticus may occur.

**How is TLE diagnosed?**

* The diagnosis of medial temporal lobe epilepsy is still by listening to a person describe their seizures or hearing observations of a witness.
* An MRI of the brain is considered the standard radiology procedure to see the characteristic abnormalities associated with medial temporal lobe epilepsy.
* An EEG is also essential - they often present with anterior temporal spike or sharp waves, which can occur in both wakefulness and/or sleep.
* Sometimes recording seizures in a video EEG monitoring unit is needed. This is often done to localize seizures and determine if surgery could be helpful.

**How is TLE treated?**

* Most patients with focal seizures will respond to medical treatment with appropriate anti-epileptic drugs. However, almost a third of patients may not respond to therapy and they may report problems with memory, socialization, and a fear of leaving their home. They may restrict their activities of daily life, which in turn leads to a decrease in quality of life.
* If seizures fail to respond to medication, then surgical approaches are an appropriate option. In individuals where the MRI shows hippocampal sclerosis in the medial temporal lobe and EEGs show abnormalities in that same area, seizures may be cured by surgery and in some cases, up to 70% of people can be rendered seizure-free with minimal problems afterwards.
* If surgery is not possible or doesn't work, devices such as vagus nerve stimulation or responsive neurostimulation may help.
* It is important to understand and recognize the features of medial temporal lobe epilepsy and how responsive treatments such as surgery and medications can be. It is important to consider the presenting aspects of how these seizures manifest in order to make the right diagnosis.

**Causes of malnutrition**

Malnutrition in developed countries is unfortunately still more common in situations of poverty, social isolation and substance misuse. However, most adult malnutrition is associated with disease and may arise due to:

* reduced dietary intake
* reduced absorption of macro- and/or micronutrients
* increased losses or altered requirements
* increased energy expenditure (in specific disease processes).[2](http://www.rcpjournal.org/content/10/6/624.full#ref-2)

**Dietary intake**

Probably the single most important aetiological factor in disease-related malnutrition is reduced dietary intake. This is thought to occur due to reductions in appetite sensation as a result of changes in cytokines, glucocorticoids, insulin and insulin-like growth factors.[6](http://www.rcpjournal.org/content/10/6/624.full#ref-6) The problem may be compounded in hospital patients by failure to provide regular nutritious meals in an environment where they are protected from routine clinical activities, and where they are offered help and support with feeding when required.[7](http://www.rcpjournal.org/content/10/6/624.full#ref-7)

**Malabsorption**

For patients with intestinal failure and those undergoing abdominal surgical procedures, malabsorption represents an independent risk factor for weight loss and malnutrition.

**Increased losses or altered requirements**

In some circumstances, such as enterocutaneous fistulae or burns, patients may have excessive and/or specific nutrient losses; their nutritional requirements are usually very different from normal metabolism.

**Energy expenditure**

It was thought for many years that increased energy expenditure was predominantly responsible for disease-related malnutrition. There is now clear evidence that in many disease states total energy expenditure is actually less than in normal health. The basal hypermetabolism of disease is offset by a reduction in physical activity, with studies in intensive care patients demonstrating that energy expenditure is usually below 2,000 kcal/day. The exception is patients with major trauma, head injury or burns where energy expenditure may be considerably higher, although only for a short period of time.[8](http://www.rcpjournal.org/content/10/6/624.full#ref-8),[9](http://www.rcpjournal.org/content/10/6/624.full" \l "ref-9)

**Consequences of malnutrition**

Malnutrition affects the function and recovery of every organ system.

**Muscle function**

Weight loss due to depletion of fat and muscle mass, including organ mass, is often the most obvious sign of malnutrition. Muscle function declines before changes in muscle mass occur, suggesting that altered nutrient intake has an important impact independent of the effects on muscle mass. Similarly, improvements in muscle function with nutrition support occur more rapidly than can be accounted for by replacement of muscle mass alone.[2](http://www.rcpjournal.org/content/10/6/624.full#ref-2),[9](http://www.rcpjournal.org/content/10/6/624.full" \l "ref-9)

Downregulation of energy dependent cellular membrane pumping, or reductive adaptation, is one explanation for these findings. This may occur following only a short period of starvation. If, however, dietary intake is insufficient to meet requirements over a more prolonged period of time the body draws on functional reserves in tissues such as muscle, adipose tissue and bone leading to changes in body composition. With time, there are direct consequences for tissue function, leading to loss of functional capacity and a brittle, but stable, metabolic state. Rapid decompensation occurs with insults such as infection and trauma. Importantly, unbalanced or sudden excessive increases in energy intake also put malnourished patients at risk of decompensation and refeeding syndrome.[6](http://www.rcpjournal.org/content/10/6/624.full#ref-6)

**Cardio-respiratory function**

Reduction in cardiac muscle mass is recognised in malnourished individuals. The resulting decrease in cardiac output has a corresponding impact on renal function by reducing renal perfusion and glomerular filtration rate. Micronutrient and electrolyte deficiencies (eg thiamine) may also affect cardiac function, particularly during refeeding. Poor diaphragmatic and respiratory muscle function reduces cough pressure and expectoration of secretions, delaying recovery from respiratory tract infections.

**Gastrointestinal function**

Adequate nutrition is important for preserving GI function: chronic malnutrition results in changes in pancreatic exocrine function, intestinal blood flow, villous architecture and intestinal permeability. The colon loses its ability to reabsorb water and electrolytes, and secretion of ions and fluid occurs in the small and large bowel. This may result in diarrhoea, which is associated with a high mortality rate in severely malnourished patients.

**Immunity and wound healing**

Immune function is also affected, increasing the risk of infection due to impaired cell-mediated immunity and cytokine, complement and phagocyte function. Delayed wound healing is also well described in malnourished surgical patients.[2](http://www.rcpjournal.org/content/10/6/624.full#ref-2),[9](http://www.rcpjournal.org/content/10/6/624.full" \l "ref-9)

**Psychosocial effects**

In addition to these physical consequences, malnutrition also results in psychosocial effects such as apathy, depression, anxiety and self-neglect.

[**Dehydration Influences Mood, Cognition**](http://psychcentral.com/news/2012/02/20/dehydration-influences-mood-cognition/35037.html)

By [Rick Nauert PhD](http://psychcentral.com/news/author/news-editor/) *Senior News Editor*  
Reviewed by John M. Grohol, Psy.D. on February 20, 2012

While most understand that dehydration can have medical complications, a new study shows that even mild dehydration can influence mood, energy levels and the ability to think clearly.

Regrettably, we often use thirst as an indicator for when we need to drink — a response that experts say is too late to avoid many of the detrimental effects of dehydration.

In two recent studies, researchers at the University of Connecticut’s Human Performance Laboratory discovered the mental, mood and cognitive downside of even mild dehydration.

Investigators determined that it didn’t matter if a person had just walked for 40 minutes on a treadmill or was sitting at rest – the adverse effects from mild dehydration were the same.

Mild dehydration is defined as an approximately 1.5 percent loss in normal water volume in the body.

The take home message is that individuals need to stay hydrated at all times, not just during exercise, extreme heat or exertion.

“Our thirst sensation doesn’t really appear until we are 1 [percent] or 2 percent dehydrated. By then dehydration is already setting in and starting to impact how our mind and body perform,” says Lawrence E. Armstrong, one of the studies’ lead scientists and an international expert on hydration.

The importance for everyone to stay hydrated is a message that needs to be promoted.

“Dehydration affects all people, and staying properly hydrated is just as important for those who work all day at a computer as it is for marathon runners, who can lose up to 8 percent of their body weight as water when they compete.”

In the study, separate groups of young women and men were tested. Twenty-five women with an average age of 23 took part in one study. The men’s group consisted of 26 men with an average age of 20.

All of the participants were healthy, active individuals, who were neither high-performance athletes nor sedentary — typically exercising for 30 to 60 minutes per day.

Each participant took part in three evaluations that were separated by 28 days. All of the participants walked on a treadmill to induce dehydration, and all of the subjects were hydrated the evening before the evaluations commenced.

As part of the evaluation, the subjects were put through a battery of cognitive tests that measured vigilance, concentration, reaction time, learning, memory, and reasoning. The results were compared against a separate series of tests when the individuals were not dehydrated.

The young women experienced mild dehydration which caused headaches, fatigue, and difficulty concentrating. They also perceived tasks as more difficult when slightly dehydrated, although there was no substantive reduction in their cognitive abilities.

The research findings are published in *The Journal of Nutrition*.

In the tests involving the young men, mild dehydration caused some difficulty with mental tasks, particularly in the areas of vigilance and working memory, according to the results of the second UConn study.

While the young men also experienced fatigue, tension, and [anxiety](http://psychcentral.com/disorders/anxiety/) when mildly dehydrated, adverse changes in mood and symptoms were “substantially greater in females than in males, both at rest and during exercise,” according to the study. The men’s study was published in the *British Journal of Nutrition*.

“Even mild dehydration that can occur during the course of our ordinary daily activities can degrade how we are feeling – especially for women, who appear to be more susceptible to the adverse effects of low levels of dehydration than men,” says Harris Lieberman, one of the studies’ co-authors.

“In both sexes these adverse mood changes may limit the motivation required to engage in even moderate aerobic exercise. Mild dehydration may also interfere with other daily activities, even when there is no physical demand component present.”

Investigators are uncertain why women and men are so adversely affected by mild dehydration. One possibility is that neurons in the brain detect dehydration. These neurons may then signal parts of the brain regulating mood.

This process could be part of an ancient warning system protecting humans from more dire consequences, and alerting them to the need for water to survive.

In order to stay properly hydrated, experts like Armstrong recommend that individuals drink eight, 8-ounce glasses of water a day, which is approximately equivalent to about 2 liters of water.

People can check their hydration status by monitoring the color of their urine. Urine should be a very pale yellow in individuals who are properly hydrated.

Urine that is dark yellow or tan in color indicates greater dehydration. Proper hydration is particularly important for high-risk groups, such as the elderly, people with diabetes, and children.

**'God told us to exorcise my daughter's demons. I don't regret her death'**

By Elizabeth Day

12:01AM GMT 27 Nov 2005

At the end of an ordinary road in a little town in Bavaria stands an unexceptional house, its walls a dirty white, the window frames painted a flaking green. But behind the locked front door and the lowered shutters a dark tale of extraordinary horror lurks.

Twenty-nine years ago, the house was filled with fear. The nights were punctuated by howls and screams, the mornings filled with inhuman voices. The neighbours did not know it then, but they were hearing the exorcism of a young woman who would shortly die.

At the time, it was believed that Anneliese Michel, a 23-year-old student from Klingenberg, had been possessed by six demonic spirits who would not let her go. After enduring 67 rites of exorcism over nine months, she succumbed to starvation in 1976.

She forced herself to fast, believing that it would rid her of the influence of Satan and when she died her weight was down to 68lb. "Mother," she said, just before the end, "I'm afraid."

Last week saw the release of a film loosely based on the life and death of Anneliese Michel. The Exorcism of Emily Rose is set, as is Hollywood's way, in modern-day America and focuses not on the of the exorcism itself, but on the prosecution of the exorcists after the heroine's death. Tom Wilkinson plays Fr Moore, the rural priest who believes he has acted on the side of angels, and Laura Linney stars as his hard-nosed but reluctant defence attorney.

Anneliese's parents, Anna and Josef, were put on trial for their daughter's murder alongside the two priests who performed the exorcisms. All were found guilty of negligent homicide by allowing her to starve and given suspended six-month prison sentences and three years' probation.

Anneliese's mother, who still lives in the house where her daughter died, has never quite recovered from those terrible times. Her husband died six years ago and her three surviving daughters have moved away. So Anna Michel, now in her eighties, bears the burden of memory alone. Her bedroom overlooks the graveyard where Anneliese is buried, under a wooden cross bearing her name and the inscription "Resting with God."

The house is quieter now, but the pain is evident still. "I don't want to see the film and I don't know anything about it," Mrs Michel says, her eyes glazed with the film of cataracts. "I miss Anneliese, of course. She was my daughter. I can see her grave from the house. I visit it often, taking flowers."

For a moment, it is easy to forget her turbulent history. She looks like a benign great aunt, contoured with soft lines drawn across papery skin, her brittle white hair tucked under a floppy black hat. She clearly does not like speaking about Anneliese's death and, until now, she has maintained a public silence.

But nor does she regret her actions. A deeply religious woman, she insists that the exorcism was justified. "I know that we did the right thing because I saw the sign of Christ in her hands," she says in a voice surprisingly forceful for one so frail. "She was bearing stigmata and that was a sign from God that we should exorcise the demons. She died to save other lost souls, to atone for their sins.

"Anneliese was a kind, loving, sweet and obedient girl. But when she was possessed, it was something unnatural, something that you can't explain." She pauses. From the very beginning, Anneliese's life was governed by fear. Her family was deeply religious. Her father had considered training as a priest and three of her aunts were nuns. But the Michels had a secret.

In 1948, Anneliese's mother gave birth to an illegitimate daughter, Martha, bringing such disgrace on her family that she was forced to wear a black veil on her wedding day.

When Anneliese was born in 1952, her mother encouraged her to atone for the sins of illegitimacy through fervent devotion. But when Martha was eight, she died from complications arising from an operation to remove a kidney tumour. Anneliese, a kind-hearted and deeply sensitive girl, must have felt ever more strongly the pressure to do penance for her mother.

She found herself increasingly surrounded by evidence of sinfulness and increasingly anxious to be rid of it. While other children in the 1960s were rebelling testing the limits of their freedom, Anneliese slept on a bare stone floor to atone for the sins of the drug addicts who slept rough at the local train station.

In 1968, aged 17, she began to suffer convulsions. Although initially diagnosed with grand mal epilepsy, she started experiencing devilish hallucinations while praying. By 1973, she was suffering severe depression and considering suicide. Voices in her head told her she was damned. She asked the local priest for exorcism and was twice refused.

But gradually, Anneliese slipped further into the abyss. She would perform 600 genuflections a day, eventually rupturing her knee ligaments. She crawled under a table, barking like a dog for two days. She ate spiders, coal and bit the head off a dead bird. She even licked her own urine off the floor and could be heard through the walls screaming for hours.

In 1975, her third request for exorcism was granted by the Bishop of Wurzburg. "I don't regret it," says Anna Michel firmly. "There was no other way."

We shall never know if there was. By this stage, Anneliese had refused further medical intervention from the Psychiatric Clinic Wurzburg. Her symptoms have subsequently been compared to schizophrenia and should have responded to treatment.

There has also been speculation that Anneliese might have been influenced by the release of William Friedkin's The Exorcist, in 1973. But whatever lay behind her disturbance, the exorcism could have caused Anneliese to believe her own hallucinations.

There was certainly no doubting the extent of Anneliese's turmoil. Her exorcism was performed by Fr Arnold Renz and Pastor Ernst Alt according to the 1614 Rituale Romanum. One or two four-hour sessions a week were held over nine months. The priests identified several demons, including Lucifer, Judas Iscariot, Nero, Cain and Adolf Hitler, who spoke with the correct Austrian inflections.

Forty-two hours of the process were recorded and the tapes are said to make terrifying listening. Barely human growls mingle with throaty gurgles, screamed obscenities and a series of dialogues between each of the demons about the horrors of Hell. The sessions often resulted in such brutality that Anneliese would be held down or chained to her chair.

By the spring of 1976, Anneliese was suffering from pneumonia and emaciation. Gradually weakened and exhausted to the point of fever, she died on July 1. Her parents buried her next to Martha at the outer edges of the cemetery - ground normally reserved for illegitimate children and suicides. Even in death, Anneliese was not free of the sinfulness she fought so hard to repent of.

Today, the 2,000 inhabitants of Klingenberg are unwilling to speak of Anneliese Michel. A gentle enquiry to passers-by is greeted with hostile glares and a shake of the head. "The town is ashamed," says Christiana Metzler, 42, who works in the tourist office. "I was at school when it happened and there were a lot of things covered up. People don't want to talk about it. There is a feeling that it was the parents' fault because they were so religious they didn't see what was happening. Sometimes Catholic pilgrims come to her grave because they think she can save lost souls. But there are not many of them. Now there is this film coming out, we are worried it will all be stirred up again."

It is a past that the Church is ashamed of, too. In 1984, German bishops petitioned Rome to review the exorcism rite in the light of the Michel case. Although their recommendations were not adopted, the Vatican published a revised exorcism rite in 1999 - the first update since the 17th century - and has introduced a qualification in exorcism that maks priests undergo medical training.

"I wouldn't have carried out the exorcism [on Anneliese Michel]," admits Fr Dieter Feineis, the current priest at St Pankratius Church in Klingenberg. "But both Anna Michel and her husband remained absolutely convinced that what they had done was right. The view of the Church is that it is possible to be possessed, but in Germany there are no more exorcisms."

In Italy, however, it is a different matter. According to the Italian Association of Psychiatrists and Psychologists, half a million Italians seek exorcisms each year. There are about 350 practising exorcists worldwide. Earlier this year, a priest and several nuns in a Romanian Orthodox convent in Tanacu believed that Maricia Irina Cornici, a 23-year-old nun, was possessed. They carried out an exorcism ritual and tied her to a cross, pushing a towel in her mouth and denying her food or water, She was dead three days later.

Was this death, or Anneliese's, the work of Satan or was the act of exorcism itself to blame? It is a question that tests the limits of faith and science. But for Anneliese's mother, sitting in her bedroom and looking out over the snow-covered graveyard, there is no uncertainty. "I give out a prayer to pilgrims who come to visit her grave," she says. "They are prayers to be said every day and they thank God for her giving her young life for other sinners so that we can be shown how to devote ourselves to the will of God."

As she shuffles slowly on her visits to leave flowers at the graves of her dead daughters, she cuts a lonely figure among the grey headstones. For Anna Michel, faith is all she has left.

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