Guillain-Barré Syndrome

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Arizona Department of Health Services

Office of Surveillance, Epidemiology, and Laboratory Services
Scientific Education and Professional Development Program Office

CDC

Objectives

- Pathophysiology of Guillain Barré Syndrome (GBS)
- Epidemiology
- Signs and symptoms
- Review of GBS subtypes
- Diagnosis, treatment, prognosis
- Outbreaks

Definition

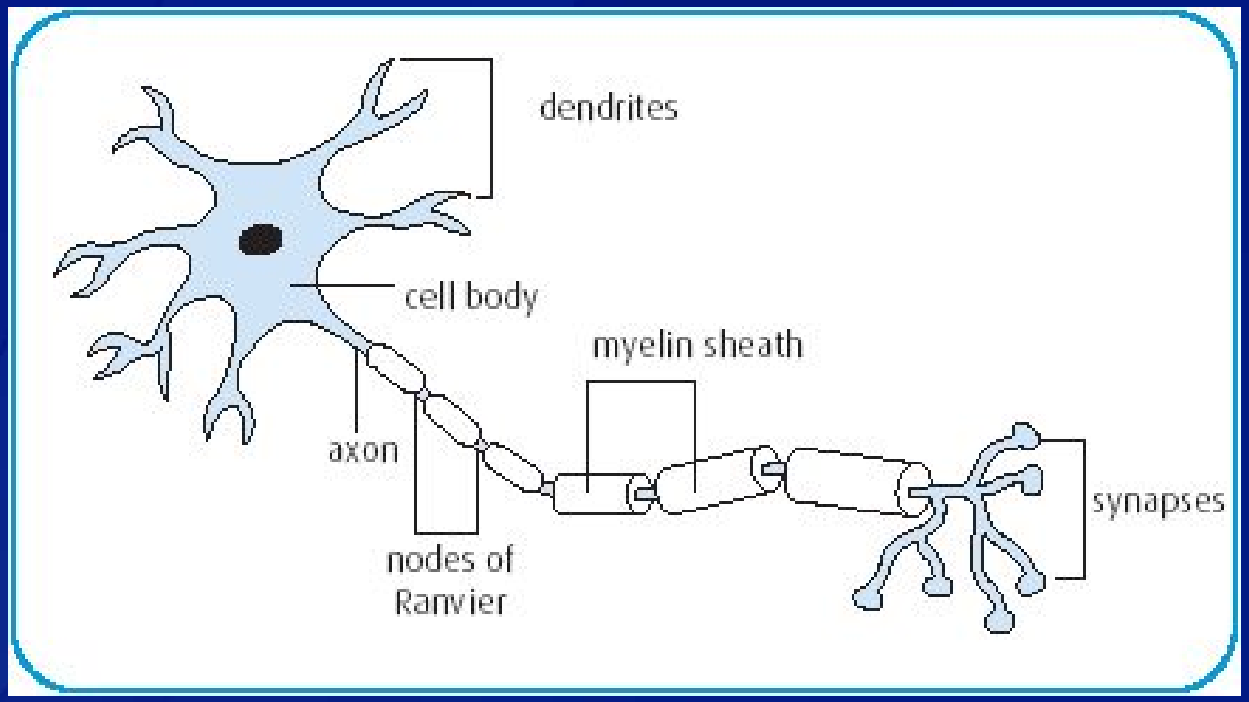
- First described in 1916
- Acute flaccid paralysis, areflexia, ↑protein in CSF
- Flaccid: Voluntary control over muscles has been lost → limp, floppy muscles
- Commonest cause of acute flaccid paralysis

Epidemiology

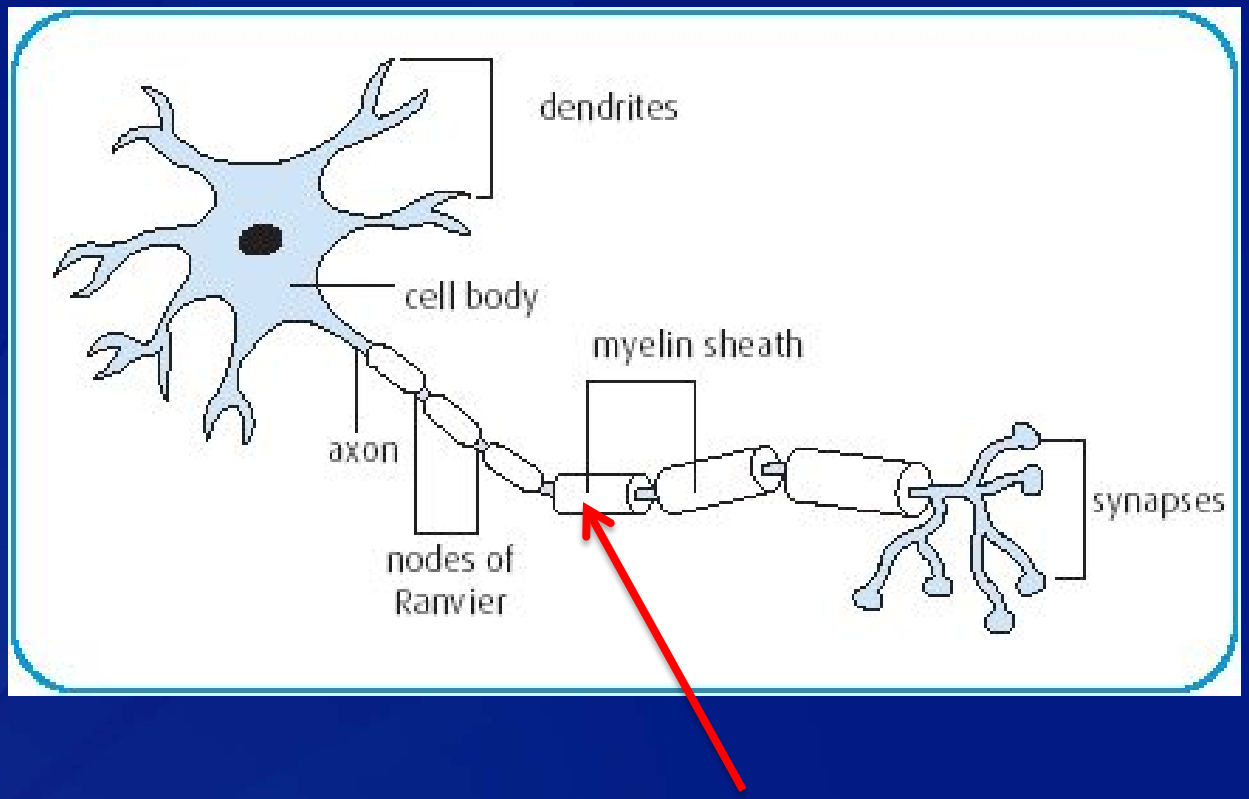
- 0.9–1.9/100,000 persons
- Incidence differs with age
  - <30 yrs: <1/100,000
  - >75 yrs: >4/100,000
- 20% increase with every 10-year rise in age
- Male to female ratio – 1.2–1.5:1

Sejvar et al, Neuroepidemiology2011; 36: 123-133

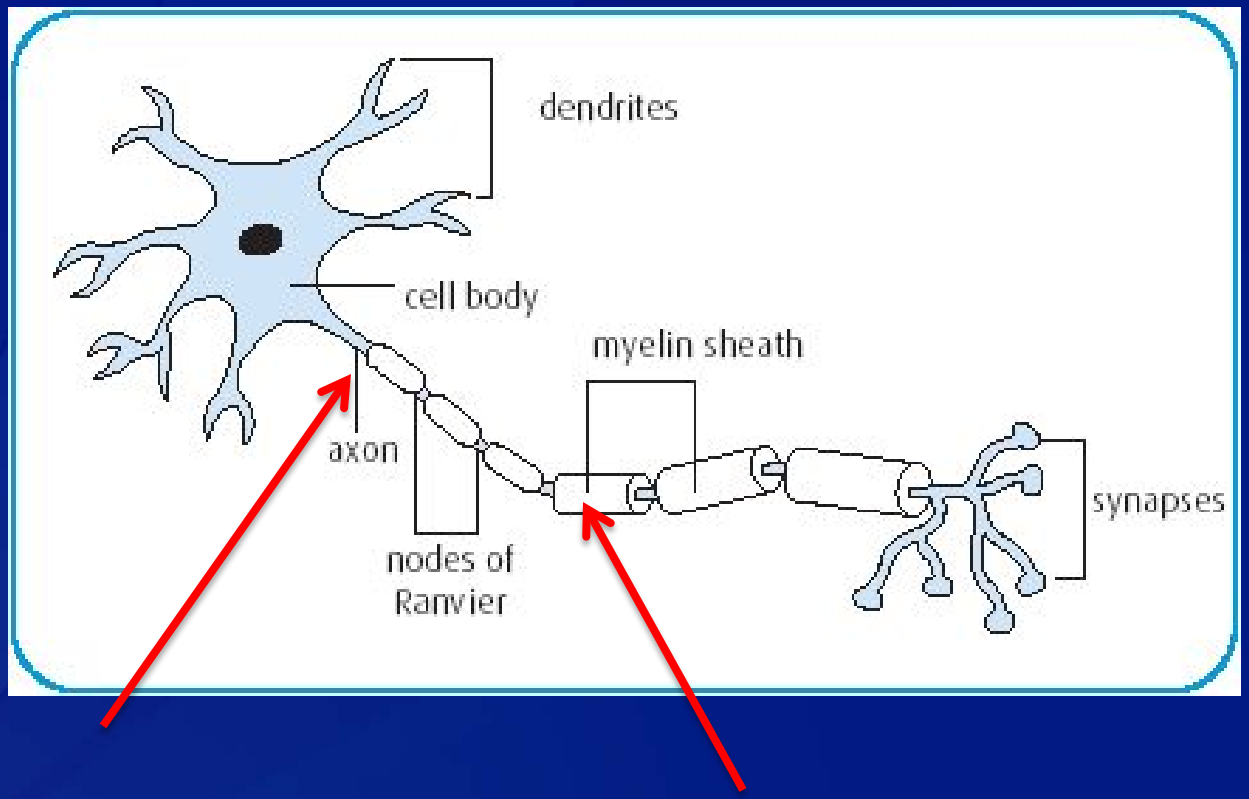
Pathophysiology



Pathophysiology

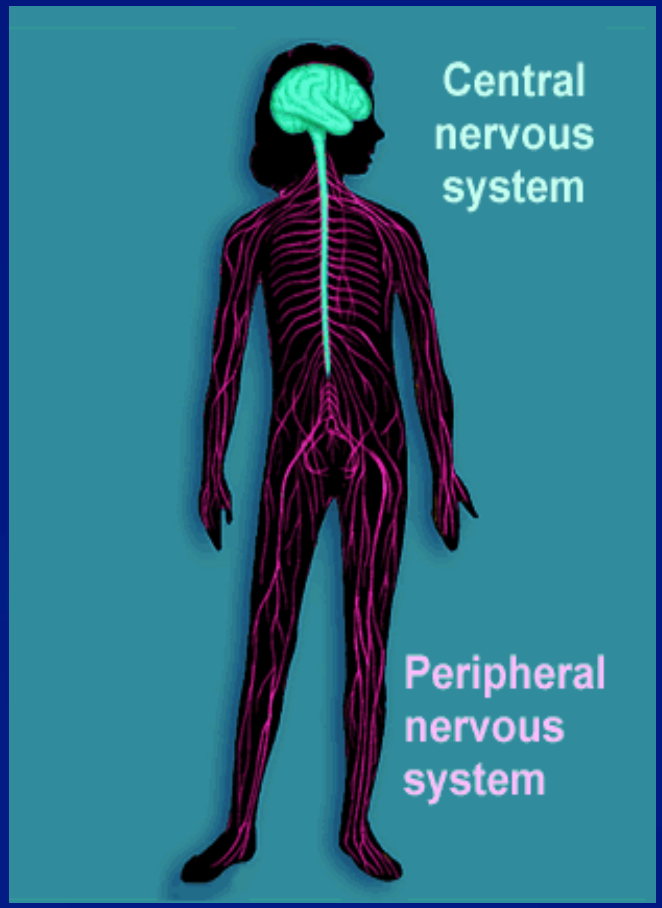


Pathophysiology



Nervous System

- Central nervous system
  - Brain and spinal cord
- Peripheral nervous system
  - Somatic - voluntary
  - Autonomic - involuntary
- GBS affects the 2 components of the peripheral nervous system



Neurology Definitions

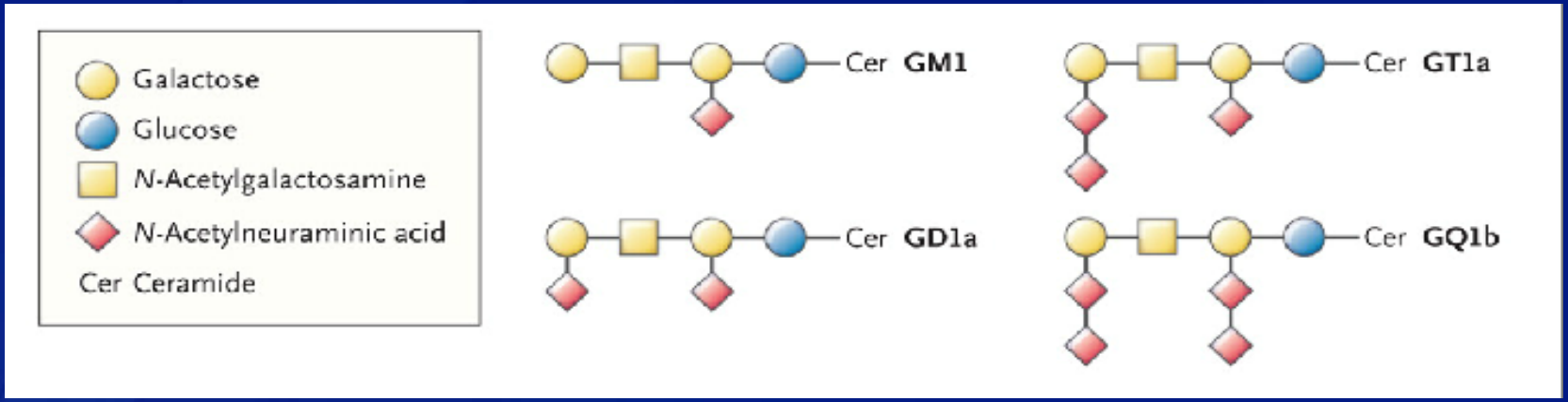
- **Paralysis – loss of voluntary muscle function**
  - Partial – affecting one muscle or one limb
  - Total – paralysis of all muscles
- **Plegia – used to describe paralysis**
  - Palsy – not used anymore except for 'Bell's palsy'
- **Paresis – weakness of voluntary movement**

Neurology Definitions

- **Hemi – arm, leg, trunk on the same side of the body**
  - Hemiplegia – total paralysis on one side of the body
  - Hemiparesis – weakness on one side of the body
- **Para – either both arms or both legs**
- **Quadri – all 4 limbs and torso**
  - Quadriplegia is the same as tetraplegia
- **Paresthesia – tingling, burning, numb sensation**

Variants

- Autoantibodies (usually IgG) attack gangliosides
  - Part of the cell membrane involved in signal transduction



N Engl J Med 2012; 366:2294-2304

Five Variants of GBS

Subtypes and variants	IgG autoantibodies to
Guillain–Barré syndrome	
Acute inflammatory demyelinating polyneuropathy	None
Facial variant: Facial diplegia and paresthesia	None
Acute motor axonal neuropathy	GM1, GD1a
More and less extensive forms	
Acute motor–sensory axonal neuropathy	GM1, GD1a
Acute motor-conduction-block neuropathy	GM1, GD1a
Pharyngeal–cervical–brachial weakness	GT1a > GQ1b >> GD1a
Miller Fisher syndrome	GQ1b, GT1a
Incomplete forms	
Acute ophthalmoparesis (without ataxia)	GQ1b, GT1a
Acute ataxic neuropathy (without ophthalmoplegia)	GQ1b, GT1a
CNS variant: Bickerstaff's brain-stem encephalitis	GQ1b, GT1a

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Geographic Distribution of GBS Subtypes

- **Demyelinating**
  - Autoantibodies attack the myelin sheath
- **Axonal**
  - Autoantibodies attack nerve axon

Geographic Distribution of GBS Subtypes

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  - Autoantibodies attack the myelin sheath
  - 90% of all cases in Europe and North America
  - 22-46% of cases in China, Japan, Bangladesh, Mexico
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  - 30-65% of all cases in China, Japan, Bangladesh, Mexico

Guillain Barré Syndrome

- Acute, ascending paralysis
- Decreased or absent reflexes
- Elevated protein in the CSF but normal cell count

- Autoantibodies to myelin sheath or axon of nerve cells

- 5 variants

Acute Inflammatory Demyelinating Polyneuropathy (AIDP)

- Commonest variant of GBS in North America, Europe
- Paresthesias in distal limbs before weakness
- Ascending paralysis, progressive weakness
  - Bilateral, symmetrical
  - At presentation, 60% of patients have weakness in all 4 limbs
  - >60% unable to walk independently when maximum weakness is reached
- Respiratory weakness
  - Presenting symptom in 40% of patients
- Autonomic dysfunction
  - Postural hypotension → syncope
  - Sinus tachycardia

Miller Fisher

- Occurs in 5% of GBS cases
- Classic triad of ophthalmoplegia, ataxia and areflexia
- Presenting complaint usually diplopia
- Elevated CSF protein but less than other types of GBS

Acute Motor Axonal Neuropathy (AMAN)

- Acute/subacute paralysis or paresis without any sensory loss
- Loss of reflexes
- Facial/oropharyngeal muscle weakness
- Associated with *Campylobacter jejuni* gastric enteritis
  - >60% seropositive

Aetiology of GBS: Triggering Event

- >60% of cases preceded by upper respiratory tract infection or diarrhea 3 days–6 weeks prior to symptoms
- *Campylobacter jejuni* most frequently identified infectious agent (30%)
  - Incidence: 0.25–0.65/1000 cases of *C.jejuni*
- Cytomegalovirus (10%)
- Epstein-Barr virus, varicella-zoster, *Mycoplasma pneumoniae*

Immunizations and GBS

- Little evidence to support a causal association with most vaccines
- Older formulations of rabies vaccine cultured in mammalian brain tissue (Semple)
- Swine flu vaccine 1976–77

Time Course

- Pain 2 weeks after triggering event
- Weakness worsens over 2 weeks
- Symptoms plateau at 4 weeks
- Recovery begins

Differential Diagnosis

- **Acute peripheral neuropathies**
  - Toxic: thallium, arsenic, lead, n-hexane, organophosphate
  - Drugs: amiodarone, perhexiline, gold
  - Alcohol
  - Porphyria
  - Systemic vasculitis
  - Poliomyelitis
  - Diphtheria
  - Tick paralysis

Differential Diagnosis

- **Disorders of Neuromuscular Transmission**
  - Botulism
  - Myasthenia gravis
- **Central Nervous System Disorders**
  - Basilar artery occlusion
  - Acute cervical transverse myelitis

Diagnosis

- History
- Examination
- Lumbar puncture
  - Elevated CSF protein *without* pleocytosis
- Nerve and muscle function tests
  - Electromyography – is muscle weakness due to the muscle itself?
  - Nerve conduction studies

Case Definition

2. Clinical case definitions: Guillain–Barré syndrome (GBS)[3,4,5]

Level 1 of diagnostic certainty

- Bilateral AND flaccid weakness of the limbs[6,7,8]
  AND
- Decreased or absent deep tendon reflexes in weak limbs[9]
  AND
- Monophasic illness pattern[10] AND interval between onset and nadir of weakness between 12 h and 28 days AND subsequent clinical plateau[11]
  AND
- Electrophysiologic findings consistent with GBS[12]
  AND
- Cytoalbuminologic dissociation (i.e., elevation of CSF protein level above laboratory normal value AND CSF total white cell count <50 cells/μl)[13]
  AND
- Absence of an identified alternative diagnosis for weakness (see Appendix A.3)[3].

Level 2 of diagnostic certainty

- Bilateral AND flaccid weakness of the limbs[6,7,8]
  AND
- Decreased or absent deep tendon reflexes in weak limbs[9]
  AND
- Monophasic illness pattern[10] AND interval between onset and nadir of weakness between 12 h and 28 days AND subsequent clinical plateau[11]
  AND
- CSF total white cell count <50 cells/μl (with or without CSF protein elevation above laboratory normal value)[13]
  OR
- IF CSF not collected or results not available, electrophysiologic studies consistent with GBS[12]
  AND
- Absence of identified alternative diagnosis for weakness (see Appendix A.3)[3].

Level 3 of diagnostic certainty

- Bilateral AND flaccid weakness of the limbs[6,7,8]
  AND
- Decreased or absent deep tendon reflexes in weak limbs[9]
  AND
- Monophasic illness pattern[10] AND interval between onset and nadir of weakness between 12 h and 28 days AND subsequent clinical plateau[11]
  AND
- Absence of identified alternative diagnosis for weakness (see Appendix A.3)[3].

J Sejvar et al, Vaccine 29 (2011) 599–612

Nerve Conduction Tests

- Motor and sensory nerves
- Nerve conduction velocity is measured
  - Conduction slowing
  - Conduction block
- F waves and H reflexes
  - Prolonged or absent

Treatment

- **Supportive care**
  - Intubation
  - Occupational therapy
  - Physiotherapy
  - Speech and language therapy
- **Specific therapy**
  - Intravenous immunoglobulins
  - Plasmapheresis

Prognosis

- Recovery starts at ~2–4 weeks after symptom onset
- Months to years
  - 20% unable to walk 6 months after symptom onset
- Time to recovery depends on many factors
  - Age
  - Severity
  - Delay in receiving treatment
- Various prognostic scales
  - Patient's age, presence/absence of antecedent diarrhea, severity
  - Time between weakness onset and admission, facial weakness
- Complications of intubation
  - Pneumonia, sepsis, PE in 60%

Prognosis Depends on Subtype

- **AIDP**
  - 5% mortality
  - >75% of patients have complete/near-complete recovery, no deficits or with mild residual fatigue and distal weakness
- **Miller Fisher**
  - Improvement begins at a median of 2 weeks
  - Full recovery takes a median of 1-3 months
- **AMAN**
  - Recovery time similar to or quicker than AIDP

GBS Surveillance

- **1976 influenza**
  - 40 million doses of influenza vaccine administered in US
  - Cluster of GBS cases noted
  - Vaccine associated with small, but statistically significant increased risk of GBS in 6 weeks post-vaccination

- **CDC Emerging Infections Program (EIP) 2009–10**
  - Active, population-based surveillance
  - Connecticut, Maryland, New Mexico, Tennessee, New York, Minnesota
  - Metropolitan areas in Georgia, Oregon, California, Colorado

Key Points

- GBS characterised by:
  - Muscle weakness or paralysis
  - Loss of reflexes
  - High protein in the CSF but a normal cell count
- Not a single disease but a group of immune-mediated neuropathies
- Autoantibodies against cell membrane gangliosides
- Clusters are rare

Outbreaks

ARTICLE | November 18, 1983

Simultaneous Outbreaks of Guillain-Barré Syndrome and Bell's Palsy in Hawaii in 1981

Jonathan E. Kaplan, MD; Joel R. Greenspan, MD; Mona Bomgaars, MD; Ned Wiebenga, MD; Robert D. Bart, Jr, MD; Kenneth Robbins, MD; Robert Wiebe, MD; Frank Tabrah, MD; John Stewart, MD; Lawrence B. Schonberger, MD

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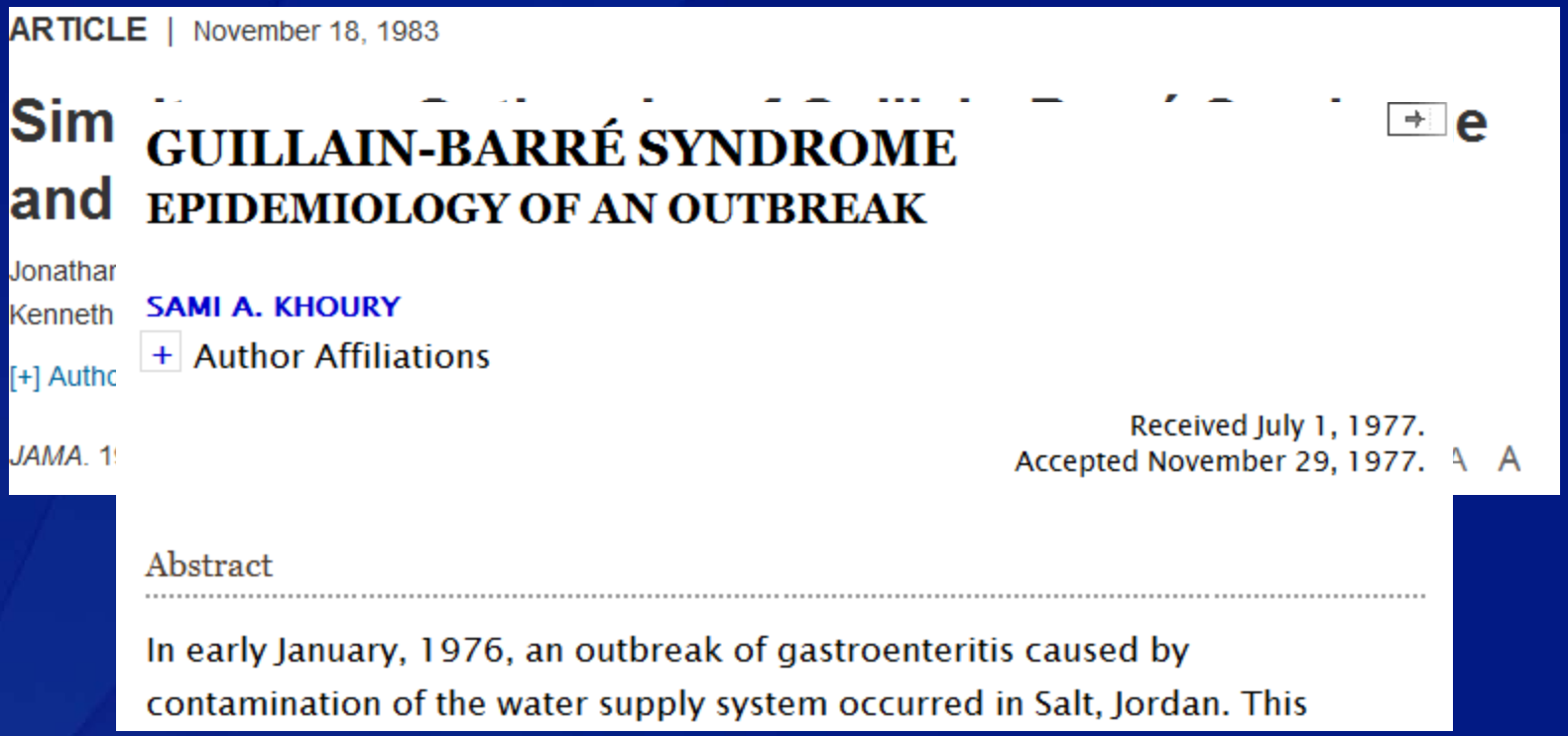
JAMA. 1983;250(19):2635-2640. doi:10.1001/jama.1983.03340190037028

Outbreaks



ARTICLE | November 18, 1983

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GUILLAIN-BARRÉ SYNDROME
EPIDEMIOLOGY OF AN OUTBREAK

SAMI A. KHOURY

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Received July 1, 1977.
Accepted November 29, 1977.

Abstract

In early January, 1976, an outbreak of gastroenteritis caused by contamination of the water supply system occurred in Salt, Jordan. This

Outbreaks

Foodborne Pathog Dis. 2010 Aug;7(8):913-9.

Association study between an outbreak of Guillain-Barre syndrome in Jilin, China, and preceding Campylobacter jejuni infection.

Zhang M, Li Q, He L, Meng F, Gu Y, Zheng M, Gong Y, Wang P, Ruan F, Zhou L, Wu J, Chen L, Fitzgerald C, Zhang J.

Department of Diagnosis, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China.

Abstract

From June to July 2007, 36 cases of Guillain-Barre syndrome (GBS) occurred in a township in north China. Serological study and bacteria culture were performed to investigate the association between preceding Campylobacter jejuni infection and this GBS outbreak. Anti-C. jejuni antibodies were found in significantly higher numbers of GBS patients (IgM 84%, IgG 87.5%) than in healthy inspection cases

In early January, 1976, an outbreak of gastroenteritis caused by contamination of the water supply system occurred in Salt, Jordan. This

Outbreaks

Guillain-Barre Syndrome Strikes AZ-Mexico Border

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Jim Sejvar

- EXTRA SLIDES

Risk Factors

- Older age
- Male
- Recent gastrointestinal or respiratory infection
- Recent surgery
- History of lymphoma, lupus, AIDS