1.0 DESCRIPTION

1.1 Definition: Ribavirin is an antiviral drug shown to have in vitro activity against respiratory syncytial virus, influenza virus, and herpes simplex virus. The drug may be aerosolized via the (Small Particle Aerosol Generator) SPAG-2 nebulizer developed specifically for this use. The generator produces aerosolized particles of ribavirin solution appropriate in size (95 percent of nebulized particles are less than five microns in diameter) for delivery to the pulmonary site of infection.

1.2 Indications: The efficacy of aerosolized ribavirin therapy remains controversial. However, ribavirin aerosolization may be indicated for patients with clinical signs and symptoms consistent with a viral pulmonary infection, especially respiratory syncytial virus, influenza virus, or herpes simplex virus.

1.3 Contraindications

1.3.1 Ribavirin is contraindicated in female patients who are or may become pregnant, or who are breastfeeding during exposure to the drug. Prior laboratory studies show there may be some potential for teratogenic effects from the drug.

1.3.2 Aerosolization of ribavirin may be contraindicated in patients with chronic cardiopulmonary diseases (such as asthma and chronic obstructive pulmonary disease) due to the potential for bronchospasm with inhalation of the drug.

1.4 Complications

1.4.1 The drug may precipitate in the patient's airways causing mucus plugging, swelling of secretions, and/or defects of oxygenation and
ventilation. Careful attention to secretion characteristics and good bronchopulmonary hygiene is imperative.

1.4.2 The aerosolized particles of ribavirin may be irritating to some patients causing bronchospasm.

1.5 Precautions

1.5.1 Health care personnel who are pregnant or breastfeeding, or who may become pregnant in the near future, should avoid caring for patients who are undergoing ribavirin therapy. Titers of ribavirin in the blood are still measurable four weeks after administration of the drug.

1.5.2 Aerosolization of ribavirin should be performed, whenever possible, in a negative flow isolation room to minimize the risk of potential effects to other patients and health care personnel, but may occur in a private room if a negative flow room is impractical. Additionally, Clinical Center policy recommends that drug therapy be administered during the hours of 7:00 p.m. and 7:00 a.m.

1.5.3 Appropriate protective clothing should be worn by all persons entering the patient's room during ribavirin aerosolization (See Equipment). When the patient’s room must be entered for care, the SPAG-2 should be turned off and safety goggles as well as an approved particulate respirator must be worn to minimize ribavirin exposure.

1.5.4 Carbon dioxide rebreathing may occur if the total gas flow to the patient device is inadequate. For patients other than infants, a high flow system will be required in addition to the SPAG-2 to provide this flow, as well as to meet the patient's inspiratory flow demands.

1.6 Adverse Reactions and Interventions

1.6.1 If the patient exhibits signs of bronchospasm, bronchodilator therapy may be appropriate. Persistent wheezing that compromises oxygenation and/or ventilation should be assessed relative to the indications for continued ribavirin aerosol therapy.

1.6.2 Anemia has been associated with ribavirin therapy. Patients should be monitored for a decrease in the red blood cell count throughout therapy.

1.6.3 Health care professionals who are particularly sensitive to the drug's aerosolization, either in exhibiting airway hyperreactivity,
eye irritation, or upper airway irritation, or who exhibit signs of rash as a result of handling the drug, should avoid caring for patients undergoing ribavirin therapy. Proper attire (See Equipment) should be worn whenever the drug is handled in any way or when entering a room during aerosol therapy.

2.0 EQUIPMENT

2.1 Negative flow isolation room
2.2 SPAG-2 nebulizer
2.3 Oxygen-air blender with appropriate high pressure gas hoses
2.4 Additional oxygen source gas hose (to connect to the SPAG-2)
2.5 Air compressor
2.6 High flow nebulizer system (if indicated)
2.7 Disposable corrugated tubing
2.8 Aerosol mask, hood, or tent
2.9 Miscellaneous adapters for connections to that patient delivery device
2.10 Ribavirin solution (as prepared by the pharmacy)
2.11 Latex gloves
2.12 Particulate respirator or HEPA filter mask
2.13 Safety goggles
2.14 "Aerosol Therapy in Progress" sign
2.15 Oxygen analyzer

3.0 PROCEDURE (See attached diagram)

3.1 Nebulizer assembly:

3.1.1 Pour the ribavirin solution into the nebulizer reservoir. NOTE: The solution is premixed in the pharmacy. Notify the "unit dose" pharmacist if there are any problems encountered in obtaining the solution.
3.1.2 Insert the nebulizer stem (with three tubings attached) into the swage fitting on the nebulizer cap and tighten.

3.1.3 Place the nebulizer cap (with gasket in place) onto the nebulizer reservoir and twist clockwise until sealed. Be certain that the nebulizer cap is tight to avoid leakage of solution during therapy. Ensure that the nebulizer tubes are not sitting flush against the bottom on the reservoir.

3.1.4 Place the assembled nebulizer into the SPAG-2 housing.

3.1.5 Connect the drying air flow (black hose) quick coupling to the larger fitting on the cap. Connect the nebulizer air flow (blue hose) quick coupling to the smaller fitting on the cap. Each of these hoses should be pressed into position while twisting until they "snap" into place.

3.1.6 Insert the drying air chamber into the side port of the SPAG-2 housing and press it firmly onto the nebulizer cap outflow port. The flow direction arrow must point away from the nebulizer.

3.2 Patient Connections

3.2.1 Assemble the high flow system (if appropriate) and connect it to the patient delivery device via corrugated tubing and adapters. Pour all the water out of the bottle.

3.2.2 Connect the SPAG-2 system to the patient delivery device via additional corrugated tubing and an appropriate adapter. The length of tubing should be as short as is practical to minimize aerosol deposition in the tubing. If applying the SPAG to a patient with an FiO2 requirement greater than 21% or less than 100%, an O2/air blender and compressor source are required.

3.2.2.1 Attach the corrugated tubing to an appropriately sized aerosol mask and add 6 inches of corrugated tubing to both side ports of the mask.

3.2.2.2 Attach the corrugated tubing to an oxygen tent if the mask is intolerable. The total flow may not be enough to for patient comfort in larger patient populations. In this situation a high flow oxygen aerosol system needs to be added. Set the FiO2 the same as the blender on leading into the SPAG Nebulizer. Analyze the FiO2 as close to the patient as possible.
3.3 Initiation of Therapy

3.3.1 Open the nebulizer flowmeter completely (approximately six turns counter-clockwise from the closed position).

3.3.2 Adjust the source gas pressure gauge on the front of the SPAG-2 to read 26 PSI on the pressure manometer.

3.3.3 Turn the drying air flow to 2-9 LPM.

3.3.4 Readjust the SPAG-2 pressure regulator to 26 PSI (if needed).

3.3.5 Verify the correct operation of the SPAG-2 according to the following parameters (the SPAG-2 should stabilize to these ranges shortly after initiation of operation):
   3.3.5.1 Regulator pressure = 26 +/- 2 PSI
   3.3.5.2 Nebulizer flow = 6-10 LPM
   3.3.5.3 Drying air flow = 2-9 LPM
   Refer to the SPAG-2 "Instructions for Use" page 11 for specific troubleshooting instructions should any of the parameters be out of range.

3.3.6 Confirm that the nebulizer is producing a good aerosol by visualizing the three "spray spots" on the wall of the reservoir. These should be approximately one inch in diameter. Optimally, the solution should be nebulized at a rate of 12.5-15.0 ml/hour. If it is noted that ribavirin solution is leaking from the nebulizer, ensure that the nebulizer cap remains tight. Refer to the SPAG-2 "Instructions for Use" for troubleshooting tips.

3.3.7 Monitor the operation of the SPAG-2 for approximately 10 minutes and adjust any settings as needed.

3.3.8 Analyze the FiO₂ delivery as close to the patient as is practical. Maintain the desired FiO₂ through adjustment of both the oxygen blender and the high flow system (if applicable) being utilized.

4.0 POST PROCEDURE

4.1 Monitor the patient throughout the therapy for adverse reactions. Continue to assess the efficiency of aerosolization and make adjustments to the flow as needed.

4.2 Disposal of ribavirin solution: Any ribavirin solution which has not been completely nebulized at the termination of therapy, or solution recalled due to the discontinuation of therapy, should be returned to the pharmacy in its
original container inside a Ziploc bag so that appropriate disposal may occur. **Do not** dispose of the solution on the unit.

4.3 Equipment Processing

4.3.1 Disassemble the nebulizer and drying chamber parts and rinse in water. Send for pasteurization.

4.3.2 Replace all disposable equipment daily at the termination of therapy. When it has been determined that no further therapy will be delivered, wipe that SPAG-2 housing with Dispatch prior to removing it from the patient's room.

5.0 CHARTING

Record the initiation and discontinuance of therapy each day. In the MICU, document on the "Comments" side of the Continuous Ventilation Record. If treatment is provided outside the MICU, documentation should be completed in the MIS system. This note should include an evaluation of the patient's tolerance of the therapy, any adverse effects and actions taken, and the efficiency of nebulization. The flowrate used for nebulization should also be noted.

6.0 REFERENCES

6.1 SPAG-2 Instructions for Use.

6.2 Virazole (ribavirin) Prescribing Information Sheet.

6.3 Communication with ICN Pharmaceuticals, Inc. Pharmacological and Technical Support [1(800)572-7400].

6.3.1 Clinical Center Policy: Guidelines for Preparation and Administration of Aerosolized Ribavirin.