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INFECTION PREVENTION: SSI AND OXYGEN

Hi, my name is Patch Dellinger.I'm a surgeon from the University of Washington, and I'm going to be talking about oxygen and what it has to do with surgical site infection.

We all learned early in our health care careers that if you have a critically ill patient, you need to pay attention to airway breathing and circulation to preserve the patient's health.The good news, when it comes to preventing surgical site infections, is that airway breathing and circulation are good starting points there as well.And it seems that it's the way in which they affect oxygen in the wound that is pretty important.Then if you add prophylactic antibiotics, you can have "D" for drugs; and we've got A, B, C, D.And after that, as we look at some of the other issues, we lose the alphabet.

So let's talk about oxygen and surgical site infections.An interesting study was done quite a number of years ago by Tom Hunt, a general surgeon at UCSF.He exposed experimental animals to a wound infection model, and he exposed them either to room air or to 45% oxygen or to 12% oxygen.And what you see is that animals that were high poxemic with low levels of oxygen had much more severe infections, whereas animals that had extra oxygen had less severe infections.

And Knighton, one of Dr. Hunt's trainees working with him, showed that if you look at white blood cell function, we can look at the percent of killing of staph aureus by white blood cells in a test tube; and we can look at the amount of oxygen provided to the white blood cells.And we see that the more oxygen, the greater the percentage of killing by normal polymorphonuclear leucocytes.But if you look at white cells from chronic granulomatous disease of childhood, this is an inherited condition where the patients have recurrent infections because their white cells do not have the metabolic machinery to use oxygen to kill bacteria.And what you see is when you deprive normal white cells of oxygen, they behave the same as white cells from patients with chronic granulomatous disease.

Now, Jimmy Lee, an interesting surgeon from Minneapolis who spent an entire career thinking about surgical site infections, has made the observations that neutrophils, or white cells, have no way of knowing what type of operation we have performed.And so they don't care what type of operation it is, but they do care how well they are able to use oxygen.

In another study by Knighton and by Hunt, they used a different type of model; and they looked at oxygen and bacterial growth in a wound chamber in rabbits.And again, they exposed the rabbits to room air, to 12% oxygen or 45% oxygen; and the animals were able to suppress the bacterial numbers substantially better if they had extra oxygen and substantially worse if they had low levels of oxygen.

Hunt and others have also shown that soft tissue oxygen depends on how well the blood flow to tissue is.And if you look at arterial oxygen tension and compare that to the tension of oxygen just in the tissues, you get this line for experimental animals with normal blood flow; and you get a much lower line if you cause vasoconstriction through the use of a presser.So vasoconstriction restricts the amount of oxygen that gets into tissue, even if the arterial oxygen tension is at a good level.

Harriet Hopf and colleagues, again working with Hunt at UCSF, looked at experimental subjects who were anemic and had volume replacement and temperature control.And they found that even if you created severe anemia, you did not change tissue oxygen tension as long as there was good blood flow.Hopf went on and looked at post-operative patients in the recovery room, and they measured tissue oxygen tensions at a point next to the wound from low to high.At the same time, they looked at the wound infection rate; and they said that the infection rate was zero, or expected infection rate, based on the National Nosocomial Infection Surveillance Risk Index.And what they observed was that for low tissue oxygen tensions, infection rates were almost 25% higher than predicted by the Standard Infection Risk Score; whereas in patients with high tissue oxygen tension levels, infection rates were about 12% lower than expected.And in fact, if you follow these lines, you get something about as close to a straight line as you ever see in human clinical research.

Ives and colleagues measured infrared oxygen saturation in the tissue adjacent to the incision at 12 hours after vascular surgery.And what they showed is that patients who developed a surgical site infection had an average tissue saturation that was considerably lower than patients who did not develop a surgical site infection.

Govinda and colleagues looked at tissue oxygen saturation in the arm following an operation.And again, they found that the infection rates were higher than expected when the tissue saturation was low, and lower than expected when the tissue saturation levels were high.

What we can conclude from this and other similar studies is that oxygen tension in the wound is important; however, how to translate that into clinical practice that lowers surgical site infection risk has been more difficult to determine.

Oxygen in the wound is not the same as arterial oxygen tension.Oxygen in the wound is affected by the inspired oxygen concentration, by the cardiac output, by the fact of whether the patient is getting regal or general anesthesia, by pain management, by fluid management, by temperature, and perhaps by other factors that are not as well understood.

Let's look first at the influence of temperature and surgical site infection.Rabkin and colleagues, again at UCSF, took patients and raised the subcutaneous temperature by 4 degrees, resulting in an increase in tissue subcutaneous oxygen tension by 40 millimeters of mercury.They also found that there was a linear correlation between temperature and oxygen tension and that there was a threefold increase in local profusion with the elevated temperature.They went on and they did this study of patients having colectomy in a multicenter trial run in Austria.All patients had a mechanical bowel prep; all patients had intravenous prophylactic antibiotics; all patients got a standard anesthetic.But they were randomized either to have aggressive warming in the operating room to keep the temperature at 36.5 or above; or they were allowed simply to have the temperature drift in the OR, which was the most common way of managing patients when I began my training in the '70s.They provided supplemental oxygen in the recovery room, and they did aggressive fluid resuscitation.What they found was that patients who were warmed and kept normal thermic had one-third the surgical site infection risk of patients whose temperatures were allowed to decrease.

In another study, Flores-Maldonado and colleagues looked at patients having open cholecystectomies and recorded whether they had a temperature below 36 or 36 and above on arrival in the recovery room

and found again that the infection rate was much higher in patients who arrived in recovery room cold compared to patients whose temperature was above 36.

Melling and colleagues in England examined local warming after short clean operations.They examined patients have elective inguinal hernia repair, varicose vein operation, or breast operations with incision of 3 centimeters or greater.What they did was take the patients and give to some of them whole body forced air warming for 30 minutes, or they placed a radiant heat bandage over the area of incision for 30 minutes before operation.And then they had a control group.When they looked at surgical site infections in follow up, patients who had either local or systemic warming had significantly lower infection rates than control patients, as well as a lower use of post-operative antibiotics.

Wong and colleagues examined patients having open abdominal operations with bowel resection.All patients were warmed in the operating room, but the study group had perioperative warming for two hours beforehand and two hours after the operation.What they found was that there was significantly less blood loss in the patients with more aggressive warming, including warming before and after the OR; and there a significantly lower rate of complications.The surgical site infection rate was also lowered; but due to small numbers of patients in the study, this did not change the traditional statistical significance.

It's worth noting that blood loss differences are not surprising because normal human coagulation is much more effective when a patient has a normal temperature, and coagulation proteins do not work well at lower temperatures.In addition, many reports show a higher risk of surgical site infection in patients with higher amounts of blood loss.

Now, what happens to your temperature when you get an anesthetic in the operating room?This has been examined; and you see that what happens is as the anesthetic is induced, there is an early, fairly rapid drop in temperature which then slows down and eventually begins to steady out at several degrees below normal core temperature.What's the reason for this?

Well, as we sit here listening to this talk, our core temperature is probably 37 degrees.But the temperature of our skin and subcutaneous tissue is anywhere from 2 to 6 degrees cooler.This is how our body maintains a normal core temperature in cooler environments.And it is maintained by vasoconstriction that preferentially directs blood to the core.However, when you have an anesthetic, that vasoconstriction is broken down.The blood vessels dilate, and there is an immediate drop in the core temperature which is caused simply by shift from the core to the subcutaneous space even before any temperature is lost to the operating room.This is the reason why prewarming the patient and actively warming the patient in the operating room is much more important than trying to increase the operating room temperature.In fact, if you raise the temperature of the operating room from 20 degrees to 27 degrees, you are still 10 degrees cooler than you want the patient's temperature to be; and yet everyone in the room is miserable, and the surgeon is at risk for perspiring and dripping in the wound and if anything, increasing the infection rate.

At my own institution, the University of Washington Medical Center, we have had an aggressive program for the last 10 to 12 years of putting every patient who checks into the preoperative area under a warming blanket for at least 30 minutes, if not longer, before they go into the operating room.With this protocol in place, 96+% of our patients in 2006 arrived in the recovery room with a temperature above 36 degrees.I think we're doing even a little better now, but I don't have more up-to-date information.

Well, now if more oxygen in the wound is good, how about just giving higher percentages of inspired oxygen during the operation?A study was actually done on this.Griffin and colleagues in the year 2000, again in a multicenter study in Austria, took patients have standardized bowel prep, standardized intravenous antibiotics, standardized anesthetic, were randomized to get either 30% or 80% inspired oxygen concentration in the operating room and for the first two hours in recovery room.All patients had a temperature maintained at or above 36 degrees, and they all had aggressive fluid resuscitation.

Now, you can see that 30% oxygen is sufficient to keep arterial oxygen saturation high at acceptable levels.But the oxygen tension was much higher in the patients who got 80% oxygen, and the oxygen tension in subcutaneous tissue and in muscle was significantly higher in patients with 80% oxygen compared to 30% oxygen.And the infection rate was dramatically lower in patients getting the higher inspired oxygen concentrations.

An early objection to giving high inspired oxygen concentration in the OR was that it might induce atelectasis.But in fact, they specifically looked for this; and through a combination of chest x-ray, CT scans, and physical examination, they showed that there was no difference in atelectasis between the groups of patients getting 30% or 80% oxygen.

This was an exciting study and one that I took notice of immediately and began requesting 80% FiO_2 for my patients in the OR.However, it was followed a couple of years later by this study from New York Hospital in which patients were randomized to 35% or 80% FiO_2.Some problems with this study, however, were that the bowel prep was not specified, parenteral antibiotics were not described, the anesthetic was not standardized, the temperature control was not described, and fluid resuscitation in the OR was not standardized.So there are a lot of areas that we know influence infection risk and influence oxygen tension in the wound that were not controlled in this study.What they found was that they actually had more infections in the group with 80% oxygen.They did not look at atelectasis, nausea, or any oxygen tension measurements.There were also significantly more patients with high BMI, twice as many obese patients, longer operations, and more blood loss in the patients randomized to 80% FiO_2.So there are serious concerns about what to conclude from this study.

The next study was published a year later; and again, it was focused on colectomy patients.This one was done as a multicenter study in Spain.Again, they standardized the bowel prep, standardized antibiotics, standardized the anesthetic, standardized temperature maintenance and fluid resuscitation and pain management; and randomized patients to 30% or 80% oxygen.And they showed, again, a similar about almost 50% -- closer to 40% -- reduction in infection rate in the group getting high FiO_2.

So if you put all these studies together, you see that there were more patients in the two studies that showed a benefit of high FiO_2,and a lower number in the study that showed a deficit.Also, when you look at the differences in infection rates, you see substantial benefits to the first and the third study.Nevertheless, we have to understand that this does give us more or less conflicting information.

Now, Myles in Australia did a study where their primary question was, "Does nitrous oxide increase or decrease infection risk?"And they randomized general surgical cases to get either 80% oxygen and 20% nitrogen, or 30% oxygen and 70% nitrous oxide.And the results of this study showed that there was a reduction in surgical site infections in the group getting 80% oxygen compared to the group getting 20%

oxygen and nitrous oxide, from 10% down to a little bit under 8%.And in terms of pulmonary complications, there was no increase in pulmonary complications in the group getting 80% oxygen.In fact, they had fewer complications than the group getting 20% oxygen and nitrous oxide.

Maragakis, in an observational study rather than in a prospective randomized study, looked at fractions of inspired oxygen in patients having spinal surgery.And they showed that patients who got surgical site infections on average received significantly lower levels of inspired oxygen than patients who did not.When they did a multivariate analysis of risk factors for surgical site infection, they found -- as you would expect -- an increased odds ratio of infection for patients with long operations, for patients with high anesthesia risk scores, for patients getting operations in the lumbosacral level compared to the cervical level, higher rates of infection for posterior approach, for instrumentation, for obese patients, and for patients being shaved with a razor, and a dramatically increased risk for patients getting less than 50% inspired oxygen tension.

Kaden and colleagues did a meta-analysis of prospective studies available at the time, and they looked at prior Greif, Belda, and Myles – the studies I've discussed – as well as another one by Mazzler – and observed that four of the five studies showed a benefit, whereas the one that I've described by Pryor showed a deficit of increased inspired oxygen.And several different methods of combining all five studies all showed significant advantage, one of them not statistically significant, looking at different ways of analyzing and combining the results from all of the studies.

This was followed by the PROXI trial, a very large study of over 1,400 patients in Denmark in which patients were randomized to get 80% oxygen or 30% oxygen and then followed for surgical site infection rate.And disappointingly, they found no difference -- 19%, 20% infection rates in the two arms, and of course this is not significantly different.They also looked at atelectasis and at respiratory failure and found no differences there either.Again, in this study, they did not control the anesthetic administration, temperature control, and a number of other elements that we know do influence oxygen content in the wound.

And so my personal conclusion from this study was that oxygen has not been shown to cause a problem in any of the studies, particularly not in terms of respiratory status, which is where the hypothetical problems might develop.And in some studies, it shows a significant reduction in surgical site infections; and in others, it fails to show that.So my own personal preference is I ask for a high FiO_2 for my surgical patients, believing that it may be beneficial and that it is not harmful.

Basically, we need to think about maneuvers to increase wound oxygen tension.And this can happen by increasing pO_2, including inspired oxygen tension concentration.But we also need to combat vasoconstriction by correcting hypovolemia, preserving normal core temperature, controlling pain, and to the extent possible, avoiding vasoconstrictive drugs, and possibly by the use of regional anesthesia in comparison to general anesthesia, although this has not been studied in a very systematic manner.

So misconceptions about oxygenation are that anemia is the culprit.And as I showed you near the beginning of this talk, anemic patients can have high tissue oxygen tension.Hemoglobin saturation in the artery is not all that informative, although saturation in tissue may be an important measurement.

Adequate arterial pO_2 does not necessarily assure adequate subcutaneous oxygen tension unless there is good blood flow and warm tissue.Transcutaneous oxygen tension is also not informative because it tells you only what's going on in the skin and not in the subcutaneous tissue.Clearly, several of these studies show that giving supplemental oxygen is not enough; you also have to make sure that the supplemental oxygen gets to the subcutaneous tissue.

And it looks like the period of effect may well be longer than the initial two to three hours after the operation, although this has not been studied in a coherent manner.So with these thoughts in mind, I'll leave you with the message that extra oxygen in the wound is good.We don't know as much as we'd like to about how to achieve that; but some of the issues that I've listed on this previous slide of combating vasoconstriction, keeping the patient warm, and increasing inspired oxygen tension are probably very helpful.

Thank you for your attention here, and I hope that over the coming period of time you see decreasing infection rates in your patients.

That's the end.