Answers to picture quiz

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1. **Rett syndrome** is a neurodevelopmental disorder of the grey matter of the brain that almost exclusively affects females but has also been found in male patients. The clinical features include small hands and feet and a deceleration of the rate of head growth (including microcephaly in some). Repetitive stereotyped hand movements, such as wringing and/or repeatedly putting hands into the mouth, are also noted. People with Rett syndrome are prone to gastrointestinal disorders and up to 80% have seizures. They typically have no verbal skills, and about 50% of individuals affected are not ambulatory. Scoliosis, growth failure, and constipation are very common and can be problematic.

   Genetically, Rett syndrome (RTT) is caused by mutations in the gene MECP2 located on the X chromosome, and can arise sporadically or from germline mutations. In less than 10% of RTT cases, mutations in the genes CDKL5 or FOXG1 have also been found to resemble it. Rett syndrome was initially diagnosed by clinical observation, but the diagnosis is definitive when there is a genetic defect in the MECP2 gene. In some very rare cases, no known mutated gene can be found suggesting changes in MECP2 that are not identified by presently used techniques or mutations in other genes that may result in clinical similarities.

2. ***Naegleria fowleri*** is a free-living excavate form of protozoa typically found in warm bodies of fresh water, such as ponds, lakes, rivers, and hot springs. It is also found in soil, near warm-water discharges of industrial plants, and unchlorinated or poorly chlorinated swimming pools in an amoeboid or temporary flagellate stage. There is no evidence of this organism living in ocean (salt) water. Rarely, it can appear in inadequately treated samples of home-based tap water that is not treated enough to be entirely potable, though this is not the usual method of contracting the illness unless the water is very deeply inhaled, usually deliberately.

   N. fowleri can invade and attack the human nervous system. Although this occurs rarely, such an infection nearly always results in the death of the victim. The case fatality rate is estimated at 98%. From July to October 2012, 22 people died in the southern part of Pakistan within a week from Naegleria infection. At least 13 cases has been reported in Karachi, Pakistan, who had no history of aquatic activities. Infection likely occurred through ablution with tap water. It may be attributed to rising temperatures, reduced levels of chlorine in potable water, or deteriorating water distribution systems.

   In humans, *N. fowleri* can invade the central nervous system via the nose (specifically through the olfactory mucosa and cribriform plate of the nasal tissues). The penetration initially results in significant necrosis of and haemorrhaging in the olfactory bulbs. From there, the amoeba climbs along nerve fibers through the floor of the cranium via the cribriform plate and into the brain. The organism begins to consume cells of the brain piecemeal by means of a unique sucking apparatus extended from its cell surface. It then becomes pathogenic, causing primary amoebic meningoencephalitis (PAM or PAME). PAM is a syndrome affecting the central nervous system. PAM usually occurs in healthy children or young adults with no prior history of immune compromise who have recently been exposed to bodies of fresh water. Amphotericin B is effective against *N. fowleri in vitro*, but the prognosis remains bleak for those who contract PAM, and survival remains less than 1%.

3. **Rasmussen's encephalitis,** also known as chronic focal encephalitis (CFE), is a rare inflammatory neurological disorder, characterized by frequent and severe seizures, loss of motor skills and speech, hemiparesis (paralysis on one side of the body), encephalitis (inflammation of the brain), and dementia. The disorder, which affects a single cerebral hemisphere, generally occurs in children under the age of 15.

   The cause of the inflammation is not known: infection by a virus has been suggested, but the evidence for this is inconclusive. In the 1990s it was suggested that auto-antibodies against the glutamate receptor GluR3 were important in causing the disease, but this is no longer thought to be the case. However, more recent studies report **the presence of autoantibodies against the NMDA-type glutamate receptor subunit GluRepsilon2 (anti-NR2A antibodies)** in a subset of patients with Rasmussen's encephalitis.

   The condition mostly affects children, with an average age of 6 years. However, one in ten people with the condition develops it in adulthood. There are two main stages, sometimes preceded by a 'prodromal stage' of a few months. In the acute stage, lasting four to eight months, the inflammation is active and the symptoms become progressively worse. These include weakness of one side of the body (hemiparesis), loss of vision for one side of the visual field (hemianopia), and cognitive difficulties (affecting learning, memory or language, for example). Epileptic seizures are also a major part of the illness, although these are often partial. Focal motor seizures or epilepsia partialis continua are particularly common, and may be very difficult to control with drugs. In the chronic or *residual stage*, the inflammation is no longer active, but the sufferer is left with some or all of the symptoms because of the damage that the inflammation has caused. In the long term, most patients are left with some epilepsy, paralysis and cognitive problems, but the severity varies considerably.

4. **Ring chromosome 20, ring-shaped chromosome 20** or **r(20) syndrome** is a rare human chromosome abnormality where the two arms of chromosome 20 fuse to form a ring chromosome. The syndrome is associated with epileptic seizures, behaviour disorders and mental retardation. When only one copy of chromosome 20 forms a ring, the individual suffers from ring 20 chromosomal mosaicism.

   Ring chromosome 20 syndrome is thought to be an underdiagnosed condition. Since chromosomal analysis or karyotype testing is not a routine investigation for patients with epilepsy, the diagnosis of ring chromosome 20 syndrome is typically delayed or unrecognized. Individuals from the ages of 0-17 years should be considered for ring 20 chromosome analysis if they have: predominantly complex partial seizures, medically refractory crytogenic epilepsy, Lennox-Gastaut-like features with no cause identified, frequent subtle nocturnal seizures, an EEG showing prolonged high voltage frontally dominant slowing intermixed with spikes or sharp waves, an EEG showing overlapping features of continuous slow spike and wave discharges in sleep (CSWS) and electrical status epilepticus in sleep (ESES), and/ or subsequent cognitive impairment/learning difficulties/mild retardation. These patients will typically have a normal childhood development until onset of epilepsy and lack evidence of dysmorphism or other congenital malformations.