

# Aluminium adjuvanted vaccines: the position of the French Advisory Committee on Immunisation Practices

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# Aluminium adjuvanted vaccines

## Long duration collective experience

- Aluminium salts have been added to vaccine antigens since 1926 . These vaccines have been used all over the world for more than eighty years and milliard of doses were inoculated.
- Tolerance is fair. **Adverse effects are scarce** : mainly local reaction (pain, inflammatory reaction), seldom general (fever); **these reactions happen early**.
- **No country or official body calls into question the validity of this addition or the safety of vaccines containing aluminium salts.**

# Macrophagic Myofasciitis (MMF)

- MMF is defined by microscopic [lesions](#) found in muscles biopsies : infiltration of muscle tissue by [PAS-positive macrophages](#).
- In patients suffering from musculoskeletal symptoms, Gherardi, Authier and Cherin at the French Reference Center for Neuromuscular Diseases (GERMAAD), observed MMF in biopsy obtained from deltoid muscle. Macrophages contained aluminium particles provided by inoculated vaccines.
- Since 1998, this team gathered more than 1000 observations of MMF. Biopsies were done 65 months in average between the inoculation of an adjuvanted vaccine **in the deltoid**.

Table 1 – Summary of reported clinical symptoms [12]

Symptoms	Percentage of patients
Myalgias	88–91
Arthralgias	57–68
Marked asthenia	55
Muscle weakness	45
Fever	20–32
Elevated CK levels	29–50
Increased ESR	37
Myopathic EMG	35
Demyelinating CNS disorder	9
Multiple sclerosis diagnosis	33
Chronic fatigue	50–93
Hashimoto's thyroiditis	2.7
Other autoimmune-related diseases (RA, Sjogren)	6.7

## Latest aluminium vaccine received before diagnosis.

Vaccine	N	%
Vaccine against hepatitis B	289	69.3
Vaccine against tetanus	21	5.0
Revaxis®	11	2.6
Vaccine against hepatitis A	11	2.6
Vaccine against hepatitis B + Vaccine against hepatitis A	8	1.9
Vaccine against hepatitis B + Vaccine against tetanus	2	0.5
Vaccine against hepatitis B + Tetravac®	1	0.2
Vaccine against hepatitis A + Revaxis®	1	0.2
Infanrix®	1	0.2
Gardasil®	1	0.2
Tetravac®	1	0.2
HPV Vac	1	0.2
<b>Not specified</b>	<b>69</b>	<b>16.5</b>
<b>Total</b>	<b>417</b>	<b>100.0</b>

# Macrophagic myofasciitis controversy

- An epidemiological study was set by the French Ministry of Health (2002 – 3):
  - MMF is an indisputable histological entity whose association with aluminium used as an adjuvant in vaccines is recognized.
  - But case-control study demonstrated there was no specific clinical entity could be demonstrated to be related with the use of aluminium adjuvanted vaccine.
- In 2004, the Global Advisory Committee on Vaccine Safety (WHO) reviewed the data of the case–control study performed in France and also concluded that “ **the persistence of aluminium-containing macrophages at the site of a previous vaccination is not associated with specific clinical symptoms or disease** “.

# MMF suggested pathogenesis

Several successive hypothesis were challenged :

- 1<sup>st</sup> (1998): diffuse muscle disease,
- 2<sup>nd</sup> (1999): autoimmune process related with aluminium,
- 3<sup>rd</sup> (2001): Chronic fatigue syndrome,
- 4<sup>th</sup> (2009) : Direct cerebral toxicity due to aluminium nanoparticles,
- 5<sup>th</sup> (2011) : ASIA syndrome (autoimmune?),
- 6<sup>th</sup> (2013) : cerebral toxicity due to aluminium loaded monocytes
- ...

# Chronic Fatigue Syndrom (CFS)

- 1. Unexplained, persistent fatigue** present for  $\geq 6$  months that is not substantially relieved by rest, is of new onset (not lifelong) and results in a significant reduction in previous levels of activity.
- 2. Four or more of the following symptoms** are present for six months or more:
  - Impaired memory or concentration,
  - Postexertional malaise (extreme, prolonged exhaustion and sickness following physical or mental activity),
  - Unrefreshing sleep,
  - Muscle pain,
  - Multijoint pain without swelling or redness,
  - Headaches of a new type or severity,
  - Sore throat that's frequent or recurring,
  - Tender cervical or axillary lymph nodes.



# From MMF to CFS

The GERMMAD worked to demonstrate that MMF was associated with neuropsychological problems linked to cerebral lesion.

Experimental studies were done:

- In mice, 1 year after IM injection of aluminium containing vaccine, Al deposits are detected in brain. Injected labelled materials can be followed up to brain, suggesting that macrophages loaded with nanoparticles are able to migrate and to access to cerebral area especially grey matter.
- In altered blood-brain barrier mice (BBB), they demonstrated a progressive diffusion into the cerebral grey matter suggesting an active process via macrophages containing nanoparticles that cross the blood-brain barrier : “Trojan horse” mechanism.
- In CCL2 deficient mice, substitution modulates the cerebral intake of aluminium labelled particles captured by monocytes.

# Pointed out uncertainties

- **Cerebral impairment does not explain all the symptoms which the MMF patients suffered.**
- Al-Rho particles are not representative of the aluminium used as a vaccine adjuvant.
- the experiment conducted in mice whose BBB integrity is deficient shows that increased permeability can amplify the phenomenon but does not prove that BBB is involved in the translocation.
- In the MCP-1 deficient mice loss experiment, it is not possible to ascertain whether the loss of function is linked to the primary recruitment of macrophages in the injected muscle and/or their translocation towards the brain and other organs.
- **the presence of aluminium inclusions in the CNS does not signify the automatic existence of a “neurotoxicity”.**

# **The Haut Conseil de la santé publique**

- **“Deems that the scientific data available today do not allow the safety of vaccines containing aluminium to be called into question with regard to their risk/benefit balance,**
- **Recommends the continuation of vaccinations according to the vaccine schedule in force,**
- **Warns of the consequences, in terms of the reappearance of infectious diseases, that could result from a decrease in vaccine coverage due to aluminium-containing vaccines being called into question without any scientific justification,**
- **Encourages the pursuit of research that aims to evaluate the safety of adjuvants that are available and in development”.**