

## About Pathogenesis of the Vaccine Mumps Meningitis

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### Abstract

Meningeal reactions are common with mumps patients. It is considered that such reactions are due to the direct impact of the mumps virus on meningitis. With the development of the mumps vaccines, this opinion also included the vaccinated people who are considered at risk of serious post vaccinal meningitis. In this article, the author expresses the opinion that these reactions are pathogenetically conditioned and inevitable, and are due to inflammation of the choroid plexus, caused by both virulent and vaccinal strains. The inflammation leads to enhanced secretion of cerebrospinal fluid, causing an increase in the intracranial pressure and marked meningeal symptoms. On the basis of the morphological changes in the choroid plexus in experiments with monkeys, as well as on the clinical symptoms of meningeal reactions in vaccinated children - rare, in a mild form, shortlived, and without any consequences - the author believes these reactions to be forms of meningism, not of meningitis.

**Key words:** mumps virus, choroid plexus, meningitis, meningisms

### Резюме

Менингиалните реакции са чести при болните от паротит. Съществува мнението, че се дължат на прякото действие на паротитния вирус върху меките мозъчни обвивки, менингите. Със създаването на паротитни ваксини това сановище се прехвърли и върху менингиалните реакции, появяващи се и при ваксинираните и считани за сериозни постваксинални усложнения. В настоящата статия, авторът изразява становището, че тези реакции са патогенетично обусловени и неизбежни и, че не се дължат на пряко засягане на менингите от паротитния вирус, а на възпаление на плексус хороидеус предизвикано от вируса. Това възпаление повишава секрецията на ликвора, увеличава интракраниалното налягане и с това предизвиква менингиалните симптоми. Базирайки се на морфологичните промени в плексус хороидеус при експерименти с маймуни и на клиничните симптоми на реакциите при ваксинираните деца: редки, леко протичащи, бързо преходни и без никакви последици, авторът счита, че тези реакции не са менингити, а менингизми.

Aseptic meningitis was considered to be a serious and common reaction of the mumps infection. This type of meningitis is explained with the direct attack on the meninges by the virus. After the development of mumps vaccine strains, this opinion was also addressed to them. This fact has an adverse effect on the mass vaccine prophylaxis of mumps.

It is widely known that the mumps virus has a tropism for the excretory cells of the salivary, testicles, pancreas as well as choroid plexus glands. The mumps virus has its own surface receptors corresponding to the relevant receptors on the excretory

cells of the above mentioned glands. The virus does not affect the cells with endocrine function (enzymes expression as insulin, testosterone, amylase etc.) of the above mentioned glands since they have not similar receptors.

Once the virus has entered the body through respiratory tract, it moves to the regional lymph nodes and thereafter to the blood flow. It proliferates in the blood system (in the lymphocytes), and causes viremia (Fleischer and Kroeth, 1971). This fact has been proven by isolation of the mumps virus from blood, saliva, urine and liquor. Having interacted with the relevant receptors of the cited excretory cells, mumps virions enter them, reproduce and cause inflammation.

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The present standpoint primarily view the relationship of the mumps virus (virulent and vaccine strains) with choroid plexus.(Noback *et al.*, 1996) (Fig. 1). As a single-stranded negative RNA, the virus replicates in the cytoplasm, leaving the cell nucleic acid unaffected.

Newly produced virions leave the endothelial cells of the plexus by budding, do not destroy the membranes of the cells but cause a benign inflammatory process. This process increases the function of secretory granules and the volume of cytoplasm as well as the permeability of the cell membranes, and causes hyperemia, augments the capillary volume and increases the count of perivascular lymphocyte infiltrates among the braided vascular plexus. These lesions increase the secretion of cerebrospinal fluid (CSF) and cause disorder in CSF dynamics. As a result, the brain ventricles overflow, liquor enters the intercellular space and swells it. All these processes increase the intracranial pressure and cause meningeal syndrome - meningism.

The outwandering of the surplus liquor containing virus is a continuous process (Bernard, 2014). It escapes from the fourth ventricles into the cistern magna of the sub-arachnoid space, moves slowly and finally reaches the superior sagittal sinus and by the Pacchioni granules leaves the cranial cavity carrying both the virus and the waste products of excess fluid. Meningeal symptoms disappear without any consequences.

During its stay in the cerebrospinal fluid and in the intra-cerebral space the virus contacts neuronal, glial and meningeal cells. However, the mumps virus does not enter and proliferate into them since they have no receptors corresponding to this causer.

Mumps vaccines are live and vaccine strains replicate the pathway of the wild mumps virus. Unlike it, however, the inflammatory processes provoked by them are significantly weaker, intracranial pressure remains largely lower and meningitis symptoms are manifold scarcer, milder and fast transient, due to which their clinical presentation is incidental.

The degree of inflammation of choroid plexus depends on the degree of attenuation of a strain and viral load in the blood and correlates with the intensity of the immune response.

The leading role of choroid plexus inflammation was supported also by experiments in monkeys with mumps vaccine strains Leningrad-3, Sofia-6 and Jeril Lynn (Rosina *et al.*, 1978; Rosina and Hilgenfeldt, 1985).

The role of the choroid plexus is also in line with clinical observations in vaccinated individuals manifesting meningeal symptoms a dissociation of the clinical symptoms and liquor finding: mild clinical signs, most often cervical rigidity, *against* clear liquor, outflow under pressure with puncture, with higher pleocytosis and increased protein (Odisseev, 1971; Radev *et al.*, 1980; Kaneva *et al.*, 1982).

The above facts give us a reason to suggest that the main cause of the occurrence of vaccine "mumps meningitis" reactions in some of the vaccinated individuals is not the inflammation of the meninges but inflammation of the choroid plexus and the surplus liquor secretion causes the increased pressure in the intracranial space, hence the mumps meningism is pathogenetically conditioned and inevitable, but acceptable. Given the above, we maintain that the term mumps chroiditis compliance with the concurrent parotitis, pancreatitis and orchitis. This is particularly valid for the leaflets of routinely used vaccines, in which the term meningitis, where it appears, is considered a serious syndrome and this gives parents a reason to deny children vaccination. We believe the term should be modified into meningism, which is the result of a mild inflammation of choroid plexus (excreting little liquor), with mild clinical signs and without any consequences.

Vaccine meningeal reactions, which are considered to be an inflammation of the meninges, were the object of in-depth discussions in the WHO at international and national forums worldwide and an abundance of papers. As a matter of fact, we have defended our statement in discussions and papers and also have expressed it to the WHO (Odisseev, 2006). In the beginning of 2007, the WHO concluded: "that in terms of safety, all mumps vaccine preparations for which relevant data are available and acceptable for use in immunization programmes" (WHO, 2007).

The problem of mumps vaccines was terminated and it does not present in the further plans of the WHO. From now on they will be seamlessly included in the combination with measles-mumps-rubella (MMR) and measles-mumps-rubella-varicella (MMRV) vaccines and distributed parallel with them.

However, when used in the vaccine information leaflets, the term "mumps meningitis - inflammation of the soft cerebral lining that covers the brain" ( for instance in leaflet of the vaccine Priorix applicable in Bulgaria ) has an adverse impact in the course of immunization process with mumps

vaccines, hence we suggest that this term should be modified into the meaning proposed above – meningism.

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