UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

WEEK 2 ANSWER TO QUESTION 4
STEP 3.3 ASK MARK

So we've come to the final and fourth question and here it is, for this week, it says: as a medical doctor, I find this course fascinating. I'd love you to address the role of deep anesthesia and the mind, how the states of consciousness could be controlled by the means of chemicals and then reversed. Also, what is to be learnt from it when a state of almost brain stem death has been achieved.

So I thank you for that question. I think most learners will be alarmed possibly, certainly surprised to learn how much we don't know about general anesthesia. There's a very great deal that we don't yet understand as to how general anesthetics work. So this a work in progress. What I can say on some general principles. One is that there is not only one kind of general anesthesia. There is a range of general substances used. They work in different ways and that applies not only to the development of anesthesia over the century past, little more than a century past, but also even in the present day there's a variety of different substances that are used for general anesthesia and they work in different ways.

The second thing to say, and here is part of where the alarm comes in and it is perhaps even compounded by this, which is that when I say that they work in different ways, part of what I am referring to is that some of them have analgesic properties, in other words, they act on pain mechanisms, whereas others have hypnotic properties. Some act on consciousness-generating mechanisms and a third set acts on memory mechanisms and I don't mean that they work exclusively on the one or the other, but when we compare different anesthetic substances, general anesthetic substances in use today, we see that they vary one from the other in the extent to which they are operating on not operating on, for example, memory mechanisms versus consciousness mechanisms versus pain mechanisms.

The third thing I'd like to say is that although there is variability, one thing that characterises general anesthetics more than people might have assumed is that they don't act on one part of the brain, they act on nerve cells and so the effect is quite general. I know that it is partly contradicting what I said earlier, but it depends on what aspect of the cellular process the mechanism is operant as to which sorts of nerve cells are more or less susceptible or susceptible earlier at a lower doses than others to the physiological effects that the anesthetic substance is seeking. So are talking about, for example, one very common general anesthetic adapts on GABA, GABA receptors. GABA is an inhibitory neural transmitter. So it is just a matter of inhibiting, shutting down the brain and shutting down the brain at all GABA receptors. Why I say that it's

not totally the case that this is ubiquitous in all substances and that it affects all cells, because all cells thank heavens are different, is that it obviously cannot be true that all nervous activity is shut down - that would be death! There are core brain stem structures, which monitor the state of the body and regulates the state of the body in terms of these certain parametres, which are absolutely essential to the preservation of life and if those nuclei and their connections are switched off as it were, then your body would shut down - the brain regulates the body. So those brain stems structures always have to be functioning, even under deep anesthesia. Now the interesting thing is that it is also in the brain stem that those cells or those cell groups, which are most essential for consciousness and for pain perception in the upper brain stem, that is also where those cells are located. We have in the past focused much too much on cortex and we've learnt in recent years how much really it is the brain stem that's in charge. So it's a very delicate balance, what these anesthetic substances are doing, which is why one really wants to know what's going on. It is, as I say, a little alarming.

Now one recent tool that's been used, and I'll end with this because as you could see I can't answer the question, because we simply don't have the knowledge, but one recent tool that's been used to try and explore where in the brain the different anesthetic substances are operating, there is of course FMRI, Functional Magnetic Resonance Imaging, where you can see in the brain which areas are relatively metabolically active or deactivated under certain conditions. The problem with FMRI, and there's been quite a few studies recently regarding where in the brain is the general anesthetic operating, let's look at the FMRI - it will tell us. Well, not necessarily because when you get down to the brain stem, which is relatively speaking very much smaller than the forebrain. And you look for signals of relative degrees of metabolic activity - a tiny little nucleus in the upper brain stem is not going to register relative to a vast expansive activation of cortex - that doesn't mean that the vast expansive activation or deactivation of cortex is where the causal mechanism lies. That may be a knock-on effect of something happening in a very tiny brain stem nucleus, which doesn't register fairly in the competition for signal in an FMRI scanner.

So with that incomplete answer, remembering we don't know everything, let's end this session for this week and I hope you enjoyed the course this week and I look forward to talking to you again in seven days time. Bye-bye!