



Updating the Vaccine Injury Table: Guillain-Barré Syndrome (GBS) and Seasonal Influenza Vaccines

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Objective: To seek advice and concurrence on the proposed changes to the VICP's Vaccine Injury Table (VIT)



- Overall key concepts of the presentation:
 - Changes are proposed based on policy
 - Changes proposed address Guillain-Barré Syndrome (GBS) in relationship to seasonal influenza vaccines (current and future)
- Focus is on proposed changes conceptually to:
 - Vaccine Injury Table (VIT)



Guillain-Barré Syndrome (GBS)



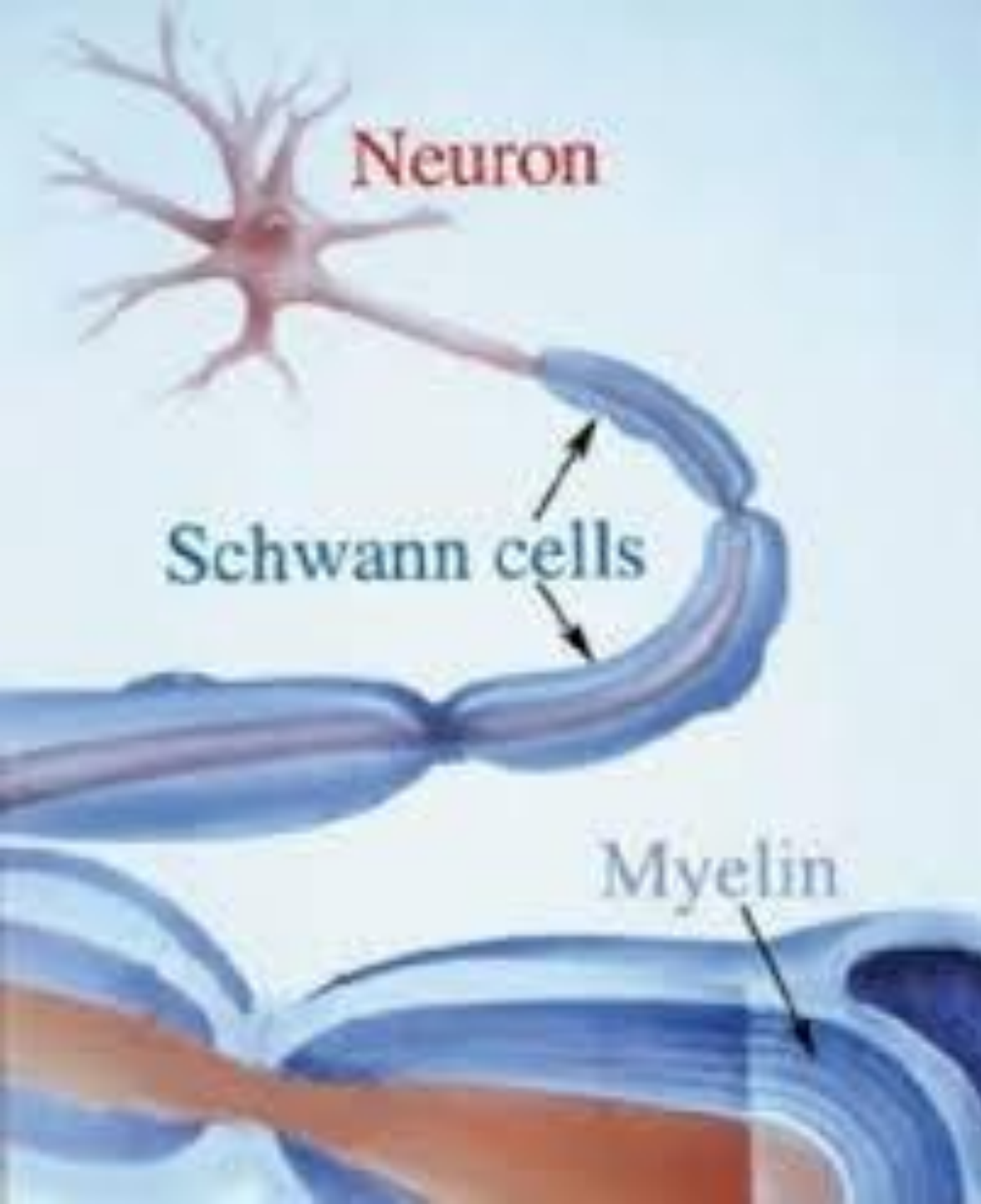
- GBS is a rare acute paralysis caused by dysfunction in the peripheral nervous system (the nervous system outside the brain and spinal cord) that may manifest with weakness, abnormal sensations, and/or abnormalities in the autonomic (involuntary) nervous system.
- The syndrome is generally thought of as an acute demyelinating disorder (damage to the myelin sheath of the peripheral nervous system nerve cells).



Guillain-Barré Syndrome (GBS)

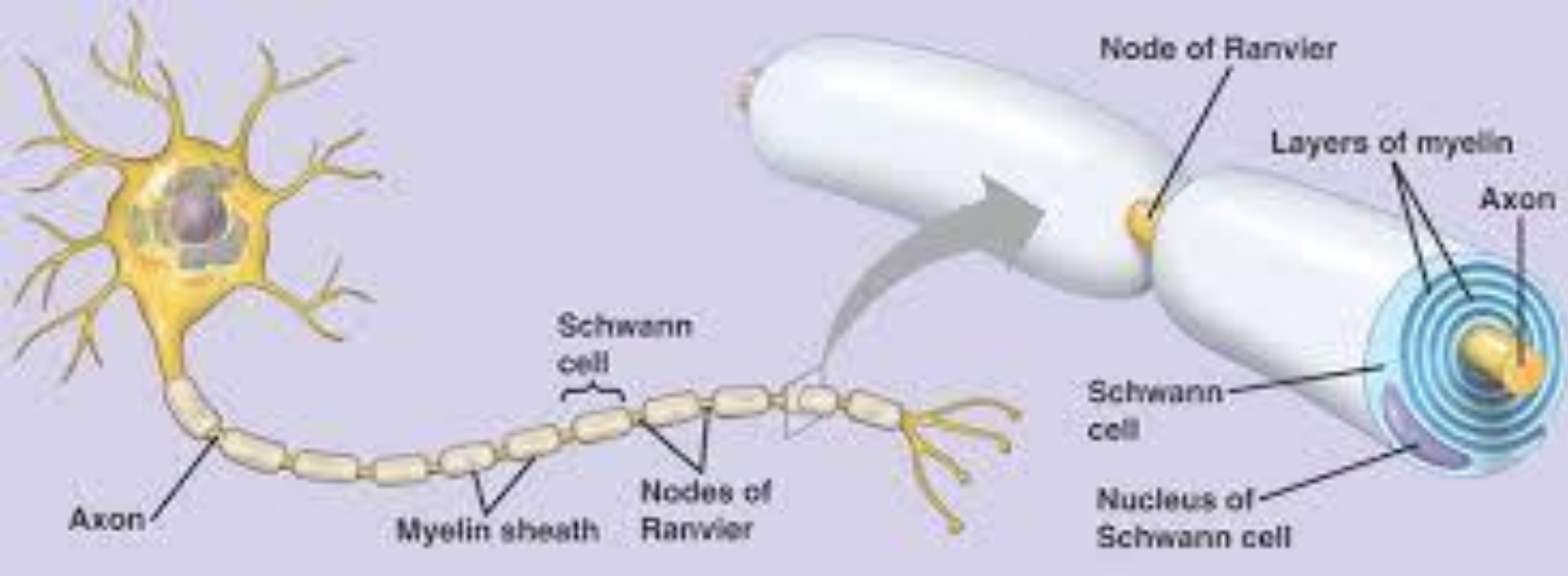


- Typical GBS involves ascending weakness with or without facial weakness and with or without respiratory failure. Most people fully recover from GBS, but some people can either develop permanent disability or die due to respiratory difficulties. Death, if it occurs, usually involves respiratory compromise secondary to paralysis of the muscles involved in breathing; or from complications, such as infection/sepsis.



Vocabulary

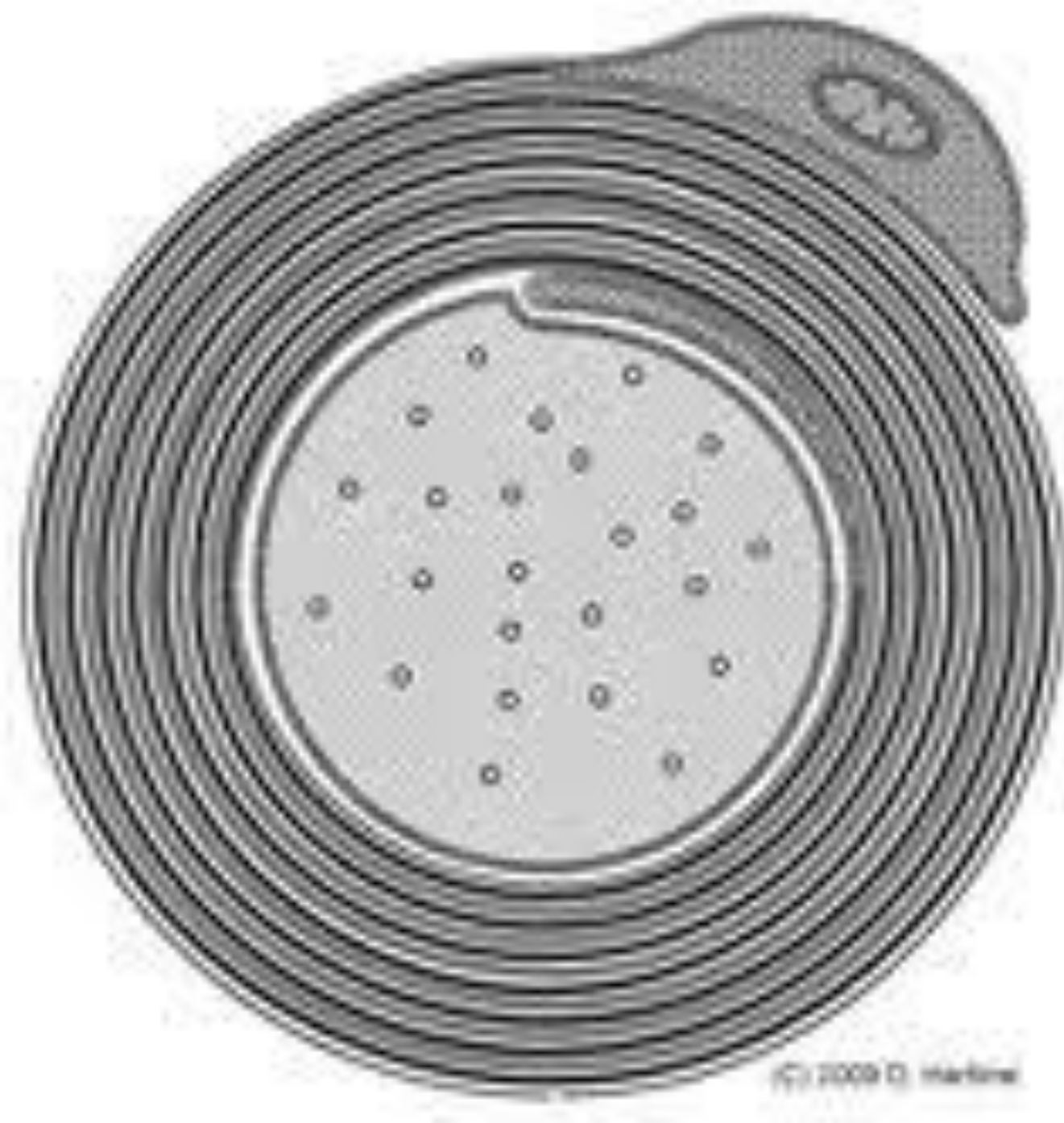
- Neuron: the nerve cell itself (all of it)
- Schwann cells: cells that create the myelin by wrapping over and over around the long axon of the nerve cell (lengthy arm stretching to where the signal needs to get to)



- The myelin sheath is therefore a series of segments of layers of the Schwann cells wrapped over and over around the axon all the way down the axon. There are separations (“Nodes of Ranvier”) between the many individual Schwann cells.

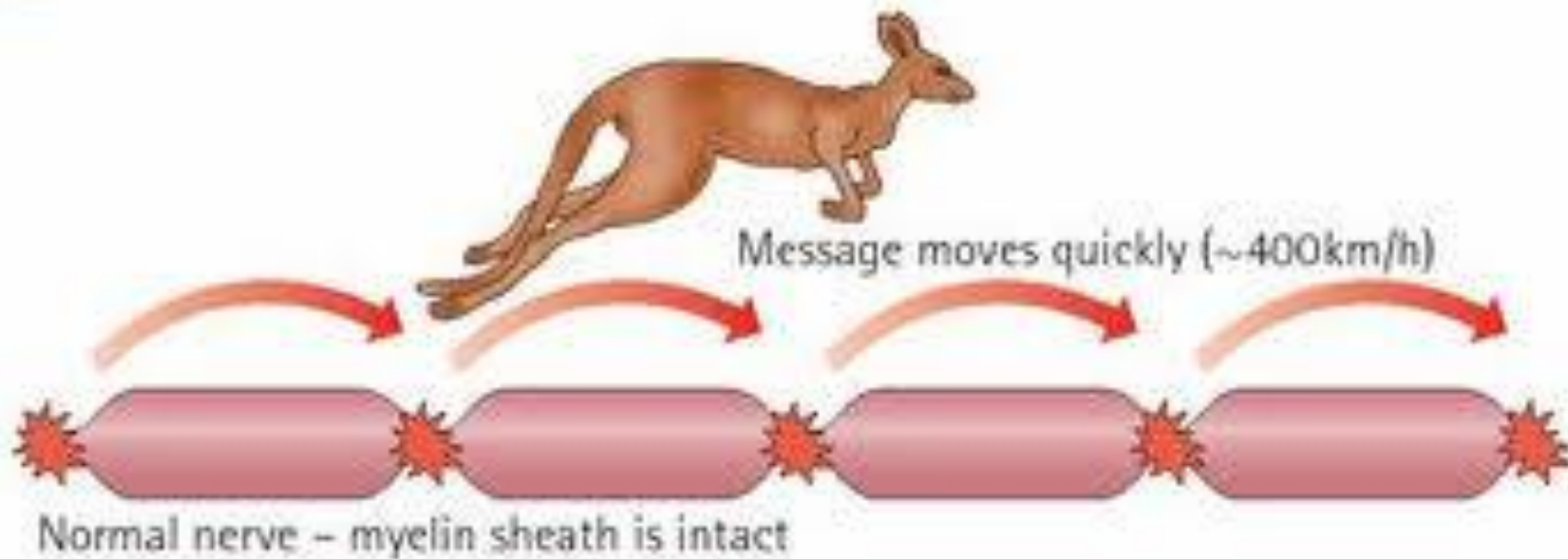


- The nucleus of any given Schwann cell is somewhat separated from the axon of the nerve cell itself (by the layers of myelin wrapping)



View in Cross Section Cut:

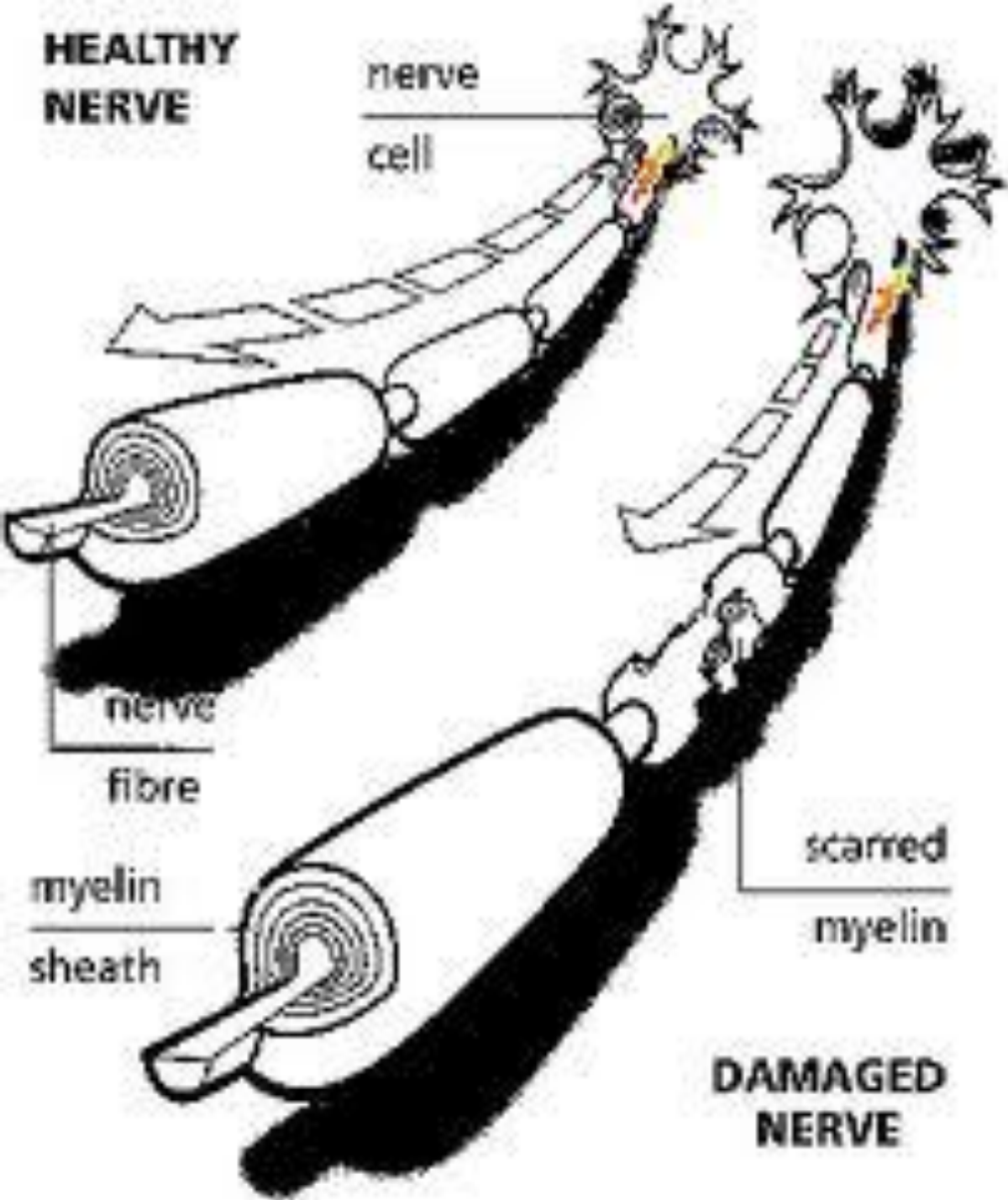
- 1) the axon is in the middle;
- 2) layers of myelin are around it;
- 3) nucleus of Schwann Cell is separate from actual nerve axon



- Nodes of Ranvier structure help to move the electrical signal much more quickly by skipping the signal faster than would happen without it

HEALTHY NERVE

nerve
cell



GBS Functional Signal Damage:

- Healthy nerve at the left is able to move the signal fast
- The damaged nerve is not able to do so - or is slower

Major Variants

- GBS historically considered a single disorder
- Now recognized as heterogeneous syndrome that includes multiple major variants:
 - Acute inflammatory demyelinating polyneuropathy (AIDP)
 - Fisher Syndrome (FS) (aka: Miller-Fisher Syndrome)
 - Acute motor axonal neuropathy (AMAN)
 - Acute motor & sensory axonal neuropathy (AMSAN)

Context for ACCV Consideration Today

- Key Issues:
 - Flu vaccine linkage to GBS in Vaccine Injury Table
 - What we are proposing to be added to VIT
 - And why: in English (not medical or legal jargon)
- Changes are being proposed for policy reasons (in context of current science status)
- Factoid: VICP to date has settled 90.1 % of flu/GBS claims that have been adjudicated

2010-2011-2012-2013-2014

- Following the H1N1 influenza pandemic, the H1N1 antigen was included in the 2010-2011 and 2011-2012 Trivalent Influenza Vaccine (TIV) formulations.
- It is in the 2012-2013 formulation and also will be included in the 2013-2014 version.

GBS VIT Background

- In March 2012, a presentation was made on behalf of the Influenza Working Group Task Force which “discussed a number of IOM findings where evidence was insufficient to accept or reject a causal relationship between vaccination and the adverse event or the findings did not warrant a Table change” – including GBS.

2012 ACCV Decision to Wait

- The March 2012 ACCV meeting decided to defer further ACCV decisions on linkage of GBS and TIV until formal peer review and publication was completed and the results of the studies were publicly available.

GBS and 2009 Influenza A (H1N1)

- A variety of studies on the risk of Guillain-Barré syndrome (GBS) and 2009 influenza A (H1N1) monovalent vaccine have been published.
- 3 large government sponsored studies published in May 2012 showed compelling evidence for a rare, small increase for GBS caused by 2009 H1N1 flu vaccine.

2013 Meta-Analysis

- A new meta-analysis study was published in March 2013 focused on association of GBS and 2009 influenza A (H1N1) monovalent vaccine and showed a small increased risk of GBS, which translated into about 1.6 excess cases of GBS per million people vaccinated.
- Note: 2009 H1N1 monovalent vaccine is not covered by VICP - but is covered by the Countermeasures Injury Compensation Program

- The Agency for Healthcare Research and Quality (AHRQ) has developed a new report for the Office of the Assistant Secretary of Health that now has been published asking for public comment. The report is not yet final.
- This report reviewed all routinely recommended vaccines; IOM studies; and the science of GBS association with influenza vaccines; leading to the understanding that there was not enough power in the epidemiological studies done to date to resolve completely the science issues at this time.

- The report leaves us understanding that the **strength of evidence and association is high** between (2009) H1N1 vaccines and GBS.
- And that **post-licensure studies report mixed results** regarding the association of seasonal influenza vaccines, including those containing H1N1 strains, with GBS.

Policy Implications

- The scientific basis for including GBS in the VIT is not yet resolved, and recommendation for this change is made for policy reasons, as well as the science which exists up to now.
- DVIC recommends that the ACCV support the proposed changes to the VIT.



Proposed Modification to VIT



Vaccine	Illness, disability, injury, or condition covered	Time Period for first symptom or manifestation of onset or of significant aggravation after vaccine administration
Trivalent Influenza Vaccines Seasonal Influenza Vaccines	A. Anaphylaxis B. Shoulder Injury Related to Vaccine Administration C. Vasovagal syncope D. Guillain-Barré Syndrome	4 hours 48 hours 1 hour 3 - 42 days



Statutory Authority



- National Childhood Vaccine Injury Act of 1986
 - Section 2114: Administrative Revision of Table
 - Secretary may promulgate regulations to modify Table
 - Anyone may petition Secretary including ACCV
 - ACCV mandated to review proposed changes



Modifying the VIT



- Secretary has authority to change the Vaccine Injury Table (VIT)
 - Adding/removing injuries/conditions/timeframes
 - Adding/removing vaccines



ACCV Recommendation Choices



1. ACCV concurs with the proposed change(s) to the VIT and would like to move forward (with or without comments).
2. ACCV does not concur with proposed change(s) to the VIT and would not like to move forward.
3. ACCV would like to defer a recommendation on the proposed change(s) to the VIT pending further review at this meeting, or the next ACCV meeting of December 5, 2013.



ACCV Guiding Principles



- In 2006, the ACCV developed “Guiding Principles” for recommending revisions to the Table.
- The Table should be scientifically and medically credible.
- Where there is credible scientific and medical evidence both to support and to reject a proposed change to the Table, the change should, whenever possible, be made to the benefit of petitioners.



ACCV Guiding Principles



- Guidelines for what is “scientifically and medically credible”
 - If IOM study: conclusions of the IOM should be deemed credible but should not limit deliberations of the ACCV.
 - For data sources other than IOM report, assess the relative strength. Also assess consistency if there is no IOM report. Consistency across multiple sources of evidence is an indication of credibility.



- Hierarchy of evidence (strongest to weakest)
 - Randomized controlled clinical trials
 - Controlled observational studies (e.g., cohort and case control studies), including but not limited to studies based upon data from the Vaccine Safety Datalink (VSD) database
 - Uncontrolled observational studies (e.g., ecological studies)
 - Case series
 - Data from passive surveillance systems, including but not limited to the Vaccine Adverse Event Reporting System (VAERS)
 - Case reports
 - Editorial articles on scientific presentations
 - Non-peer reviewed publications

(DVIC is available to help assess strength of evidence.)



ACCV Guiding Principles



- Remain aware of policy considerations underlying the Table.
 - Awards to vaccine-injured persons are to be made quickly, easily, and with certainty and generosity.
 - Congress intended to compensate serious injuries caused by vaccines
- If there is a split in credible scientific evidence, ACCV members should tend toward adding or retaining the proposed injury.



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Questions To Run On



To open the conversation of the whole:

- What are key insights that this presentation maybe has generated for you?
- Do you have any questions DVIC staff can address to make your deliberations easier?