

Guillain-Barré syndrome/Fisher syndrome

Summary: To perform active prospective surveillance for Guillain-Barré Syndrome (GBS) and Fisher syndrome (FS) in children using the system developed by British Paediatric Surveillance Unit. We work closely with Professor Elizabeth Miller, the Head of Vaccination, the Health Protection Agency (HPA).

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Background: Guillain-Barré syndrome is an important cause of acute flaccid paralysis worldwide and it is believed that immune stimulation plays a central role in its pathogenesis. Fisher syndrome was described in 1956 and was hypothesised to be a form of GBS. In some cases the clinical findings have features of both GBS and FS so it makes sense to include both conditions in this study.

GBS was an identified risk with swine flu vaccines used in the United States in 1976 (1) – it is thought that 1 extra case of GBS occurred with every 100,000 doses of vaccine. The exact reason why the 1976 vaccine increased the risk of GBS remains unknown. Many studies have since looked at whether other flu vaccines used since 1976 may carry a risk of GBS and no robust evidence of a risk has been found. No cases of GBS have been found in clinical trials of H5N1. A recent epidemiological study used in the UK found no evidence of an increased risk of GBS after seasonal influenza vaccine but there was a greatly increased risk after influenza like illness (2). It is therefore possible that even if swine influenza vaccines do cause GBS, this risk may be offset by the protection they offer against influenza itself. Thus, both vaccination and swine influenza illness need to be evaluated as potential risk factors for GBS.

Coverage: United Kingdom

Duration: September 2009 to September 2011

Objective: To determine how many new cases of Guillain-Barré syndrome/Fisher syndrome in children and young people (aged 16 years or under) are being seen by paediatricians each month and to determine the proportion of these that are temporally associated with a recent influenza infection or vaccination.

Clinical Case Definition: Guillain-Barré syndrome (GBS)

The presence of

- Acute onset of bilateral and relatively symmetric flaccid weakness/paralysis of the limbs with or without involvement of respiratory or cranial nerve-innervated muscles **AND**
- Decreased or absent deep tendon reflexes at least in affected limbs **AND**
- Monophasic illness pattern, with weakness nadir reached between 12 hours and 28 days, followed by clinical plateau and subsequent improvement, or death **AND**
- Electrophysiologic findings with GBS **AND**
- Presence of cytoalbuminologic dissociation (elevation of cerebrospinal fluid (CSF) protein level above laboratory normal value, and CSF total white cell count <50 cells/mm³) **AND**

ABSENCE OF AN ALTERNATIVE DIAGNOSIS FOR WEAKNESS

Cont.

Clinical Case Definition: Fisher Syndrome (FS)

- Acute onset of all three of: bilateral ophthalmoparesis, bilateral reduced or absent tendon reflexes, and ataxia.
Ophthalmoparesis, tendon reflexes, and ataxia are relatively symmetric. Ptosis or pupillary abnormalities may be present in the setting of the ophthalmoplegia. The clinical severity of each component may vary from partial to complete. **AND**
- Absence of limb weakness** **AND**
- Monophasic illness pattern, with clinical nadir reached between 12 hours and 28 days, followed by clinical improvement, with or without treatment **AND**
- Presence of cytoalbuminologic dissociation (elevation of cerebrospinal protein above the laboratory normal, with total CSF white cell count <50 cells/mm³) **AND**
- Nerve conduction studies, if performed, are normal, or indicate involvement of sensory nerves only **AND**
- Brain magnetic resonance imaging (MRI) normal, or if abnormal, absence of brainstem lesions consistent with encephalitis **AND**

An alternative diagnosis is not evident (Including, but not limited to Wernicke's encephalopathy, botulism, diphtheria)

**While the classic triad is often clinically recognized and occurs in the absence of limb weakness, in some cases there is clinical overlap with GBS, with limb weakness present

These are the criteria that provide the highest level of diagnostic certainty for GBS and Fisher syndrome, but the diagnosis can still be made if not all the criteria are met so if there is any uncertainty please report all suspected cases.

For further clarification we refer to the Brighton collaboration document
http://www.brightoncollaboration.org/intranet/en/tools/public_tools/intranet_login.html

Reporting Instructions: Please report any new suspected or confirmed cases seen in the past month in children under the age of 16 years.

Methods: A questionnaire will be sent to each paediatrician who reports a case via the BPSU office. The questionnaire will ask about the clinical history, relevant physical findings and results of investigations in children with GBS. Patient identifiers and General Practitioner's name and address will be posted to Professor Miller on an information form with a reply slip to confirm receipt. The team at the HPA will then be able to contact the GP or health clinic to obtain information about any vaccinations (type, batch number etc) given to the child (this information would not be available to us via the child's hospital notes).

Six months after the initial notification to us we will send a brief follow up questionnaire to paediatricians asking about clinical outcome and the results of any outstanding diagnostic tests.

We recently e-mailed all paediatricians via the BPSU advising them about the pathological specimens that they should consider collecting in children they see with GBS – these samples will be for clinical and not for research purposes. In addition the HPA will provide advice to paediatricians if necessary. Blood samples from cases will be requested for testing for antibodies to swine influenza. Samples collected locally will be sent to the HPA – this is an established pathway for clinical specimens. No specimens will be sent to the surveillance team in Cambridge.

Ethics Approval: Trent Research Ethics Committee, REC reference number: 09/H0405/45 and National Information Governance Board reference number: ECC/BPSU 5-02 (FT1)

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References:

1. Schonberger LB, Bergman DJ, Sullivan-Bolyai JZ et al. Guillain-Barré syndrome following vaccination in the National Influenza Immunization Program, United States, 1976-1977. *Am J Epidemiol.* 1979;110:105-123
2. Stowe J, Andrews N, Wise L, Miller E. Investigation of the temporal association between Guillain-Barré syndrome and influenza vaccine and influenza-like illness using the UK General Practice Research Database. *Am J Epidemiol.* 2009 Feb 1;169(3):382-8.