QUESTION 8 Infectious Disease
A 42-year-old man in the intensive care unit following a motor vehicle accident develops *Staphylococcus aureus* bacteraemia. He is commenced on vancomycin. Following the first infusion he develops a rash involving the face and upper trunk. His blood pressure falls to 100/70 mmHg.

What is the most appropriate next step?
A. Stop vancomycin, commence linezolid.
B. Stop vancomycin, commence dalfopristin/quinupristin.
C. Commence rapid desensitisation for vancomycin.
D. Continue vancomycin but slow the rate of infusion.
E. Continue vancomycin but premedicate with hydrocortisone.

Vancomycin hypersensitivity
- “red man syndrome” does not represent a true allergic response
- wide range reactions from localized skin reactions to generalized cardiovascular collapse

Mechanism
1) IgE-mediated anaphylaxis
2) “Pseydo-allergic” anaphylactoid reaction

Anaphylaxis (IgE MEDIATED)
Immunologically-mediated reactions involving IgE antibodies
Rare with vancomycin
Occurs after subsequent administrations after dev of IgE antibodies to the drug

Anaphylactoid reaction (NON-IgE MEDIATED)
Non-immunologically mediated response
Can develop with 1st administration
Direct mast cell-mediated release of mediators such as histamine
- affected by opiates
- induce a dose or rate-related mast cell degranulation
- other agents include radiocontrast dye, muscle relaxants (potentiate mast cell degranulation)

Red Man syndrome
Most common adverse reaction, not life-threatening
Infusion-related histamine-like reaction
Characterized by flushing (upper body more that lower body), pruritus, chest pain, muscle spasms and occasionally hypotension
Frequency of syndrome: 10% - 70-90% (large range)
Prevention: pretreatment with anti-histamines
   Slower infusion rates

Hypersensitivity Manifestations
1) Skin rash
   a) Maculopapular/urticarial skin eruptions
   b) Vancomycin-related linear IgA bullous dermatosis (LABD)
   - IgA autoantibodies deposited in linear pattern along epidermal basement membrane
   - Rare but under-recognised
   - Discontinue vancomycin or try prednisolone
2) Hematologic
   a) Leukocytosis
   b) Eosinophilia
   c) Neutropenia
   d) Thrombocytopenia
   e) Agranulocytosis (rare)
3) Renal
   - 5 pts developed acute interstitial nephritis

Investigations
RMS is the most common reaction but does not represent true hypersensitivity, better to distinguish RMS from hypersensitivity reactions to avoid falsely labeling a pt as allergic or discontinuing the drug unnecessarily.

1) Histamine vs tryptase levels
   - no replicable test for differentiating true hypersensitivity from anaphylactoid reactions to vancomycin
   - if tryptase levels are high, greater likelihood that reaction is IgE-mediated.

Management

1) Severe symptoms: bronchospasm, respiratory distress, hypotension
   - discontinue vancomycin

2) RMS
   - slow infusion rate
   - treatment with antihistamine
   - if reactions do not disappear with measures, cease vancomycin
   - consider desensitization procedures

Alternative treatments to vancomycin

1) Quinupristin-dalfopristin
   - used for tx of vancomycin resistant enterococcal infections and complicated skin infections due to MSSA
   - synergy against MRSA when quinupristin-dalfopristin combined with vancomycin
   - overall response rate is 71%
   - adverse reactions: arthralgia, myalgias, nausea and hyperbilirubinemia

2) Linezoid
   - bacteriostatic antistaphylococcal agent
   - used for nosocomial pneumonia and complicated skin infections
   - excellent tissue distribution and taken orally as well as IV
   - added advantage of inhibiting bacterial toxin production

3) Daptomycin
   - new class of antibiotics (cyclic lipopeptides)
   - disrupt bacterial membrane function
   - approved for use in complicated skin and soft tissue infections and bacteremia with or without endocarditis due to S.aureus
   - cannot be used for gram +ve pneumonia as does not achieve sufficiently high concentrations in resp
   - tract and it is inactivated by surfactant

4) Tigecyclin
   - novel glycyclcline antibiotic
   - strong activity against gram +ve, gram –ve, aerobic, anaerobic and atypical bacterial species (VRE, MRSA, penicillin resistant streptococcus pneymoniae)
   - approved for complicated skin infections and complicated intraabdominal infections but not approved for
   - use in bloodstream infections

5) Teicoplanin
   - same spectrum of activity as vancomycin
   - less side effects
   - teicoplanin compared to linezolid- no sig difference in clinical success or microbiological success

Back to the Question

This is a tricky question once again, as the patient develops a rash in his upper trunk and also hypotension. It does sound like red man syndrome although having hypotension would be a more severe form of RMS.
Year 2005 Paper two: Questions supplied by Ilynn

1 Quote from Up to Date

“The syndrome may be effectively prevented by pretreatment with anti-histamines [13], and slower infusion rates of vancomycin may reduce the frequency and severity of the reactions. One study in 10 normal volunteers analyzing histamine levels, occurrence and severity of RMS, and vancomycin infusion time found a higher incidence of RMS and increased severity when vancomycin was infused over one hour compared to when the same volunteers received the drug over two hours; peak plasma histamine levels and the total release of histamine were greater during the one-hour infusion [15].”

Answer D – Slow infusion rate down.

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1 Up to date: Vancomycin hypersensitivity