Identification and management of Guillain-Barré syndrome in the context of Zika virus

Interim guidance

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1. Introduction

1.1 Background

Guillain-Barré syndrome (GBS) is a disorder in which the body's own immune system attacks part of the peripheral nervous system. GBS can be triggered by a variety of infections, including dengue and chikungunya viruses. The syndrome can affect the peripheral nerves that control muscle strength as well as those that transmit feelings of pain, temperature and touch. This can result in muscle weakness and loss of sensation in the legs and/or arms. Approximately 25% of GBS patients require intensive care and 3-5% die even with appropriate supportive care, due to complications related to: paralysis of the muscles that control breathing; cardiac arrest; or blood clots (1).

Currently, health authorities in Brazil, Colombia, El Salvador, Suriname and Venezuela have reported increases in cases of GBS in the context of widespread Zika virus transmission. In French Polynesia, all 42 GBS cases identified during an outbreak of Zika virus from 2013–2014 on retrospective analysis (seroneutralisation test) tested positive for both dengue and Zika virus infection (2). The cause of the increase in incidence of GBS observed in Brazil, Colombia, El Salvador and Suriname remains unknown, especially as dengue, chikungunya and Zika viruses all circulate simultaneously in the Americas. Investigations to establish the cause, risk factors, and consequences of these clusters of GBS cases and other neurological complications are currently underway.

This document aims to provide interim guidance on the case definition of GBS and strategies to manage the syndrome, in the context of Zika virus and its potential association with GBS. This document is intended to inform the development of local clinical protocols and health policies related to the care of patients with GBS. An expert meeting will be organized in March 2016 to develop additional guidance to identify and manage GBS and other possible neurological disorders in the context of Zika virus transmission.

1.2 Target audience

The primary audience for this guidance are health care professionals including family medicine physicians, general practitioners, neurologists, emergency medicine physicians, critical care physicians and nurses. This guidance may also be used by those responsible for developing local and national health protocols and policies, and policy-makers in regions affected by Zika virus transmission.

2. Interim recommendations

a. Health care providers should be trained in the recognition, evaluation and management of patients with GBS. Specifically, neurological examination skills and training in the acute management of GBS should be strengthened.

b. The Brighton criteria (3) should be used for the case definition of GBS (see below). Neurological examinations should be performed on all patients with suspected GBS, and ancillary testing with nerve conduction studies/electromyography and lumbar puncture if available.

c. The risk of death in patients with GBS is associated with complications including respiratory failure, cardiac arrhythmias, and blood clots. Optimal supportive care including frequent neurological assessments, vital sign and respiratory function monitoring should be provided to patients with GBS.

d. Intravenous immunoglobulin therapy or therapeutic plasma exchange should be provided to GBS patients who are unable to walk or who have rapidly progressive symptoms. Access to these medications and training for their appropriate administration should be made available.

e. Hospital beds for patients with severe manifestations of GBS should be made available, so that patients can receive optimal supportive care.

3. Case definition of Guillain-Barré syndrome using the Brighton Criteria

The Brighton criteria (3) should be used as the case definition of GBS. These are based on presenting clinical findings and ancillary testing including neurophysiology and lumbar puncture findings. Patients are categorized as level 1 (the highest level of diagnostic certainty) to level 3 (the lowest level of diagnostic certainty) These criteria were

developed to standardize collection and assessment of information on GBS, and are applicable in: study settings with different availability of resources; health care settings that differ by availability of and access to health care; and different geographic regions. It should be stressed that, although potentially applicable in a clinical setting, the level of diagnostic certainty is primarily intended for epidemiologic purposes and not as a criterion for treatment (3).

Table 1. Brighton criteria for case definition of Guillain-Barré syndrome

Level 1 of diagnostic certainty	Level 2 of diagnostic certainty	Level 3 of diagnostic certainty
• Bilateral and flaccid weakness of the limbs; **AND** • Decreased of absent deep tendon reflexes in weak limbs; **AND** • Monophasic illness pattern; and interval between onset and nadir of weakness between 12h and 28 days; and subsequent clinical plateau; **AND** • Absence of identified alternative diagnosis for weakness; **AND** • Cytoalbuminologic dissociation (i.e. elevation of CSF* protein level above laboratory normal value and CSF total white cell count <50 cells/µl; **AND** • Electrophysiologic findings consistent with GBS	• Bilateral and flaccid weakness of the limbs; **AND** • Decreased or absent deep tendon reflexes in weak limbs; **AND** • Monophasic illness pattern; and interval between onset and nadir of weakness between 12h and 28 days; and subsequent clinical plateau; **AND** • Absence of identified alternative diagnosis for weakness; **AND** • CSF total white cell count <50 cells/µl (with or without CSF protein elevation above laboratory normal value); **OR** electrophysiologic studies consistent with GBS if CSF not collected or results not available.	• Bilateral and flaccid weakness of the limbs; **AND** • Decreased or absent deep tendon reflexes in weak limbs; **AND** • Monophasic illness pattern; and interval between onset and nadir of weakness between 12h and 28 days; and subsequent clinical plateau; **AND** • Absence of identified alternative diagnosis for weakness

* Cerebrospinal fluid (CSF)

4. Guidance development

4.1 Acknowledgements

The following individuals contributed to the development of this interim guidance: Professor Gretchen Birbeck (Neurology and Epidemiology, University of Rochester School of Medicine, Rochester, USA); Dr Francisco Javier Carod-Artal (Consultant Neurologist, Raigmore Hospital UK, Inverness UK; Professor Igor Koralnik (Neurology, Beth Israel Deaconess Medical Center, Boston, USA); Dr Constantine Malama (Virologist, Ministry of Health Zambia, Lusaka, Zambia); Dr Farrah Mateen (Assistant Professor, Harvard Medical School, Boston, USA): Professor Avindra Nath (Senior Investigator, National Institute of Health, Bethesda, USA); Dr Erwan Oehler (Hospital Physician in General Medicine, Tahiti, French Polynesia); Professor Lyda Osorio (Epidemiology, University of Valle, Cali, Valle del Cauca, Colombia); Dr Carlos Pardo (Director of the Johns Hopkins Transverse Myelitis Center, Johns Hopkins University, Baltimore, USA); Professor Laura Rodrigues (Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK); Dr James Sejvar (Neurologist and Epidemiologist, Center for Disease Control and Prevention, Atlanta, USA); Professor Tom Solomon (Director of the Institute of Infection and Global Health, University of Liverpool, Liverpool, UK); Dr Kiran Thakur (Assistant Professor, Department of Neurology, Columbia University College of Physicians and Surgeons, New York, USA); Professor Joseph Zunt (Neurology and Global Health, University of Washington, Seattle, USA).

Staff from the Department of Mental Health and Substance Abuse, WHO Geneva (Tarun Dua, Shekhar Saxena and Marius Vollberg) and WHO Regional Office for the Americas (Armando Vasquez) contributed to this guidance.

4.2 Guidance development methods

Global experts in the areas of neurological infections, neuroimmunology and GBS were identified through existing networks of neurologists. This included experts from Africa, the Americas, south-east Asia, Europe and the Pacific. Due to limited time, it was not possible to identify and include experts from other areas.

A conference call was convened by the WHO Geneva Department of Mental Health and Substance Abuse on 9 February 2016. Notes for the record were documented. Based on these, an interim guidance was prepared. The notes for the record and draft interim guidance were circulated to the experts. Comments and references proposed by the experts were included in the revised guidance.

4.3 Declaration of interests

F Mateen declared that she is the recipient of an American Brain Foundation in 2010–2012 to study GBS in India using polio surveillance data. This interest was deemed non-conflicting, and the individual participated fully in the guidance development process. No other competing interests were identified. No specific funds were used to develop this interim guidance.

4.4 Review date

These recommendations have been produced under emergency procedures and will remain valid until August 2016. The Departments of Mental Health and Substance Abuse at WHO Geneva will be responsible for reviewing this guideline before or at that time, and updating it as appropriate.

5. References

1. Yuki N, Hartung HP. Guillain–Barré syndrome. N Engl J Med. 2012 Jun; 366(24):2294-304.
2. World Health Organization [Internet]. Zika situation report 12 February 2016; 2016 [cited 2016 Feb 22]. Available from: http://www.who.int/emergencies/zika-virus/situation-report/12-february-2016/en/
3. Sejvar JJ, Kohl KS, Gidudu J, Amato A, Bakshi N, Baxter R, Burwen DR, Cornblath DR, Cleerbout J, Edwards KM, Heininger U. Guillain–Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011 Jan 10; 29(3):599–612.