

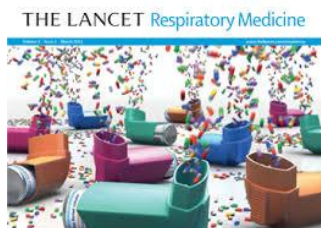
## Anatomy of an Exacerbation

By John R. Goodman BS RRT

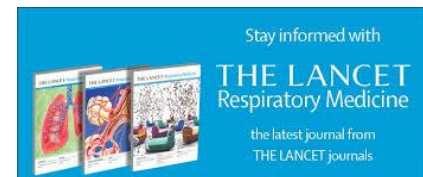
In April of 2012, the British journal Lancet published an enormous overview and update on COPD. Among other things it estimated that globally about 10% of people older than 40 had some form of mild to moderate airway obstruction. Up to 60-85% of those patients were yet to be diagnosed, and again globally, COPD is the 4<sup>th</sup> leading cause of death, expected to pass cardiovascular disease as the 3<sup>rd</sup> leading cause of death in the next 20 years. The inherited form of emphysema, Alpha-1 antitrypsin deficiency presents in 1-2% of people with COPD, again mostly unrecognized. It is true that COPD is a chronic and progressive disease in many patients, but progression between individuals is highly variable. Recent research suggests that the majority of patients with COPD will experience declines in lung function no more rapid than the average non-smoker.



First blood transfusion shown in 1829

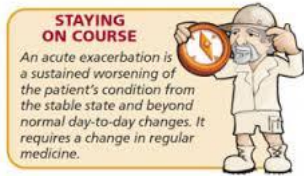


Lancet first published in 1823



The Lancet name came from the from the idea of using a “lancet” to explore what is underneath

Given this information, it can be seen that COPD is a very complex disease with great variability from patient to patient. One “event” that seems to be common to all COPD patients however, is the occasional exacerbation or “flare up.” Most exacerbations occur at home resulting in an increased reliance on inhaled bronchodilators, increased cough with or without sputum, increased shortness of breath, and decreased function and overall quality of life. The mainstay of treatment for many years has been the prescription of antibiotics, steroids, and hospitalization if necessary. People with moderate COPD average about one exacerbation per year, more severe patient’s perhaps two exacerbations per year. These averages can be misleading as many patients never or almost never have exacerbations, while others can have them almost monthly. COPD exacerbations result in just under a million hospitalizations in the United States alone, with nearly 50% of those patients spending more than 9 days in the hospital.



**STAYING ON COURSE**  
 An acute exacerbation is a sustained worsening of the patient's condition from the stable state and beyond normal day-to-day changes. It requires a change in regular medicine.

TABLE 6  
 Indications for the Hospitalization of Patients With Exacerbation of Chronic Obstructive Pulmonary Disease<sup>a</sup>

Poor response to outpatient treatment Inability to walk, eat, or sleep because of dyspnea Inadequate home care Serious comorbidity (congestive heart failure, decompensated diabetes mellitus, cardiac ischemia, etc) Altered mental state: confusion or lethargy Severe hypoxemia or hypercapnia Respiratory muscle fatigue (paradoxical abdominal motion) Need for invasive or noninvasive assisted ventilation
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Table 1 Causative Agents in COPD Exacerbations
<b>Bacteria (40% – 50%)</b> <i>Haemophilus influenzae</i> <i>Streptococcus pneumoniae</i> <i>Moraxella catarrhalis</i>
<b>Viruses (30%)</b> Influenza Parainfluenza Rhinovirus
<b>Other (10% – 25%)</b> Air pollution
<b>Atypical bacteria (5% – 10%)</b> <i>Chlamydia pneumoniae</i>
Source: References 8, 15

Definition of Exacerbation      Indications for hospitalization      Common causes

By far infections cause the vast majority (80%) of COPD exacerbations. These can be of bacterial or viral origin. Other conditions such as heart failure, systemic infection, pulmonary emboli (blood clot), or pneumonia may either cause or worsen the exacerbation. If you have had an exacerbation all the evidenced based medicine in the world won't make you feel or get better any sooner. In fact, there is quite a bit of controversy surrounding the treatment of COPD exacerbation. For many years a "cocktail" of long acting bronchodilator and inhaled corticosteroid, perhaps a drug like tiotropium, and of course oxygen have been used to slow down or reverse the symptoms of an exacerbation. After many years, and many well designed studies the evidence is still inconclusive. Let's also not forget the possible side effect profiles of each of these drugs. Sometimes the cure is worse than the disease!



COPD exacerbation has been studied for many years



Cough is one of the hallmark signs of an exacerbation



The medical staff will evaluate all the medical data accumulated



And the decision to admit to the hospital or not will be made

So is there anything we can take to the bank regarding pharmacologic treatment with COPD exacerbation? If we follow the science, it leads us to the use of Azithromycin (Zithromax) as an antibiotic that seems to be quite effective in preventing COPD exacerbations. Another large study was published by the New England Journal of Medicine (NEJM) in July 2012.



Actual article in NEJM



Zithromax comes in many dosages and preparations



Hearing loss may be severe

1142 patients with severe COPD were randomized to either 250mg of Azithromycin every day or a placebo and followed for a full year. At the end of the study the group that took the Azithromycin had far fewer exacerbations than the placebo group. In fact, there was a big difference (92 days) until the first exacerbation in the Azithromycin group compared to the placebo group. So the evidence proved that Azithromycin reduced the number of exacerbations and significantly extended the number of days until the first exacerbation showed up. The evidence was so strong the authors concluded that it was only necessary to give the Azithromycin 3 times a week instead of daily.

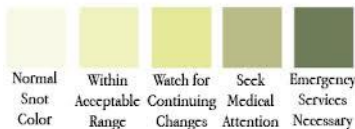
Now all this needs to be balanced against the well known side effects of Azithromycin which primarily involved hearing loss. Although the majority of patients reporting hearing loss had their hearing restored upon discontinuation of the Azithromycin, it is still cause for alarm. Also, taking an antibiotic routinely can certainly result in antibiotic resistance. The clinical importance of this finding has not yet been adequately studied. Some of the best clinical investigators in the world believe more questions have been generated than answered. It is expected the debate will continue for some time.

One of the most debated areas concerns changes in sputum color. Increased cough with sputum production is a common symptom in patients having an exacerbation. For many, many years both patients and their physicians have associated yellow or green sputum with a bacterial infection. Theoretically, this should respond better to antibiotic treatment than a viral infection. But let's not jump so quickly to the conclusion. Another well done study published in the European Respiratory



ERJ

Snot Color Analysis Chart



Snot color chart



Yellow mucus plug



Green mucus plug

Journal (ERJ) studied over 3,000 patients in 14 different medical centers. In politics it is usually a case of “following the money,” in medicine it is usually the case of “following the evidence.” The research showed that patients reporting colored sputum were far more likely to have an antibiotic prescribed, BUT there was no evidence that giving the antibiotics resulted in a greater rate of improving symptoms, or even their severity in this very large group of patients. It became clear that both clinicians and patients were likely to be over interpreting the importance of changes in sputum color, and the decision on whether or not to prescribe an antibiotic. So once again, when the science is done correctly we are left with the usual conundrum of years and years of “the way it is” against the weight of the new information. Sometimes this is a very large ship to try to turn around in a very large ocean.

It is pretty well established that steroids can definitely help resolve a COPD exacerbation, but steroids have their own very long list of side effects...many unpleasant or certainly unwanted. The question then becomes, “How long should steroids be given for a COPD exacerbation?” Once again a well designed study was published in the Journal of the American Medical Association (JAMA) in May 2013. In this study 314 patients with severe COPD all came through the emergency room and subsequently 92% were hospitalized for the exacerbation. One group got 5 days of 40 mg of prednisone followed by 9 days of placebo. The other group got 14 days of 40mg of Prednisone. The primary end-point was how did each group do regarding exacerbations within the next 6 months. The results were surprising to the investigators. There was virtually no difference in percentage of patients who had an exacerbation within the 6 month window. The exacerbation data showed 37% of the patients who took prednisone for 14 days vs. 36% of the patient who took prednisone for just 5 days. In point of fact, there was virtually no difference between the two groups. It was pretty clear that for most patients with COPD exacerbations, taking longer courses of steroids probably doesn’t help all that much. Much like the automatic use of antibiotics for sputum color changes,

this seems to fly in the face of common sense, but the *evidence* is now quite clear.



Steroids by mouth.....or inhaled



One size does not fit all....but does fit many....and so it goes.



plus antibiotic



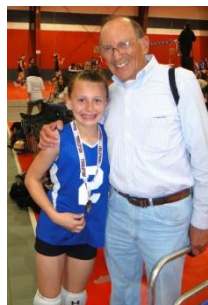
and mucolytic

Another thing that should be clear to the reader at this point is that there really is no such thing as a “universal exacerbation.” Much like the Supreme Court justice who said he couldn’t necessarily define pornography, but he knew it when he saw it, we may have difficulty in accurately describing a COPD exacerbation or flare up, but patients certainly do know one when they have one. That is why I hope the following actual description of a COPD patient who recently had an exacerbation requiring hospitalization may be more helpful and illustrative than any systematic review of the literature that I could do for you.

The patient has given me full permission to tell his story as I asked him to describe how this exacerbation happened to him. Some of you who monitor the EFFORTS website know him as Richard. There is much more to this story than a first name. Richard Harris (aka Dick) is a retired physician who also happens to be a patient with long diagnosed COPD. Dick opted for a transtracheal catheter a couple of years ago and leads a very active lifestyle. As you read Dick’s story, see if there are any common threads that you may have noticed over the years. Perhaps even when you had an exacerbation of your own underlying lung disease. Here in Dick’s own words is *the anatomy of an exacerbation*.



Dick Harris MD



With Granddaughter Megan



Getting ready to hit a few



“Excuse me Dr. Harris, just one more question.”

I have had COPD diagnosed for over 11 years, although I had symptoms for several years prior to that in my estimation. Over the course of time, I have had an exacerbation approximately every 18 months, always treated as an outpatient with antibiotics and prednisone for one to two weeks and never requiring hospitalization. I have severe COPD with bilateral bullous emphysema involving both upper lobes and an FEV<sub>1</sub> of 30%. Three years ago I started on 24/7 oxygen and had only one exacerbation during that time. I remain very active with pulmonary rehabilitation for 90 minutes twice a week, golf twice a week, serving on several boards, working in my shop, going to various sports activities and doing very well maintaining an SpO<sub>2</sub> of 95-97% on my SmartDose portable LOX conserver.

I had a complete annual physical examination on June 20<sup>th</sup> of this year by an internist that I had been going to for years. A complete exam including an ECG was normal except for mild renal insufficiency that I have had laboratory evidence of for years, but for causes not quite known. I was looking forward to my 83<sup>rd</sup> birthday on July 11<sup>th</sup>, however on July 6<sup>th</sup> I experienced non-productive coughing, right shoulder discomfort, as well as some right sided chest pain of a pleuritic type which was aggravated by my breathing and accompanied by some shortness of breath. These symptoms required me to increase my oxygen liter flow from 2 to 3 L/min. I was especially short of breath upon awakening on the morning of July 7<sup>th</sup>. This was in spite of the fact that I had now bumped my oxygen up from 2 to 5 L/min. I did not have any fever, chills, or loss of appetite, but I just felt generally ill. Being a physician is not the best situation as I tried to self-diagnose and imagined a small pneumothorax (collapse of part of the lung) that would probably take care of itself. I also thought that perhaps I had pulmonary emboli (blood clot in the lung) although there was no precipitating cause for this and so...I decided to wait another day. Although I still had no fever, I was having considerable non-productive coughing.

By the morning of July the 8<sup>th</sup>, I was extremely short of breath and had difficulty with *any* activity. Getting dressed caused major shortness of breath and I saw my pulmonologist that very day. After examination, I was advised to enter the hospital ASAP. I was actually relieved to hear this as I was feeling very weak and with increasing shortness of breath I knew that I could not be treated at home.

Following admission I had a chest x-ray, a ventilation /perfusion scan to rule out the blood clot, and was found to have bilateral pneumonia with an elevated white blood cell count indicating what turned out to be a “community acquired infection...probably viral.” Treatment consisted of IV fluids, IV steroids, IV antibiotics, and a myriad of other meds, most of which I was too sick to care about.

Taking a shower was an ordeal, as was just walking in the room. Respiratory therapy treatments helped immeasurably. I had to change my own transtracheal catheter as there was no one familiar with it and none actually willing to learn. To make a long story short, after 6 days in bed with minimal activity, I was breathing well, had multiple prescription changes from those taken prior to hospitalization, and was allowed to go home in quite a weakened condition.

I felt like I was cutting the umbilical cord, as I was now on my own and no longer had the nurses and RT's to depend upon. I also had been cut way back on my LOX deliveries by Apria from every two weeks to once a month. Since I was on a LOX setting of 4 L/min continuous, I knew that a once a month refill would not suffice. Nor would the concentrator that I had found very irritating. Consequently, I changed to a local company that provides me with as much LOX as necessary. Once they were all aboard, I fired Apria, who I feel could have cared less.

I was told by my pulmonologist that it would require 2-3 months to return to my previous level of activity, but I decided to try to hasten recovery as much as possible. On discharge from the hospital I asked my pulmonogist when I should resume respiratory therapy and he said "tomorrow." A month has now passed since my discharge and I am almost back to my previous level of exercise and was able to play golf recently without any problems. I am now back to 2L/min on my LOX portable, and with both diaphragmatic and pursed lipped breathing am able to maintain my oxygen saturation at my previously normal levels.

I have learned several lessons from my exacerbation odyssey:

1. COPD exacerbations can develop quickly at any time, and often when least expected.
2. Don't try to self-diagnose and don't rely on on-line sites (Web MD's everywhere take note) for emergent situations. Contact your PCP or Pulmonologist ASAP.
3. The earlier treatment is started, the more benign the course of the illness.
4. Pulmonary Rehab exercises are an absolute must for anyone with COPD.
5. Push yourself in the rehabilitation process following an exacerbation even though you don't feel like it.
6. If you are a TTO patient, be sure that someone in your family is able to change your catheter in the proper manner.

This may be the first recorded transcription of an actual patient very observant of his symptoms that had what might be described as a textbook exacerbation of his underlying COPD. Note how he was treated with hospitalization, IV fluids, IV

steroids, and IV antibiotics.....in spite of everything I reported in the introduction of this piece leading up to Dr. Harris's case study. Old habits DO die hard. Dr. Harris DID get better using the tried and true approach to exacerbation. We will never know if he had been taking Azithromycin 3 times a week would have prevented his hospitalization. But history has taught us that practice patterns in medicine do change over time. In just one generation COPD has gone from a universally progressive and fatal diagnosis to a disease that is eminently treatable with a full spectrum of therapies up to and including lung transplantation. It's hard to hurry up and wait when it's YOU. Science and medicine don't always make the breakthrough discoveries as quickly as we'd like, but they always do...don't they?