Summary: Introduction. In spite of the human, social and economic impact of schizophrenia and to be considered a disease of organic origin by several evidences, there are relatively few studies about this disease using electron microscope techniques and methods. For 25 years we have made studies about the viral hypothesis of schizophrenia by means of this technique. We have studied limbic structure samples from young adults and schizophrenic patients, from fetuses of schizophrenic mothers and from chicken embryos experimentally inoculated with cerebrospinal fluid from schizophrenic patients. In the last ten years we have performed studies of blood and cerebrospinal fluid samples from young schizophrenic patients. We have found some alterations, with the same characteristics to those observed in the central nervous system, which are compatible with:
a) the viral hypothesis and b) with herpes simplex hominis type I virus when immuno-electron microscopic techniques were used. Results and conclusion. The results obtained in this work can constitute a new element favoring the possible viral etiology of schizophrenia.

Organic character of the disease

Structural alterations in schizophrenic brains in an important proportion of patients that has been shown by imagenologic and morphometric studies which point out to deeper structural atrophies in the limbic system (amygdaline nucleus and hippocampus) specially in the left cerebral hemisphere.

Schizophrenia: electron microscopy

Young adults
Fetuses from schizophrenic mothers
Chicken embryos inoculated with CSF
Blood and cerebrospinal fluid
Schizophrenia: electron microscopy.

Central nervous system findings:
- Nuclear bodies
- Membrane alterations
- Particles with viral morphology

Blood and cerebrospinal fluid findings:
- Membrane alterations, vacuoles, spherical and hexagonal particles, glycogen increase, morphological alterations

Nuclear bodies

Intranuclear particles

Particles with viral morphology
Particles with viral morphology: below, herpes simplex virus. Above (arrow) particle observed in schizophrenia.

The image below is from Dennis Kunkel’s excellent *Microscopy Science and Photography Through a Microscope*.

**Immuno-electronmicroscopy**
- Particle labeled with anti-herpes simplex hominis type I antisera

**Electron microscopy studies**

**Fetuses and chicken embryos**

**Cytoplasm**
- Foetus of schizophrenic mother

**Particles. Immuno-electronmicroscopy**

**Foetus from schizophrenic mother**

**Digital analysis of the particles within the nucleus**

**Foetus from schizophrenic mother**

- Particle labeled with anti-herpes simplex antibody (arrow)
- Digital analysis of the particle reveals a central core and a hexagonal capsule.
Particle (vertical arrow) related to membrane structure (oblique arrow).

Brain sample of chicken embryo inoculated with CSF

Particles and membrane structures labeled with the antibody (anti HSV-1 antibody).

Antigen antibody reaction.

Spherical particle labeled with coloidal gold conjugated to anti HSV1 antibody.

Cerebrospinal fluid spherical particles.

Blood: particles without labeling.
An agglutination reaction is observed in 45% of schizophrenic patients when plasma and CSF are joined together. This agglutination is formed by platelets.

**Schizophrenia: Biological Test**

- Macroscopic agglutination reaction
- Optic microscopy
- Fluorescence
- Electron microscopy
- Immuno-electron microscopy

**Blood biological test**

**Platelet agglutination**
Agglutination reaction
Electron microscopy negative staining

Immuno-fluorescence
Antiherpes antibody

Platelet

Immuno-electronmicroscopy negative staining and coloidal gold

Within the big vacuoles (arrows) hexagonal particles are observed. These particles are similar to those observed in the central nervous system and are also related to membrane structures. See next slide at higher magnification.

Hexagonal particles