GUILLAIN BARRE SYNDROME

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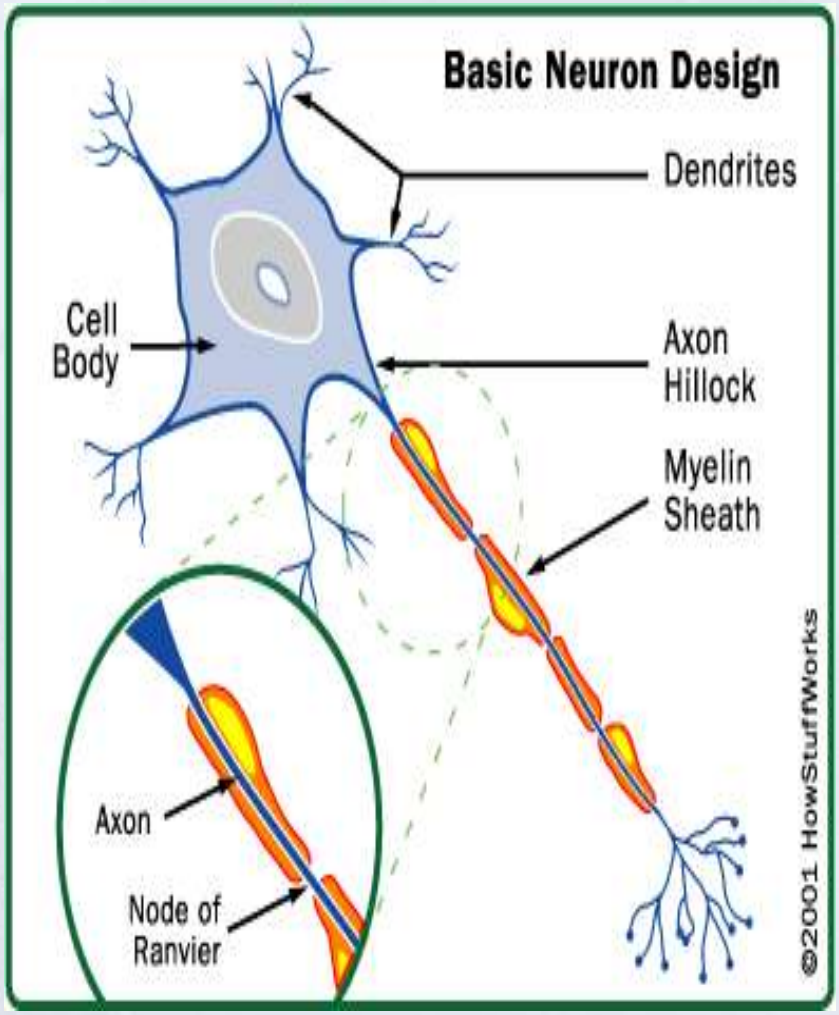
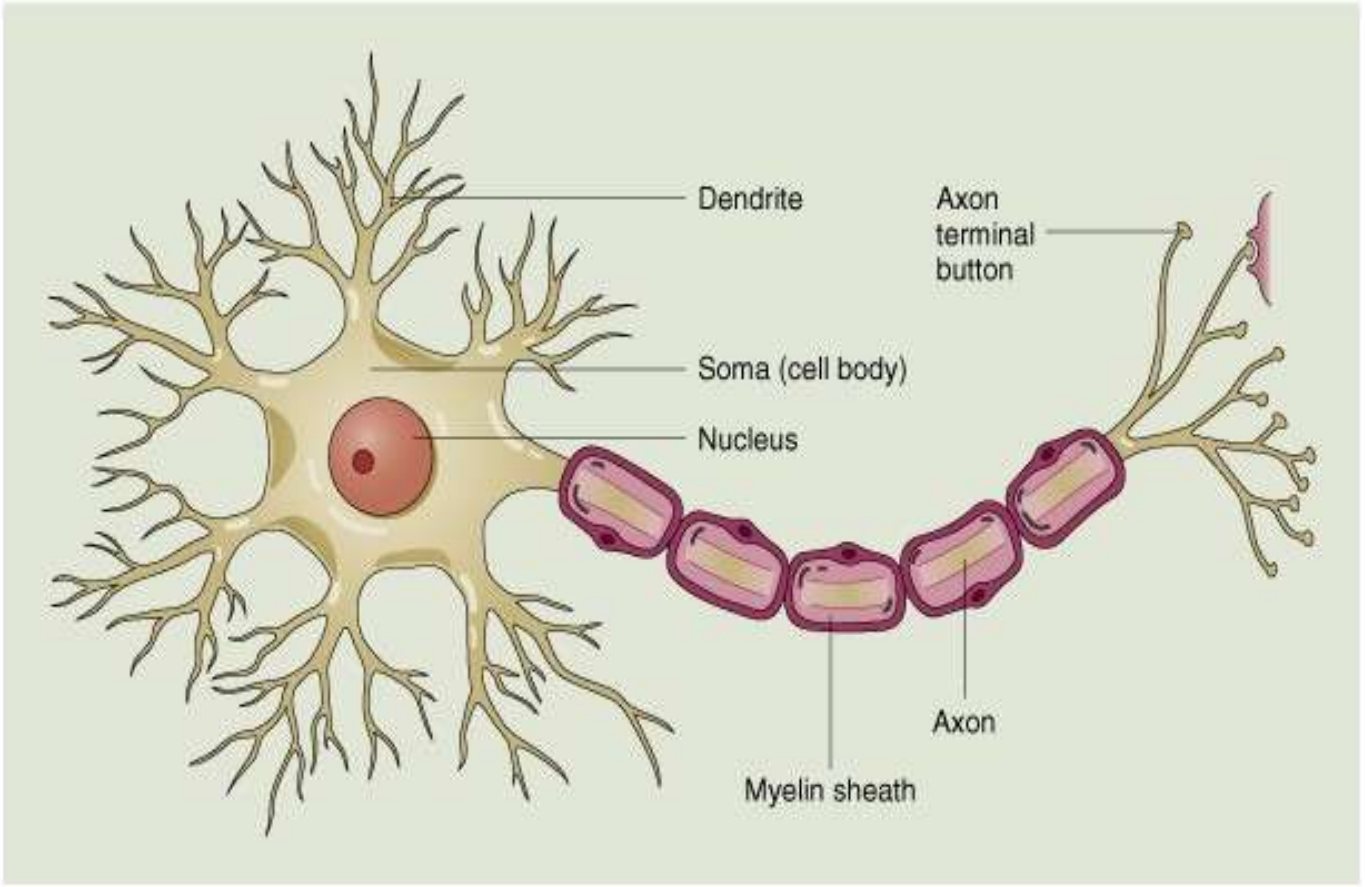
Neuron



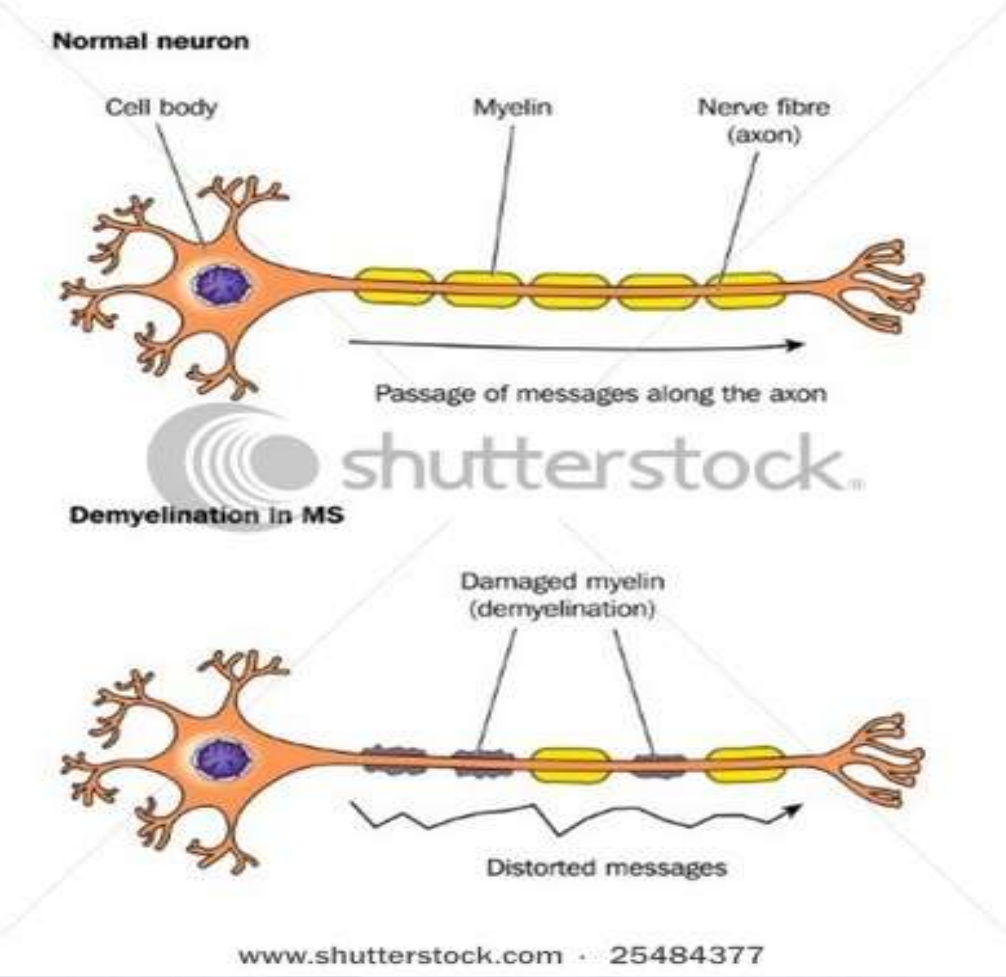
- A typical neuron possesses a cell body (often called the soma), dendrites, and an axon.
- Dendrites are thin structures that arise from the cell body, a complex "dendritic tree".
- An axon is a special cellular extension that arises from the cell body at a site called the axon hillock .
- The cell body of a neuron frequently gives rise to multiple dendrites, but never to more than one axon, although the axon may branch hundreds of times before it terminates.
- At the majority of synapses, signals are sent from the axon of one neuron to a dendrite of another.
- exceptions to these rules: neurons that lack dendrites, neurons that have no axon, synapses that connect an axon to another axon or a dendrite to another dendrite, etc.

NEURON



DEMYELINATION

- A **demyelinating disease** is any disease of the nervous system in which the myelin sheath of neurons is damaged.
- This impairs the conduction of signals in the affected nerves, causing impairment in sensation, movement, cogn ition, or other functions depending on which nerves are involved.



MOLECULAR MIMICRY

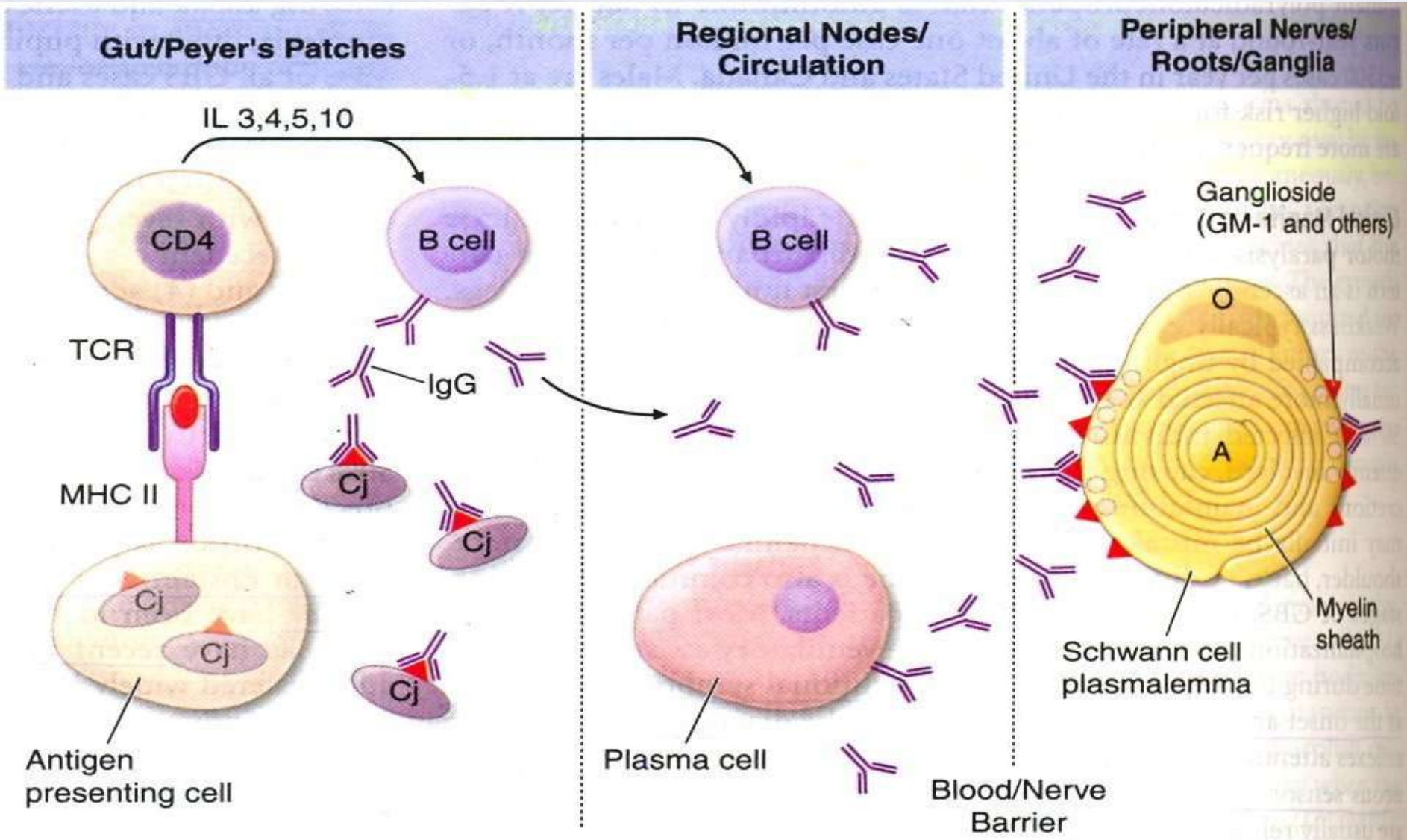
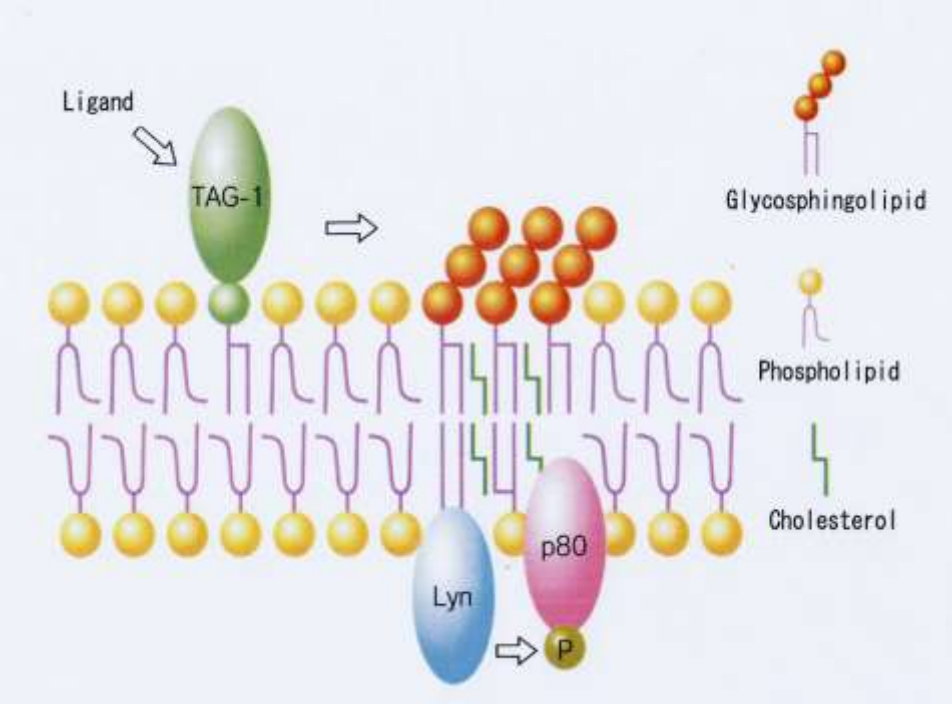


FIGURE 380-1 Postulated immunopathogenesis of GBS associated with *C. jejuni* infection. B cells recognize glycoconjugates on *C. jejuni* (Cj) (triangles) that cross-react with ganglioside present on Schwann cell surface and subjacent peripheral nerve myelin. Some B cells, activated via a T cell–in-

GANGLIOSIDES

- Complex glycosphingolipids
- One or more sialic acid residues.
- Involved in cell-cell interactions,modulation of receptors,regulation of growth.
- Seen on plasma membrane of cells.
- Targets for antibody mediated attack
- Abundant in human nervous tissue,nodes of ranvier.



TERMS

- Dysesthesias – an UNPLEASANT ABNORMAL sensation produced by NORMAL stimuli.
- Paresthesias – an abnormal sensation in ABSENCE of external stimulus.
- Allodynia – pain from NON NOXIOUS STIMULUS to normal skin.
- Hyperpathia – abnormal EXAGGERATED response to PAINFUL stimuli.

CASE

- *A 15 yr old male,came to ED with complaints of pain in the calf of the right leg on Tuesday,followed by weakness of the both lower limbs the next day morning.was bed ridden after the onset of weakness.his bowel and bladder are intact.he is able to feel sensation of clothes over the lower limbs.he felt heaviness of the limbs..taken to local hospital was given treatment..where he noticed weakness in the upper limbs also.*
- *no symptoms of cranial nerve involvement.*
- *no h/o fever at the onset of weakness.*
- *no h/o recent immunization or no h/o dog bite.*
- *no h/o seizures episodes.*
- *no h/o similar complaints in the past.*
- *no h/o similar complaints in the family.*

Clinical examination

- Patient was consciuos coherent
- no pallor ,icterus,clubbing,lymphadenopathy,edema.
- His BP is 110/70 mm Hg in supine,100/70 mm Hg on standing.no postural hypotension.
- Pulse -82/min regular,all peripheral pulses felt.
- Respiratory rate -18 /min.breath holding time –able to count upto 45 in single breath.

NERVOUS SYSTEM

- Higher intellectual functions intact
- Cranial nerves normal
- Motor system showed hypotonia of all four limbs.
- Grade 3/5 in upperlimbs,2/5 across the hip joint,knee joint,o/5 power across ankle joint.
- Hyporeflexia all DTRs,absent ankle
- Foot drop b/l
- Babinski negative,abdominal present
- Sensory intact
- Gait –stance narrow based
- Buckling of knees while walking.
- Waddling gait..high stepping gait
- Other systems normal.

Key points

- Rapid progressive ascending paralysis.
- Acute onset
- Motor paralysis
- Intact sensory
- No cranial nerve involvement
- No bladder involvement
- No fever at onset of weakness
- Diagnosis……??????????????

DIAGNOSIS

Guillain Barre Syndrome

OTHER NAMES

- LANDRY'S ASCENDING PARALYSIS
- ACUTE INFLAMMATORY DEMYELINATING POLYNEUROPATHY (AIDP)
- ACUTE IDIOPATHIC POLYRADICULONEURITIS
- ACUTE IDIOPATHIC POLYNEURITIS
- FRENCH POLIO
- LANDRY GUILLAIN BARRE SYNDROME

INTRODUCTION

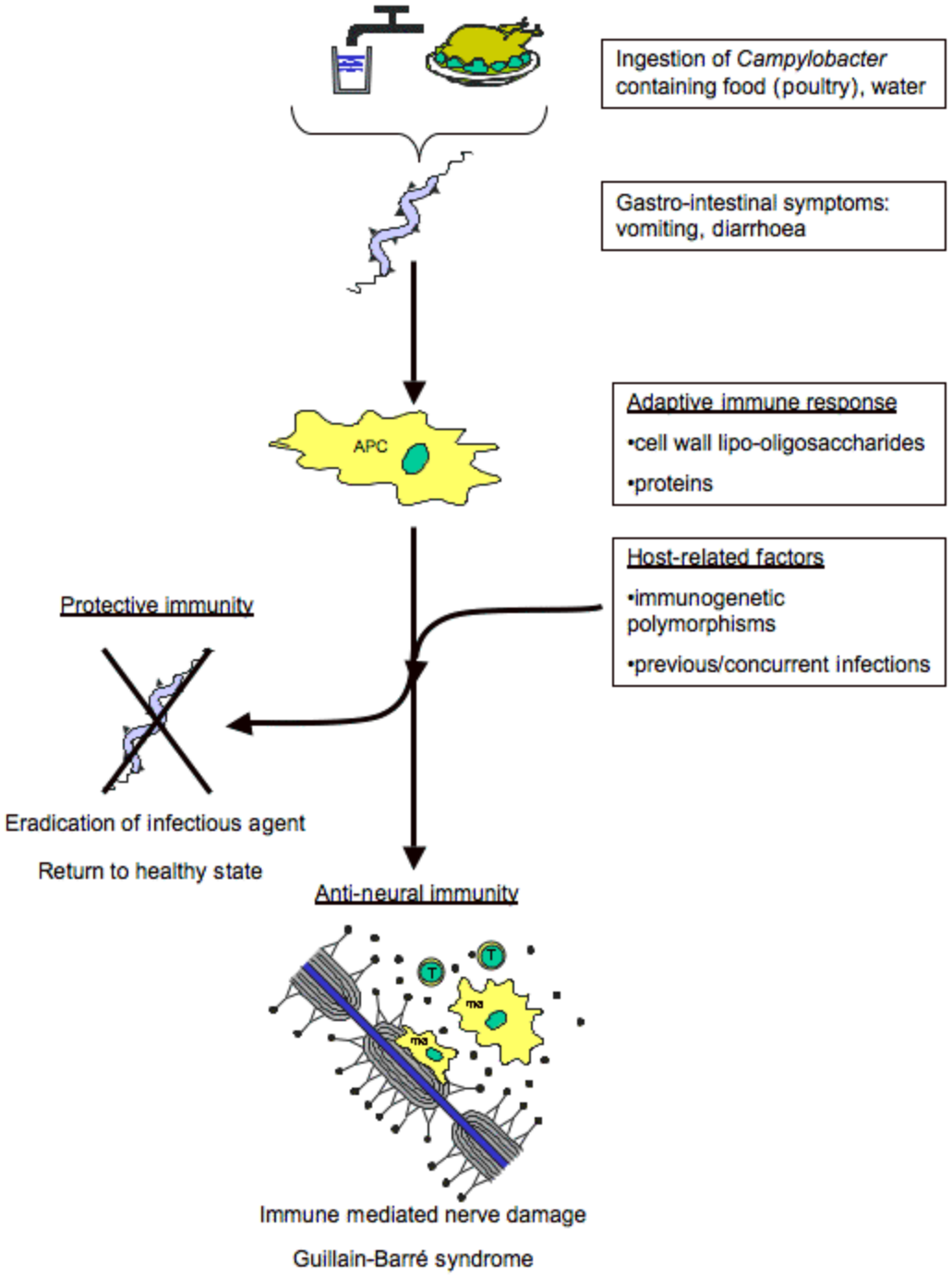
- *Acute,frequently severe and fulminant polyradiculoneuropathy that is autoimmune in nature*.

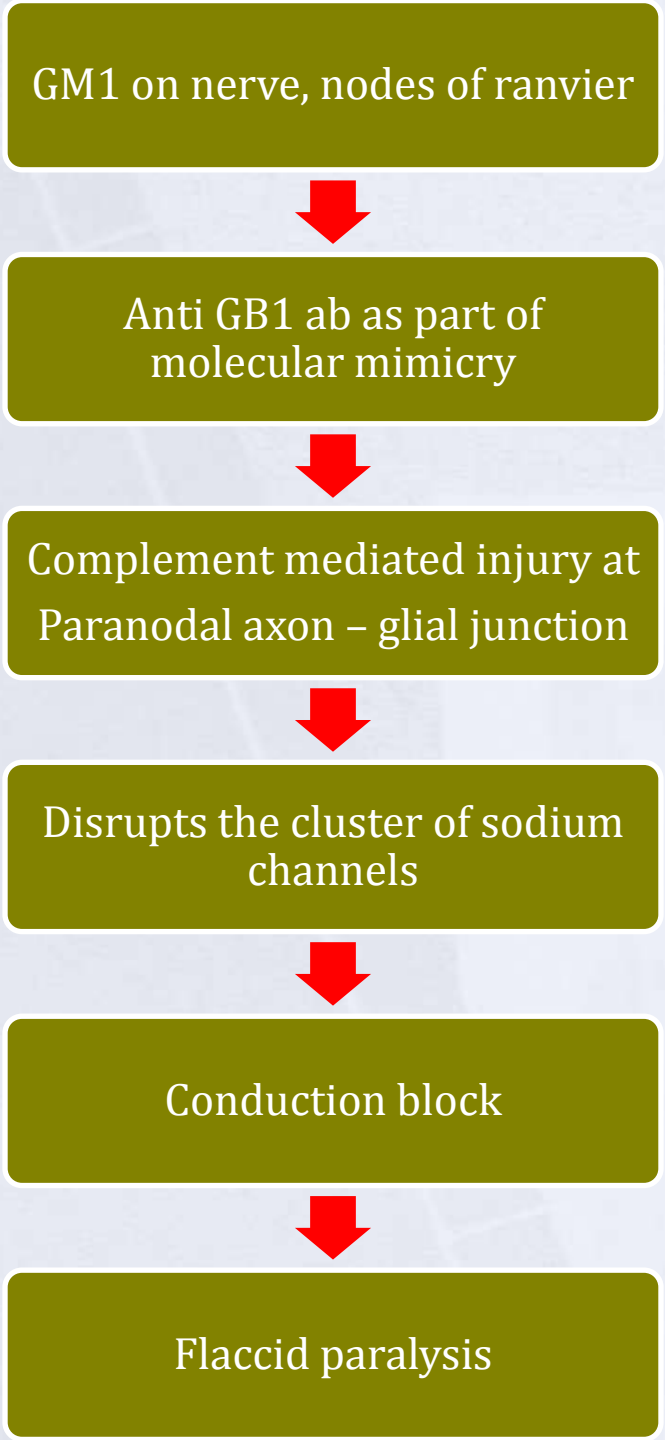
Antecedent events (causes)

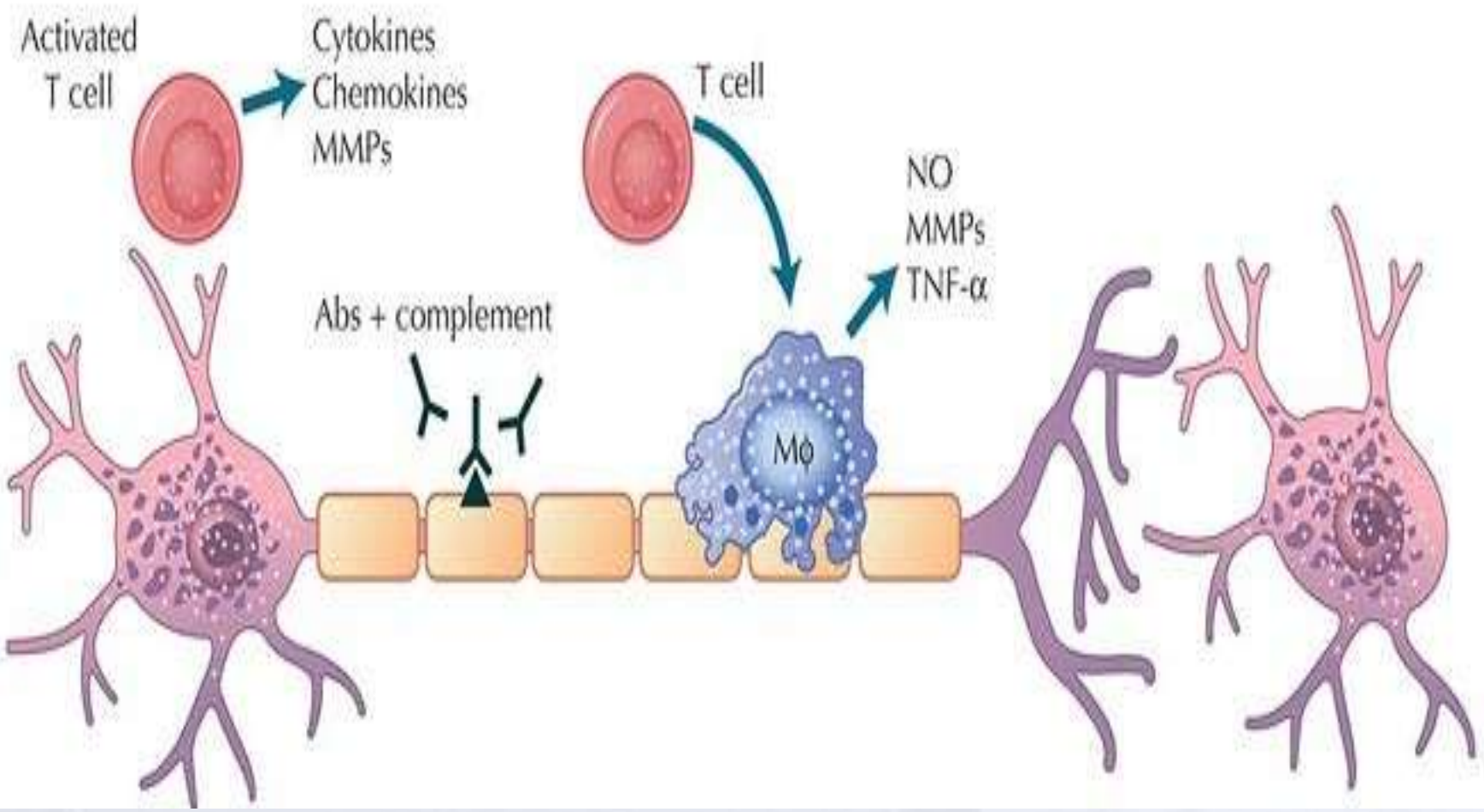
- 70% cases –post infectious .
  - 1-3 weeks after an acute infectious process respiratory or GIT.
  - 20-30% cases –campylobacter jejuni
  - Other agents –HHV (EBV,CMV)
  - Mycoplasma pneumoniae
- Recent immunisation –swine influenza vaccine,older rabies vaccine (nervous system)
- Can be seen in patients with lymphoma,HIV positive,SLE.

IMMUNOPATHOGENESIS

- An autoimmune basis.
- Both cellular and humoral immunity involved.
- T cells activation –IL2,IL2 receptor,IL-6,TNF alpha,IFN gamma.
- All GBS results from immune responses to non self anitgnes(infectious agents,vaccines) that misdirect to host nerve tissue through a resemblance of epitope(molecular mimicry).
- Neural targets are gangliosides.
- Anti ganglioside ab –GM1 (20-50% cases of C.jejuni)
- Anti GQ1b ab - >90% MFS


Ingestion of *Campylobacter* containing food (poultry), water
Gastro-intestinal symptoms: vomiting, diarrhoea
APC
Adaptive immune response
•cell wall lipo-oligosaccharides
•proteins
Host-related factors
•immunogenetic polymorphisms
•previous/concurrent infections
Protective immunity
Eradication of infectious agent
Return to healthy state
Anti-neural immunity
Immune mediated nerve damage
Guillain-Barré syndrome


GM1 on nerve, nodes of ranvier
Anti GB1 ab as part of molecular mimicry
Complement mediated injury at Paranodal axon – glial junction
Disrupts the cluster of sodium channels
Conduction block
Flaccid paralysis


Activated
T cell
Cytokines
Chemokines
MMPs
T cell
NO
MMPs
TNF-α
Abs + complement
Mφ

AIDP

- Adults > children
- Rapid recovery
- Anti GM1 ab (50%)
- Demyelinating
- First attack on schwann cell surface
- Widespread myelin damage
- Lymphocyte infiltration
- Variable sec axonal damage

AMAN (ACUTE MOTOR AXONAL NEUROPATHY)

- Children ,young adults
- Seasonal
- Recovery rapid
- Anti GD1 a ab
- Axonal
- First attack on motor nodes of ranvier
- Macrophage activation
- Axonal damage is variable

MILLER FISCHER VARIANT**

- Adults,children
- Uncommon
- Anti GQ 1 b anitbodies >90%

(Not seen in other forms of GBS
Unless there is EOM invovlement)

- More of GQ1b gangliosides in EOM
- cause conduction block
- Pupillary paralysis
- Only 5% GBS

***2marks

Clinical history

- respiratory or GI tract infection prior to onset of weakness – 1-3 weeks.
- h/o recent immunisation (rabies)
- Sudden or progressive weakness over 2-3 days.
- NO FEVER AT THE ONSET OF WEAKNESS.

FEVER AND CONSTITUTIONAL SYMPTOMS ARE ABSENT AT THE ONSET AND IF PRESENT ,CAST DOUBT ON DIAGNOSIS.

Clinical manifestations

MOTOR SYSTEM :

- Rapidly evolving areflexic motor paralysis with or without sensory disturbance.
- Ascending type of paralysis
- RUBBERY LEGS.
- Weakness evolves over hours –days.
- Legs>arms
- Accompanied by dysesthesias of extremities.

DEEPTENDON REFLEXES:

Reflexes attenuate,disappear in few days of onset.

CRANIAL NERVES:

Facial diparesis seen in 50% affected individuals.

Lower cranial nerves affected –bulbar weakness – difficulty in handling secretions,maintaining airway.

Ophthalmoplegia –miller fischer variant

Pupillary paralysis

Optic atrophy

SENSORY SYSTEM:

Largely myelinated fibres are severely affected.

Proprioception is more affected than pain temperature sensation.

BLADDER:

Only in severe cases,transiently.

If bladder dysfunction is a prominent feature and comes early in the course,think other than GBS – spinal cord disease.

- **PAIN:**
- Deep aching pain may be present the previous day in weakened muscles.
- Initially at onset –neck,shoulder,back,diffusely over spine - 50% cases.
- Dysesthetic pain in extremities
- Self limited usually
- Responds to analgesics

- **AUTONOMIC INVOLVEMENT:**
- Common
- Seen even in mild cases
- Wide fluctuation in blood pressure
- Postural hypotension
- Cardiac dysrryhthmias
- Close monitoring and management
- Can be fatal.

- All require hospitalisation
- 30% require ventilatory support

course

- Pattern of rapidly progressive (evolving) paralysis with areflexia
- Usually does not progress beyond four weeks after reaching a plateau.

Differential diagnosis

- Acute myelopathy – back pain,sphincter disturbances
- Botulism –early loss of pupillary activity,descending paralysis
- Diphtheria –early oropharyngeal involvement
- Lyme disease polyradiculitis
- Porphyria –abdominal pain,seizure,psychosis
- Vasculitic neuropathy
- Poliomyelitis with fever,meningeal signs
- Brain stem ischemia
- Critical illness neuropathy
- Myasthenia gravis
- OP poisoning

Lab features

CSF :

- Raised CSF protein 1-10 g/l (100-1000mg/dl)
- Without accompanied by pleocytosis
- ALBUMINOCYTOLOGICAL DISSOSCIATION
- Usually normal in <48 hrs
- Increased proteins at the end of first week
- 10-100/ul elevation
- Think of HIV ,CMV in case of pleocytosis.

ELECTRODIAGNOSTIC TESTS:

May be normal

Lags behind clinical events

demyelination - prolonged distal latencies,conduction velocity slowing,condcution block.

Reduced amplitude of compound action potential without conduction slowing

Asbury Criteria for diagnosis

REQUIRED :

- 1.progressive weakness of 2 or more limbs due to neuropathy.
- 2.areflexia
- 3.disease course < 4 weeks
- 4 exclusion of other causes (vasculitis,PAN,SLE,churg strauss syndrome,toxins,lead,botulism,diptheria,porphyria.,cauda equinal syndrome)

SUPPORTIVE:

- 1.relatively symmetric weakness
- 2.mild sensory involvement
- 3.facial nerve or other cranial nerve involvement
- 4.absence of fever
- 5.typical CSF profile(aceelualr,increase in protein level)
- 6.electrophysiologic evidence of demyelination

treatment

- Initiate as soon as possible.
- Each day counts
- 2 weeks after the first motor symptoms – immunotherapy is no longer effective.
- IVIg
- Plasmapheresis
- Combination is not effective
- IVIg-first choice,easy to administer
- Five daily infusions 2g/kg body weight
- Plasmapheresis 40-50ml/kg four times a week
- Treatment reduces need for ventilation by half.,increases full recovery at an year.
- Glucocorticoids are not effective in GBS.
- Conservative management in mild cases.

Severe cases

- Critical care setting
- Attention to vital capacity,heart rhythm,blood pressure,nutrition,DVT,CV status,tracheotomy,chest physiotherapy.
- 30% require ventilation
- Some for prolonged time
- Phsyiotherapy is also imp.

SUMMARY

- 1.acute rapidly evolving areflexic ascending motor paralysis with or without sensory disturbances.
- 2.fever is absent at the onset of weakness
- 3.bladder involvement in severe cases –transient
- 4.campylobacter jejuni 20-30 % cases
- 5.autoimmune basis ,molecular mimicry
- 6.anti GM1 ab (MC),anti GD1a,anti GQ1b (MFS)
- 7.autonomic involvement is common
- 8.facial nerve is the one most commonly affected,optic nerve.
- 9.30% require ventilatory support.

- 10.course is usually < 4 weeks
- 11 .typical CSF profile shows high protein,no pleocytosis
- 12.electrographically conduction block present
- 13.treatment as soon as possible
- 14.IVIg,plasmapheresis –both are equally good
- 15.glucocorticoids are not effective in GBS
- 16.think of miller fischer variant in presence of ophthalmoplegia,ataxia,areflexia.

CIDP

- Chronic course.
- Gradual onset.
- >9 weeks from onset –deterioration
- Both motor and sensory involved
- Can be asymmetric
- Tremor in 10 % cases
- Death is uncommon
- Biopsy reveals onion bulb changes (imbricated layers of attentuated schwann cell processes surrounding an axon)
- Responds to glucocorticoids


Thank you