Marine Biology as Applied to Cardiac Research

Lecture by David Jensen
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Speaker: David Jensen

Transcribed by: Samantha Muñoz

Time	Transcription
0:00	David Jensen: Thank you very much. Pleasure to be here with you this afternoon to discuss certain aspects of marine biology related to cardiac or heart research. Normally when you think of the heart in its simplest terms, it is merely a pump. And I think in a sense, it's a good way to start out this discussion by reminding ourselves of this fact. Now the form of this pump varies widely depending on the animal we're discussing. In the kingdom of marine animals, there are a great number of diverse types of hearts which in the final analysis all serve the same purpose, namely to circulate the body fluids. Now I'd like to discuss very briefly a couple of types of hearts. There's an organism which you've probably seen many times down in the [San Diego] Bay on pilings and on wharves, they're called sea squirts, or tunicates. Now, they look something like a plant or a vegetable but actually, they're an animal. Although they do live attached by the stalk to the piling.
1:23	David Jensen: Now these animals possess an extremely unique type of heart. It is only one cell layer thick. It’s approximately, it looks, it’s shaped somewhat like a J. It's transparent and it beats with a very rhythmic action. However, it has a very unique property. It'll beat for a while, starting at one end, and then the contractions stop, and then the contraction start from the other end and it beats in the reverse direction. This is, to say the least, a rather unique type of heart. A second type of marine animal possessing a very unique heart is the common clam, oysters, and even the mussels. They may wonder what use these hearts have to researchers, but they have a great deal. I'll give you one specific example. They're extremely sensitive to various types of drugs and therefore make a useful method of determining the concentrations of these drugs in amounts, which are not detectable by regular chemical methods.
2:32	David Jensen: A third type of heart belongs to crabs, lobsters, and on the East Coast, the horseshoe crab, which you may have heard of, the limulus. Now, these hearts are very peculiar in that within their walls, the muscular walls, they have nerve cells and the beat is initiated by nerve cells within the muscular wall of the heart. However, we must ask ourself one question. These hearts, by the way, are called neurogenic. That is, their beat is initiated by nerve impulses. The made, the regular type of heart such as yours and mine is called myogenic. That is the impulse which causes the rhythmic contraction occurs spontaneously within the muscle itself. There are no nerves involved except to speed up and to slow down the heart. This is the type of heart we possess.
3:33	David Jensen: Well, some years ago I became interested in how the muscle tissue is capable of inducing a spontaneous contraction. In other words, able to beat spontaneously and rhythmically. And for some time I conducted my research on the hearts of guinea pigs, rats, and rabbits, the normal standard laboratory mammals. But they all had one thing which confused the interpretation of the results specifically, there were nerve elements present in the hearts. Now it was very difficult to interpret

the results because you did not know whether the treatment you were giving to the particular heart was acting directly on the muscle or the pacemaker, which fires off and causes the spontaneous beat, or whether it was acting on the nerves present in the heart and they, in turn, were affecting the muscle. Consequently, began looking for an animal which had no nerves either in its heart or running to its heart. As you may imagine this is a, perhaps not too easy a thing to accomplish. Embryonic hearts have no nerves in them, but they're too small to work with satisfactorily.

4:44 David Jensen: Now, made a study of the various animal groups, and I found that there was one creature that can be obtained in reasonable quantities and which possesses a heart fulfilling these requirements. It beats spontaneously and rhythmically, and yet it has no nerves in it or running to it and this was the heart of the hagfish. Now, the first slide will, is just a shot of my laboratory and it shows the type of equipment I use to record the heartbeat. So I'd like to discuss that very briefly. The heart is removed from the animal and placed in a small plastic container of seawater kept at constant temperature. And every time it contracts, you can record the contractions when it beats. When it's isolated you record these contractions and we will see records of these contractions shortly. The first slide - if I may have the light in the front dimmed, Peggy - this shows the type of recording equipment used. This is the tape coming out of the oscillograph as it's called, is called. And essentially what you come up with, these are amplifiers - I can't see – that's one of the amplifiers. Essentially what you come up with is a hi-fi [high fidelity] recording of the activity of the heart. And this can be recorded continuously. In other words for hours or if necessary even days during the course of the experiment.

6:12 David Jensen: Now, I think at this time - if we could dim the lights [unclear]. Can you all see this reasonably well? Or is it a little faint? No? That's fine. Whoops. Okay. Swell. Now, these are the amplifiers and this is the actual tape coming out of the oscillograph as it's called. The next slide. [crosstalk] Well, the next slide we'll introduce our friend the California hagfish. Now, I did not select these animals because of their beauty but because of their biological interest. I'd like to discuss these creatures very briefly. You probably all heard of lampreys and these are the first cousins. They're strictly marine; their eyes are covered with skin. This is an average-sized specimen. Could you focus that a little sharper, Peg?

7:36 David Jensen: Swell, thank you. Thank you. On the front end, they have four pairs of whiskers. Their eyes are covered with skin. These white spots are gill openings. They have this particular - kind of hard to show - twelve pairs of gills. These tiny white dots are openings of slime pores. In fact, that's one of this fish's most notorious habits. It is capable of converting, literally gallons of seawater into a sort of a mucus by means of slime secreted from these pores. You'll notice that they have no fins except the tail. And they have no scales. They resemble eels and then certain parts of the world are called slime eels, although they are nowhere nearly related to the true eel which is a bony fish. Now, actually, these animals have three hearts. They have one in their tail.

They have one in their liver, going to their liver, and then they have the main or systemic heart which is the one I'm using in my research.

8:42 David Jensen: Now, if I may have the next slide, we'll see the inside of this animal here. This is a dissection of the same fish. These are eggs. These are the slime glands, and this is the heart that I use in my work. It pumps the blood forward and through the gills. This large mass is the liver. This is the intestine. This is the blood vessel running along the backside of the body. But this will give you some idea of the size of the organ I use in my work. You can see there's a centimeter scale at the bottom of the chart. Now the next slide illustrates the microscopic anatomy of this heart. This is an electron photomicrograph at about 5,000 diameters. It's a cross-section of the muscle and these little things here are muscle's cells. I just put these slides in to show you what the microscopic anatomy is like. It's very spongy as you can see. Even at this magnification, the muscle cells are not packed tightly together as they are in higher animals. This is a nucleus of a cell cut in half. If the next slide shows the same similar tissue or is cut in long section. And these little elements or dark longitudinal stripes are the muscle fibers themselves, which actually undergo the contraction.

10:11 David Jensen: The next slide illustrates the effect of a drug on this heart. Now, these lines here are produced when the heart contracts in the chamber, it pulls on an instrument and makes a recording. Now the height of these lines is proportional to the amount of force the heart exerts when it pulls on this little thread. You will recall, I said earlier that the heart is removed from the animal for these experiments. Now, at this point, I added a drug which is called acetylcholine. It's a very powerful drug, but as you can see, it has absolutely no effect on the heartbeat of this animal. In other words, the rate of the beat and the force of the beat did not change at all after application of this drug. I would also point out that the concentration used was approximately 20,000 times greater than that necessary to completely stop the heart of say a rabbit or a clam. In other words, this heart is refractory to the effects of this drug. Now, this is quite interesting for the simple reason that this acetylcholine, or this chemical, is thought or was thought to be a hormone. And with that, acting as a hormone in a higher animals, it would actually produce a heartbeat. Well, now you see in these hagfish it exerts no effect whatsoever on the beat.

11:44 David Jensen: The next slide shows a very interesting finding that I made some time ago. In A we have a recording of the normal heartbeat from a hagfish just after it has been removed from the animal. B is approximately 26 hours later. You can see the rate has slowed markedly and there's a certain irregularity in the rhythm between the beats. At this mark where I say H H E, I added a crude saltwater extract prepared from the hearts of several other hagfish. Now you'll notice that both the rate and the regularity or the rhythm, the beat became very much more regular and faster. At C, this extract was washed out of the chamber and you'll note that the beat returned to what it was before it was added. Now, this experiment was done after I tested a whole series of drugs and chemicals, which are known to affect the heart rate of most animals and they had no effect on the hagfish heart. I became curious as to whether or not the tissue itself or the muscle itself contains some type of a chemical capable of inducing a rhythmic contraction. This proved to be the case. In other words, the hagfish heart contains within itself, a chemical capable of stimulating its own beat. This was kind of an interesting finding.

13:20 David Jensen: The next slide shows what happens when you add this hagfish heart extract to the heart of a clam. In other words, this clam heart was not beating when it was isolated. It had not been beating for some hours. Application of a small quantity of this material caused a regular beat to be resumed. As you can see it's quite rhythmical. It's slow because clam hearts usually beat quite slowly. And also, the temperature at which the experiments are conducted is quite low. But suffice it to say that this material prepared from the hagfish heart works on the hearts of other animals. Now the next slide illustrates something quite interesting. This is the effect of these hagfish heart extracts on frog heart. Now, without going into too much detail, the top record represents the electrocardiograph or the electrical record produced when the heart contracts. This little contract peak here is the auricle of the frog heart contracting and this large one is the ventricle. At this point, I added a crude extract prepared from the hagfish heart and as you can see, both the rate and the force of the contractions have increased. And this, these - C and D follow B. In other words, there is a progressive rate increase in the frog as well as in the hagfish and the clam.

14:48 David Jensen: Could I have the next slide, please? This shows another very interesting feature of this extract produced from these hearts. And that is the fact, in this record, this bottom one is a time signal in each case of one second. Now here you can see there's no electrocardiograph and there is no ventricular contraction. I presume you're familiar with the anatomy of the frog heart and that it has two auricles in one ventricle and the excitation occurs from auricles to ventricle. At any rate between A and B, B represents about five minutes after adding some of this crude hagfish heart extract. And here you can see the ventricle is beginning to contract. Although the auricle was contracting normally here, the ventricle was beginning to contract here, and this is sometime later, and this is an hour later. In other words, the material from the hagfish heart is capable of permitting the normal excitation of the frog heart to occur when it was disturbed experimentally as in A. In other words, it produced a normal rhythm from an abnormal rhythm.

16:03 David Jensen: The next slide shows a control experiment. In other words, an experiment done to compare the effect of this hagfish material with a known compound or chemical. In this case, this is adrenaline. Now you can see that the rate speeds up here, very markedly, and that it returns very rapidly in C to the control rate here. In other words, in this slide adrenaline was added to the chamber where the heart was beating spontaneously. Now, the interesting thing here is this experiment shows that this material in the hagfish heart is not adrenaline because of the fact that the rhythm returns spontaneously to normal in just a few minutes. Whereas if the hagfish heart extract is permitted to remain in contact with the heart, it will stay there for quite some time. I mean, you know, the rate will stay increased for quite some time. Could I have the next slide, please Peggy?

17:06 David Jensen: Where is this material manufactured in these hearts? Well, I've saved this slide to show you a picture of where I think it is manufactured. This is another electron photo micrograph of the hagfish heart and its magnified 16,000 diameters. This dark mass is connective tissue and this cell with the dark granules is what I considered to be a secretory cell. In other words, the hearts of these primitive fish are not only pumps as I said at the outset, but they're also perhaps endocrine glands, and that by secreting into the chamber of the heart, which is this area here, this material, they actually regulate the heartbeat by, in a chemical fashion. In other words, they contain within themselves the ability to manufacturing the chemical that regulates their own activity, which is a rather good trick.

18:10 David Jensen: Now, I stated at the outset that the hagfish heart has no connections to the nervous system. In fact, you cannot find any nervous tissue inside these hearts. But, what is also attempted to ask when the animal, which is normally quite sluggish, swims faster, he has to pump more blood to um, oxygenate it enough to keep up with this activity. You're all familiar with running? You breathe faster automatically, it's a reflex phenomenon. But, in this, the case of yourselves, when you run and breathe harder and faster, you have reflexes to control the rate of the heart and therefore the amount of blood that's putting out per minute. A hagfish has no such mechanism since, as I stated, he has no nerves in his heart. Now, how did they accomplish this? Well, I found out some time ago that if the quantity of blood returned to the heart is increased - that is if the heart is stretched - just stretch acts as a stimulus to accelerate the rate. Could I have the next slide, please, Peggy?

19:23 David Jensen: Here, we see the effect of injecting a small volume of blood into a hagfish ventricle. Here's the normal rate, control rate. Here, a small quantity of material was placed in. Oh, pardon me. It was between A and B. I believe four-hundredths of a cc [cubic centimeter] of blood was injected into the heart, and at this mark, it was withdrawn. Notice that it's slowing down gradually, but notice the tremendous rate increase here, how much faster it beats. This is also proven by the fact your actual electrocardiograph speeds up too. But, when the excess fluid is withdrawn, then the heart slows down to its normal rate. So we apparently have two mechanisms here in the hagfish. One is a chemical mechanism which speeds up its heart or regulates its beat. The other one is a physical mechanism. So that as the animal, I mentioned earlier too that the hackers has three hearts. They're all independent of each other. Each one pumps blood on its own and at its own rate governed by various factors. The fact is that if the animal increases its activity, he will squeeze more blood back to his heart, and therefore he will increase its rate as I've shown in this graph here. And it's quite an interesting thing that there are these two mechanisms, which governed the net rate of the hagfish heart at a given moment. And this is how the animal is able to get around the lack of nerves in controlling its heart rate.

21:00 David Jensen: Could I get the next slide, Peg? Now, this merely shows the percent rate increase with the volume of fluid injected into the heart. In this case, it was salt water. And you see within the limits there's a proportionality between the increase in rate. In other words, the more you inject the faster the heart rate becomes. However, this is within definite limits because if you inject too much fluid into the heart, as you can see the rate falls out and the beat becomes erratic and finally the heart stops. So very briefly, that is an outline of the biochemistry and physiology of the hagfish heart. At the present time, we are trying to isolate the chemical, which is responsible for producing this effect. And to this end, we're using a technique known as paper chromatography. And at the present time, we are pretty well satisfied that we have isolated the chemical in these hagfish hearts in a reasonably pure form. I'd like to be able to tell you what it is because I'd like to know myself, but at the present time, we don't know. Now, what this will do in higher animals, such as rats, at present, we cannot say. But, this merely points out that the marine animal, this lowly hagfish, has given us a great deal more insight in the mechanics of heart action. Thank you. That's it, Peg.

22:43 [applause]

22:48 Speaker: Anybody want to ask questions? Sure. Dr. Jensen is open for any question you might have regarding -