

Medicator® Cleaning Instructions and Infection Control Considerations

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Scope: Respiratory Care, Infection Control, Social Work, Pharmacy, Hospice, Durable Medical Equipment Suppliers, Home Care Patients/Family

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There are three specific instructional sections of this document: I. Instructions for [Hospitals](#), II. Instructions for [Hospices and Clinics](#), and III. Instructions for [Home Care](#). Before reading your relevant section, please read the Background Information first.

Background Information

Purpose. This document will provide information relevant to the infection control considerations of the Healthline Medicator® family of high-efficiency aerosol drug delivery devices and describe the physical procedures for cleaning the Medicator in different usage situations. It is incumbent upon the user to develop comprehensive policies and procedures for the Medicator, as well as their other aerosol delivery devices, that are compatible with their facility policies and the CDC Pneumonia Guidelines. We provide this document in the hope it will aid the end-user in the development of infection control policies & procedures relevant to their use of the Medicator.

Indications and Usage. The Medicator Aerosol Maximizer, a high-efficiency aerosol drug delivery system, is used with an attached pneumatically-powered small volume medication nebulizer (SVN) for the administration of medicated aerosol medication solutions. The Medicator may be used in the hospital, hospice, or home-care environment. The types of medication typically used with the Medicator include, but may not be limited to: bronchodilators [racemic albuterol, levalbuterol (Xopenex®), ipratropium (Atrovent®) and racemic epinephrine], steroids [budesonide (Pulmicort® Respules®)], antibiotics (Tobi®, tobramycin, pentamidine, gentamycin and others), dornase alpha (Pulmozyme®) for mucolysis, plus morphine and fentanyl for pain and/or cough control in palliative care. Other medications may be prescribed or become available in the future.

The Medicator is supplied in two main versions:

Non-filtered, Cat # MM-800
Medicator Aerosol Maximizer

Filtered, Cat # AM-602
Medicator Maximizer⁺Plus



Configurations. Both devices have a green 1 Liter neoprene (non-latex) reservoir bag, a nebulizer and a mouthpiece. The primary difference between the two devices is that the MM-800 has a smaller manifold with a hole in its top for patient exhalation and does not have an exhalation filter. The AM-602 has a larger manifold, with a 22 mm OD exhalation port to which an optional exhalation filter may be attached. Respiratory therapy filters of this type are readily available in hospitals with both “bacterial/viral” designation as well as the better “HEPA” (High-Efficiency Particulate Air) designation. The Medicator AM-6xx may be ordered from Healthline with either type filter [AM-602 (bacteria/viral), AM-602H (HEPA)] or no filter (AM-604).

Air Compressor. The Healthline Neb-3A nebulizer supplied with the Medicator should be powered by compressed air or oxygen at a flowrate between 6 and 8 L/minute with 8 L/min being the generally preferred flowrate for optimal performance. When run from a typical portable air compressor for respiratory home care, attention should be paid to periodically cleaning the air intake filter to make sure that clean air is supplied to the patient through the nebulizer drive tubing and the flow is not restricted by a dirty filter.

Residual Volume. The Medicator, with any attached nebulizer, achieves an aerosol drug delivery rate, or total drug delivery amount (when run to dryness), that is approximately 2.4 times greater than what would be achieved by the same nebulizer attached to a standard nebulizer “T” setup running under the same conditions. Nevertheless, there will still probably be ~0.75 mL of residual volume left in the nebulizer after it has begun to sputter. This residual volume must be cleaned out of the nebulizer after a treatment is concluded in order to prevent it from becoming a medium for growth of bacterial organisms and to prevent dried medication from clogging the small jet orifice in the nebulizer.

Healthline Philosophy, or Why Do We Provide Filtered Aerosol Delivery Systems?

We believe that protecting the healthcare worker from breathing collateral aerosols while administering treatments ought to be given new priority in the workplace. There may be a two-pronged risk to the respiratory therapist during aerosol therapy. First, there’s the risk of inhaling drugs that are not prescribed for the practitioner and which could conceivably be inhaled in potentially toxic amounts (in view of the chronic dose-duration exposure relationship). The source of these aerosol drugs is not only from patient-exhalation (nebulizers, MDIs, DPIs) but from aerosol delivery devices, such as liquid nebulizers that, by design, vent large amounts of aerosol into the environment during the patient’s exhalation phase.

Second, there’s a potential risk of inhaling infectious droplets during aerosol therapy, particularly from patients with a respiratory infection that has not yet been diagnosed. For example, the April 7, 2003 report in *The New England Journal of Medicine*, quickly published online in the interest of the public health, concerning the spread of Severe Acute Respiratory Syndrome (SARS), mentioned that “... the use of a jet nebulizer to administer aerosolized albuterol in the index patient had probably aggravated the spread of the disease by droplet infections.” Half of the 138 patients discussed in this report were health care workers.

These risks may exemplify sound reasons why non-indicated aerosol therapy clearly should not be given. But, to the extent that aerosol therapy IS indicated, what can be done to mitigate the risk? We do not believe that having RTs wear masks is a sufficiently adequate answer. Experts in risk management will caution against unwarranted reliance on a single engineering control. Why? Because no single system or control works 100% of the time. Redundant controls are frequently necessary. So filtered aerosol delivery devices should always be used for medications and/or patients with a high degree of risk. Masks should provide redundant protection where necessary. There are some who would even argue that we ought to be using filtered nebs even with albuterol because there is emerging suspicion that chronic low-dose exposure to beta agonist aerosols downregulates beta receptor response to beta agonists and predisposes the therapist to asthma.

I. Instructions for Hospitals

Assumption: A Medicator device used in the hospital environment will be assigned to a single patient who uses the same device a number of times daily (1 – 12 or more) for less than one week. If the length-of-stay (LOS) exceeds one week, consideration should be given to replacing the entire Medicator device on a weekly basis.

Policies:

1. The Medicator is labeled “For Single patient Use,” which means that it must be used on a single patient and then discarded. It may not be reused on a different patient even if reprocessed.

2. The CDC Guidelines state:

“Between treatments on the same patient, disinfect, rinse with sterile water, or air-dry small-volume in-line or hand-held medication nebulizers.”

Therefore, to comply with these guidelines it is recommended that the nebulizer be emptied of residual medication and rinsed with sterile water and air-dried in between treatments

Steps:

1. To clean the Healthline Neb-3A nebulizer supplied with the Medicator, remove it from the Medicator manifold by grasping it by its top half and gently pulling straight down until separates from the manifold.

2. Disassemble the nebulizer by gently pulling the two halves apart. Remove the internal venturi cap from the inner tube on the bottom half of the nebulizer (nebulizer cup) taking care to not drop or lose this part during the cleaning process. Dump residual medication into a sink drain and rinse the sink with tap water.

3. Clean and dry the three parts of the Neb-3A according to your hospital’s policy.

4. Reassemble the Neb-3A and replace it on the Medicator manifold.

5. Store the reassembled device in a clean location until next use. If it is stored in a plastic bag, be certain that both the bag and the device are completely dry before inserting device into the bag.

Comment: Conceivably, it will probably not be necessary to clean the Medicator manifold and bag in between treatments. The uni-directional flow control diaphragm (“flapper valve”) inside the manifold of the Medicator offers protection for the nebulizer and the bag against becoming contaminated by exhaled patient droplets. Surface contamination inside the manifold or bag, if it were to develop, is probably inconsequential because it is not transformed into inhalable aerosol particles.

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II. Instructions for Hospices and Clinics

Assumption: A Medicator device used in a hospice or clinic might be used intermittently on different days by the same patient. In some cases, the patient may only use the device once every 2 to 4 weeks (e.g., pentamidine prophylaxis treatments once or twice a month). If the patient uses the Medicator everyday for a series of consecutive days, follow the “Instructions for Hospitals” in the preceding section. Otherwise, follow the instructions in this section.

Steps:

1. The Medicator is labeled “For Single patient Use,” which means that it must be used on a single patient and then discarded. It may not be reused on a different patient even if reprocessed.
2. In accord with the facility’s policies, a patient’s small volume medication nebulizer will probably be required to be emptied of residual medication and cleaned in between treatments. To clean the Healthline Neb-3A nebulizer supplied with the Medicator, remove it from the Medicator manifold by grasping it by its top half and gently pulling straight down until separates from the manifold.
3. Disassemble the nebulizer by gently pulling the two halves apart. Remove the internal venturi cap from the inner tube on the bottom half of the nebulizer (nebulizer cup) taking care to not drop or lose this part during the cleaning process. Dump residual medication into a sink drain and rinse the sink with tap water.
4. Clean and dry the three parts of the Neb-3A according to your hospital’s policy.
5. Further disassemble the Medicator by removing the mouthpiece, filter (if present) and reservoir bag. If applicable, set the filter aside and be sure to not immerse it in liquid or get the internal media wet.
6. The manifold may be immersed and washed in mild detergent, thoroughly rinsed (preferably with de-ionized water to prevent water spots), and then thoroughly dried. Drying can be accomplished by ambient exposure (“air drying”) or forced drying in a moderately heated drying cabinet specifically designed for drying plastic respiratory therapy parts.
7. The neoprene reservoir bag may be immersed and washed in mild detergent, thoroughly rinsed (preferably with de-ionized water to prevent water spots), and then thoroughly dried. Drying can be accomplished by hanging it by its tail with ambient exposure (“air drying”). Forced drying in a drying cabinet is not recommended. Care should be taken at all times when handling the reservoir bag to avoid tearing or damaging it.
8. Reassemble the Neb-3A and replace it on the Medicator manifold. Complete reassembly of the Medicator by attaching the reservoir bag and mouthpiece (plus filter if applicable).
9. Hold the Medicator up to eye level and tilt it back and forth horizontally to make sure the “flapper valve” on the inside is freely moving. If the flapper valve does not open, repeat the cleaning procedure in order to free it. It is extremely rare for the flapper valve to stick due to residual medication, even in the absence of routine manifold cleaning. But if it does happen, it is easily remedied by cleaning the manifold as described above.
10. Store the reassembled device in a clean location until next use. If it is stored in a plastic bag, be certain that both the bag and the device are completely dry before inserting device into the bag.

III. Instructions for Home Care

Assumption: A Medicator device used in the home will have to be routinely cleaned and cared for by either the patient, a family member or a health care provider (e.g., visiting nurse). These instructions should be made available to anyone who requires information concerning this procedure.

Steps:

1. The Medicator is labeled “For Single patient Use,” which means that it must be used only on a single patient. If there is more than one patient in the home requiring aerosol therapy, use separate equipment for each person. Label the equipment so it may be easily identified and kept separate to avoid cross-infection.
2. The small volume medication nebulizer should be emptied of residual medication and cleaned in between treatments in order to keep it from becoming contaminated. To clean the Healthline Neb-3A nebulizer supplied with the Medicator, remove it from the Medicator manifold by grasping it by its top half and gently pulling straight down until it separates from the manifold.
3. Disassemble the nebulizer by gently pulling the two halves apart. Remove the internal venturi cap from the inner tube on the bottom half of the nebulizer (nebulizer cup) taking care to not drop or lose this part during the cleaning process. Dump residual medication into a sink drain and rinse the sink with tap water.
4. Clean and dry the three parts of the Neb-3A according to instructions for your home health provider. Your home health provider should be able to tell you how to disinfect your respiratory therapy devices using dilute bleach solution or quaternary ammonium solutions.
5. Further disassemble the Medicator by removing the mouthpiece, filter (if present) and reservoir bag. If applicable, set the filter aside and be sure to not immerse it in liquid or get the internal media wet.
6. The manifold may be immersed and washed in mild dishwashing detergent, thoroughly rinsed with tap water, and then thoroughly dried. Drying can be accomplished by ambient exposure (“air drying”) on a clean surface (preferably not in a bathroom or near a toilet that is frequently flushed).
7. The neoprene reservoir bag may be immersed and washed in mild detergent, thoroughly rinsed and then thoroughly dried. Drying can be accomplished by hanging it by its tail with ambient exposure (“air drying”).
8. Reassemble the Neb-3A and replace it on the Medicator manifold. Complete reassembly of the Medicator by attaching the reservoir bag and mouthpiece (plus filter if applicable).
9. Hold the Medicator up to eye level and tilt it back and forth horizontally to make sure the “flapper valve” on the inside is freely moving. If the flapper valve does not open, repeat the cleaning procedure in order to free it. It is extremely rare for the flapper valve to stick due to residual medication, even in the absence of routine manifold cleaning. But if it does happen, it is easily remedied by cleaning the manifold as described above.
10. Store the reassembled device in a clean location until next use. If it is stored in a plastic bag, be certain that both the bag and the device are completely dry before inserting device into the bag.

References

Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care associated pneumonia, 2003: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep* 2004; 53(RR-3): 1-36. Available at <http://www.cdc.gov/ncidod/hip/pneumonia/>.

Bibliography -- Nebulizer Cleaning

The following is a list of references and pertinent quotations concerning the risks of contaminated nebulizers and the necessity for proper cleaning.

Craven DE. et al. Contaminated medication nebulizers in mechanical ventilator circuits. *American Journal of Medicine.* 77(5):834-8, 1984 Nov.

"Contaminated in-line medication nebulizers generate small-particle bacterial aerosols that may increase the risk of ventilator-associated pneumonia and therefore should be cleaned or disinfected after each treatment rather than every 24 hours."

Kelsen SG. McGuckin M. Kelsen DP. Cherniack NS. Airborne contamination of fine-particle nebulizers. *JAMA.* 237(21):2311-4, 1977 May 23.

"Nebulizers placed in a surgical intensive care unit that had higher numbers of bacteria and a predominance of Gram-negative organisms in background air had a significantly higher incidence of nebulizer contamination (33.0%) than did nebulizers placed in a non-patient-care area that had lower bacterial counts and a predominance of Gram-positive organisms (0%) (P less than .05). The present study indicates that airborne contamination of fine-particle reservoir nebulizers occurs when bacteria present in ambient air enter the nebulizer during its operation."

Vassal S, et al. Microbiologic contamination study of nebulizers after aerosol therapy in patients with cystic fibrosis. *American Journal of Infection Control.* 28(5):347-51, 2000 Oct.

"Regarding *P aeruginosa* alone, 38% of nebulizers were contaminated after an aerosol. The addition of *Staphylococcus aureus* to *P aeruginosa* (contamination rate of 31.8%) and other targeted bacteria led to an overall contamination rate for pathogenic flora of 63.6%. This rate was underestimated because of the unavoidable loss of bacteria during collection. This finding clearly demonstrates that any negligence during disinfection is associated with the risk of allowing the persistence of bacteria, which can be nebulized in the patients' lungs. CONCLUSION: This study demonstrates that in the absence of cleaning, nebulizers of patients with cystic fibrosis who are infected with *P aeruginosa* are likely to be contaminated by a pathogenic flora."

Hutchinson GR, et al. Home-use nebulizers: a potential primary source of *Burkholderia cepacia* and other colistin-resistant, gram-negative bacteria in patients with cystic fibrosis. [erratum appears in *J Clin Microbiol* 1996 Jun;34(6):1601]. *Journal of Clinical Microbiology.* 34(3):584-7, 1996 Mar.

"Patients who followed recommended instructions for good nebulizer hygienic practice and paid particular attention to drying had minimal or no contamination of their nebulizers."

Cobben NA, et al. Outbreak of severe *Pseudomonas aeruginosa* respiratory infections due to contaminated nebulizers. *Journal of Hospital Infection.* 33(1):63-70, 1996 May.

"The data provided evidence for the relation between *P. aeruginosa* as a cause of infection and the contamination of the nebulizers."

Pegues CF, et al. Burkholderia cepacia respiratory tract acquisition: epidemiology and molecular characterization of a large nosocomial outbreak. Epidemiology & Infection. 116(3):309-17, 1996 Jun.

"Review of respiratory therapy procedures revealed opportunities for contamination of nebulizer reservoirs. This investigation suggests that careful adherence to standard procedures for administration of nebulized medications is essential to prevent nosocomial respiratory infections."

Struycken VH, et al. Problems in the use, cleaning and maintenance of nebulization equipment in the home situation. Nederlands Tijdschrift voor Geneeskunde. 140(12):654-8, 1996 Mar 23.

"Contamination by potentially pathogenic micro-organisms was present in 50% of the saline, medication cups and aerosols (Klebsiella, Enterobacter, Pseudomonas, Serratia, Escherichia coli)."

Takigawa K, et al. Nosocomial outbreak of Pseudomonas cepacia respiratory infection in immunocompromised patients associated with contaminated nebulizer devices. Kansenshogaku Zasshi - Journal of the Japanese Association for Infectious Diseases. 67(11):1115-25, 1993 Nov.

"From May 1990 to August 1991, 36 patients admitted to the Department of Internal Medicine in a medical school hospital with hematological malignancies or solid tumors, developed respiratory tract colonization with Pseudomonas cepacia. Sixteen (44.4%) of these patients developed pneumonia, and four (11.1%) died of respiratory failure due to P. cepacia pneumonia. Extensive survey of the hospital environment as well as equipment showed that nebulizer devices used by the patients for inhalation were contaminated with P. cepacia." I think this article also co-appeared in CHEST 103(6):1706-9, 1993 Jun.

Burdge DR. Nakielna EM. Noble MA. Case-control and vector studies of nosocomial acquisition of Pseudomonas cepacia in adult patients with cystic fibrosis. Infection Control & Hospital Epidemiology. 14(3):127-30, 1993 Mar.

"Reservoirs from nebulizers consistently grew P. cepacia following therapy. CONCLUSIONS: Respiratory equipment may be an important source of nosocomial acquisition of P. cepacia in adult cystic fibrosis patients."

Wexler MR. Rhame FS. Blumenthal MN. Cameron SB. Juni BA. Fish LA. Transmission of gram-negative bacilli to asthmatic children via home nebulizers. Annals of Allergy. 66(3):267-71, 1991 Mar.

"Home use of nebulizers has increased in recent years, although adequate studies have not been performed to evaluate for possible contamination or transmission of potentially harmful bacteria. This study of 20 asthmatic children demonstrated that transmission of pathogenic bacteria occurs."

Mastro TD. Fields BS. Breiman RF. Campbell J. Plikaytis BD. Spika JS. Nosocomial Legionnaires' disease and use of medication nebulizers. Journal of Infectious Diseases. 163(3):667-71, 1991 Mar.

"These findings support the recommendation that only sterile fluids be used for filling or cleaning respiratory care equipment and suggest that this guideline is not universally followed."

Botman MJ. de Krieger RA. Contamination of small-volume medication nebulizers and its association with oropharyngeal colonization. Journal of Hospital Infection. 10(2):204-8, 1987 Sep.

"Inhalation therapy had a significant effect on colonization, with a relative risk of more than four. Age over 60 years also showed a significant association with colonization. One-third of the nebulizers sampled were contaminated, 71% with Gram-negative bacilli. A direct route of contamination could be demonstrated in 28% of the patients."

Le Brun PP. et al. A review of the technical aspects of drug nebulization. Pharmacy World & Science. 22(3):75-81, 2000 Jun.

"The efficacy of nebulizer therapy is influenced by a great number of factors, including the design of the device and the characteristics of the drug solution. Incorrect cleaning, maintenance and disinfection procedures may change the nebulizer performance in time, whereas patient factors can influence the lung deposition of the generated aerosol."

Standaert TA. et al. Effects of repetitive use and cleaning techniques of disposable jet nebulizers on aerosol generation. Chest. 114(2):577-86, 1998 Aug.

A multicenter study of particle size distribution and output using saline solution alone, tobramycin, gentamicin, or a mixture of albuterol and cromolyn said "The purpose of this study was to determine if significant changes in particle size distribution or output (mL/min) occurred with reuse" they also said "For each of the four solutes tested, there was no clinically significant change in performance for up to 100 cycles, when the nebulizers were properly cleaned between uses. Unwashed units containing tobramycin started to fail by 40 runs." They also said "the Pari LC had an output rate two to three times higher than the four disposable models." (but dosing per nebulizer is another discussion). They concluded: "CONCLUSIONS: When properly maintained, there was no trend of deterioration of performance with repeated use of disposable nebulizers. Microbial contamination was not addressed in this study and must be considered prior to recommendations for the reuse of disposable nebulizers."

Struycken VH. Problems in the use, cleaning and maintenance of nebulization equipment in the home situation. Nederlands Tijdschrift voor Geneeskunde. 140(12):654-8, 1996 Mar 23.

A study of home nebulizers said "In addition, we found that the aerodynamic mass median diameter increased considerably as the nebulizer became older. In 6/10 nebulizers the particle size was below 5 microns."

Public Health Advisory: Contamination of Multi-dose Bottles of Albuterol Sulfate Solution for Inhalation (0.5%). Available at: <http://www.fda.gov/cder/drug/advisory/albuterol.htm> (Accessed June 26, 2007).

The Agency has become aware of two recent hospital outbreaks of lower respiratory tract colonization and infection with *Burkholderia cepacia* attributed to contaminated multi-dose bottles of albuterol sulfate. In addition to these recent outbreaks, there have been several previous outbreaks reported in the medical literature. In most cases, colonization or infection occurred in the ICU setting, often in patients receiving mechanical ventilation. In the recent outbreaks, the adverse outcomes attributable to the respiratory tract infections with *B. cepacia* include prolonged hospitalization, pleural space infection, complications of antibiotic use, and death. Investigations revealed that the source of the exposure was contamination of bottles of multi-dose albuterol sulfate solution, likely due to failure to adhere to good, aseptic technique on the part of the respiratory therapists administering the medication. Additionally, it appears that the practice of using a single bottle for multiple patients over time contributed to the outbreak. Institution of more aggressive infection control training and procedures resulted in a marked reduction in the incidence of these infections.

Rau JL, Restrepo RD. Nebulized bronchodilator formulations: unit-dose or multi-dose? Respir Care. 2003 Oct;48(10):926-39.

Nosocomial infections linked to the use of multi-dose bronchodilator nebulizer formulations have been reported in the literature. American hospital respiratory therapy services were surveyed to determine practice patterns, opinions, and awareness regarding unit-dose and multi-dose bronchodilator formulations. One thousand forty-seven hospitals were recruited and 409 valid surveys were completed (completion rate 39%). Only 56% of respondents knew about the evidence regarding the risk of contamination with multi-dose bottles.

Do nebulizers place therapists at risk of occupational exposure?

Asthma risk and occupation as a respiratory therapist

Christiani DC, Kern DG. Department of Environmental Health (Occupational Health Program), School of Public Health, Harvard University, Boston, MA 02115. *Am Rev Respir Dis* 1993 Sep;148(3):671-674.

In the modern hospital environment, many health care workers are exposed to hazardous substances. Among these hazards are respiratory sensitizers, irritants, and infectious agents. A previous cross-sectional study of Rhode Island respiratory therapists reported an excess risk of asthma after entry into that profession. Before the results of that study were published, we conducted a confirmatory mailed questionnaire survey of 2,086 Massachusetts respiratory therapists and 2,030 physical therapists and physical therapy assistants. Neither the survey questionnaire nor the accompanying cover letter revealed the focus of our investigation. A history of physician-diagnosed asthma was reported by 16% of respiratory therapists and 8% of control subjects. When analysis was restricted to those who developed asthma after entry into their profession, respiratory therapists still had a significant excess, 7.4 versus 2.8%. The odds ratio for respiratory therapy was 2.5 (95% CI, 1.6 to 3.3) after adjustment for age, family history, atopic history, smoking, and gender. These results confirm the previous report of excess risk of asthma among respiratory therapists. This excess risk develops after entry into the profession and does not appear to be explained by bias or confounding. Efforts should be directed to identifying potential agents responsible for this form of occupational asthma.

Second Hand (S)-albuterol: RT exposure risk following racemic albuterol

Betty Carnathan, RRT, Barbara Martin, PA-C, Gene Colice MD. Washington Hosp Ctr., Washington, DC. *Respir Care* 2001; 46; 1084.

Racemic albuterol (RAC), a 50:50 mix of (R)-albuterol[R] and (S)-albuterol [S], is commonly used by RTs. R confers all of the bronchodilatory effects, while S demonstrates proinflammatory properties in in vitro and in vivo models. S is metabolized 10-fold more slowly, resulting in higher plasma levels that remain in circulation much longer after RAC administration. RTs have a higher rate of developing asthma after entering their profession (7.4 vs 2.4%, respectively; Christiani, 1993). Whether exposure to nebulized medications such as RAC contribute to this, or some other occupational hazard is responsible, is unknown. This study was designed to determine if S and R are detectable in the plasma of RTs. Eligible subjects (at least 18 years old; no asthma or other lung disease; at least 4 hrs of RAC exposure on each of 4 study days) began the study after a 2-day work holiday. Blood was drawn for S and R levels at baseline, 2, 4, and 8 hrs after exposure on Days 1 and 4. Subjects (n=12; mean age 38 yrs) nebulized delivered were exposed to approximately 31 mg of RAC by nebulization or MDI (range 22-43 mg) for 4.3 hours (range 3.2-5.5 hours) each day. At baseline on Day 1, On Day 1, mean levels of R and S were below the limit of quantification (BLQ, <2 pg/mL) at baseline, but were detectable after 2 hrs and increased over the 8-hr period. S levels were 1.6-2.5-fold higher than R (Table). On Day 4, approximately 2416 hrs after the last exposure, baseline levels of S, but not R, were detectable (3.7 pg/mL). Peak flow improved or remained unchanged in most subjects, but decreased in 3/12 subjects by an average of 30 mL. R- and S-albuterol are detectable in RTs following administration of RAC. S achieves higher plasma levels that remain in the systemic circulation for a longer period of time.

Identification of airborne dissemination of epidemic multiresistant strains of *Pseudomonas aeruginosa* at a CF centre during a cross infection outbreak

AM Jones, JRW Govan, CJ Doherty, ME Dodd, BJ Isalska, TN Stanbridge and AK Webb Adult Cystic Fibrosis Centre, Wythenshawe Hospital, Manchester M23 9LT, UK. *Thorax* 2003;58:525-527.

Background: Chronic *Pseudomonas aeruginosa* infection is a major cause of morbidity and mortality for individuals with cystic fibrosis (CF). *P aeruginosa* cross infection outbreaks have recently been reported at CF holiday camps and specialist centres. The mechanism of cross infection is unknown. A study was performed to look for the presence of epidemic strains of *P aeruginosa* in the environment of a CF centre during a cross infection outbreak and to examine their potential modes of spread between patients. Methods: Microbiological sampling of the environment of the CF facility was performed, including room

air sampling. Individual *P aeruginosa* strains were identified by bacterial fingerprinting. The typing patterns were compared with those of epidemic strains responsible for cross infection among the patients. Results: Epidemic *P aeruginosa* strains were isolated from room air when patients performed spirometric tests, nebulisation, and airway clearance, but were not present in other areas of the inanimate environment of the CF centre. Conclusions: Aerosol dissemination may be the most important factor in patient-to-patient spread of epidemic strains of *P aeruginosa* during recent cross infection outbreaks at adult CF centres.

A Major Outbreak of Severe Acute Respiratory Syndrome in Hong Kong

Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, Ahuja A, Yung MY, Leung CB, To KF, Lui SF, Szeto CC, Chung S, Sung JJ. Department of Medicine, Chinese University of Hong Kong, Hong Kong, China.

Background: There has been an outbreak of the severe acute respiratory syndrome (SARS) worldwide. We report the clinical, laboratory, and radiologic features of 138 cases of suspected SARS during a hospital outbreak in Hong Kong. Methods: From March 11 to 25, 2003, all patients with suspected SARS after exposure to an index patient or ward were admitted to the isolation wards of the Prince of Wales Hospital. Their demographic, clinical, laboratory, and radiologic characteristics were analyzed. Clinical end points included the need for intensive care and death. Univariate and multivariate analyses were performed. Results: There were 66 male patients and 72 female patients in this cohort, 69 of whom were health care workers. The most common symptoms included fever (in 100 percent of the patients); chills, rigors, or both (73.2 percent); and myalgia (60.9 percent). Cough and headache were also reported in more than 50 percent of the patients. Other common findings were lymphopenia (in 69.6 percent), thrombocytopenia (44.8 percent), and elevated lactate dehydrogenase and creatine kinase levels (71.0 percent and 32.1 percent, respectively). Peripheral air-space consolidation was commonly observed on thoracic computed tomographic scanning. A total of 32 patients (23.2 percent) were admitted to the intensive care unit; 5 patients died, all of whom had coexisting conditions. In a multivariate analysis, the independent predictors of an adverse outcome were advanced age (odds ratio per decade of life, 1.80; 95 percent confidence interval, 1.16 to 2.81; $P=0.009$), a high peak lactate dehydrogenase level (odds ratio per 100 U per liter, 2.09; 95 percent confidence interval, 1.28 to 3.42; $P=0.003$), and an absolute neutrophil count that exceeded the upper limit of the normal range on presentation (odds ratio, 1.60; 95 percent confidence interval, 1.03 to 2.50; $P=0.04$). Conclusions: SARS is a serious respiratory illness that led to significant morbidity and mortality in our cohort.

Quote from the publication: "We suspected that the infection was transmitted by droplets and possibly by fomites, and we therefore instituted both airborne precautions (e.g., use of the N-95 respirator) and contact precautions (e.g., use of gowns and gloves), as recommended by the CDC. However, the use of a jet nebulizer to administer aerosolized albuterol in the index patient had probably aggravated the spread of the disease by droplet infections."

Chronic exposure to a beta 2-adrenoceptor agonist increases the airway response to methacholine.

Witt-Enderby PA, Yamamura HI, Halonen M, Palmer JD, Bloom JW. Department of Pharmacology, College of Medicine, University of Arizona Health Sciences Center, Tucson 85724. *Eur J Pharmacol* 1993 Sep 7;241(1):121-3.

Scheduled chronic administration of beta 2-adrenoceptor agonist bronchodilators in patients with asthma recently has been reported to be associated with a worsening of symptoms and an increase in bronchial responsiveness. We wanted to determine whether a 28-day in vivo exposure to albuterol (beta 2-adrenoceptor agonist) altered the response of rabbit airways to the cholinergic agonist methacholine. We found, using in vitro tissue bath techniques, that in mainstem bronchi from rabbits given a 28-day exposure to albuterol, maximum contraction to methacholine was increased in the albuterol-treated group (control group = 1.10 +/- 0.11 g vs. treated group = 1.50 +/- 0.13 g, $P < 0.05$). The potency (EC_{75}) was also increased in the albuterol-treated group. The potency for the control group was 5.6 microM (95% confidence limit: 2.3-13 microM) and was 1.7 microM (95% confidence limit: 1.1-2.8 microM, $P < 0.05$) for the albuterol-treated group. In a subgroup of animals, maximum contraction to KCl, a receptor-independent contractile stimulus, was not significantly different between the groups (control group = 0.79 +/- 0.23 g vs. treated group = 0.82 +/- 0.20 g). The potency (EC_{50}) for KCl-induced contractions was also not significantly different between the groups: control = 12 mM (95% confidence limit: 3.3-44 mM) vs.

treated 19 mM (95% confidence limit: 18-20 mM). These data demonstrate that chronic in vivo exposure to a beta 2-adrenoceptor agonist can alter the in vitro tissue bath response of airway smooth muscle to methacholine