Human Physiology
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Lecture – 46
Secretory functions of alimentary tract- Part 2

Now we are going to take a closer view at the gastric gland. So we have first of all, this is the stomach and I know there is a hole there, there is the gastric pit. All these cells here, they are all mucous cells, they are all what? Mucous cells. The complication happens when you enter into the gastric pit. And now let us see what happens into the gastric pit. First of all, in the gastric pit, more or less at the neck, there is a huge population of cells which is, can you read for here, read me for there? Stem cells. Now please remember, just as in your skin, huge amount of mitosis is continuously happening in your skin so that we get rid of the old cells. Are you with me? Basic, okay. Similarly, along the entire length of the image, some of the tissues, if I ask you to tell me some of the tissues where the mitosis is continuously happening, your first answer will be bone marrow.

Hello, bone marrow. And the second answer perhaps would be skin, okay, hair follicles, okay. And third answer will be, will be what? Will be lining of the alimentary canal continuously. Fourth or fifth answer may be your nasal mucosa. I will take the pendulum to the other end and tell me the name of organ where you will find minimum mitosis? Brain, okay.

Is brain devoid of mitosis altogether? No, no, okay. There are cells in the hippocampus and the sub-ventricular gray, okay. I am not going to talk neurobiology. It is very tempting. So here, so the mucosa cells, okay.

And somewhere here are parietal cells and somewhere deep inside are the chief cells. Next, step back let us find out what cell is where. It is mucosa, mucous cell, below that there is stem cells.

And please remember, the stem cells keep on coming and they, and they keep, they are dividing and they keep on moving. Some of them go towards the, towards the upper end, some of them go towards the lower end and they keep on replacing the old cells. That is, the regeneration is continuously happening in the wall of the stomach. And then a little deep inside we have the parietal cells. Parietal cells are the acid secreting cells.

So please fill in the blank. Acid secreting cell is called as what? Parietal cell. Parietal cell is also called as oxyntic cells. What did I say? Parietal cell is also called as oxyntic

cell. And what is its main function? To produce huge amount of hydrochloric acid.

What acid? Hydrochloric acid. So tell me the name of parietal cell. Good. And, and if you go deep into the pit, almost where the pit ends, okay, these cells will call as what? Chief cells.

These are the pepsinogen-contained secreting cells. And pepsinogen is a large protein molecule that will be broken down. It will give rise to pepsin, which is an enzyme which will act in the acid medium. We will talk about it shortly. Okay. Now let us see, okay, okay.

Now what author does is here is, the structure of the gastric pits taken from the fundus is slightly different from the gastric pit taken from the antrum. Have I made my point clear? We are talking of two gastric pits. The hundreds of them, I am talking two samples. One is taken from fundus and other is taken from where? Antrum. And I am trying to, I am trying to draw the distinction between the two.

And they are relatively here. Okay. So see there is a mucus layer here, there is a mucus, these are mucus cells here. These are the surface cells, they are mucus secreting cells, these are here. They are there in both but they are little more in the antrum.

But they are there in both. You are okay so far? Then let us see what are these, these bluish cells here, these are what cells? Parietal cells, but no parietal cells here. Have you, have you appreciated the major difference between the two? Whereas the fundus part is loaded, loaded with thousands and thousands of parietal cells, you hardly find any - in the case of what? In the antrum part of the stomach, you do not get them. Are you okay so far? Okay.

Then the green ones are there in both. These green ones are what? Progenitor cells which means stem cells, which we have already seen the previous one. So you have them, you have them here, you have them here. Progenitor cells have to be there everywhere. Okay, good.

Then there is something. Now this character is coming for the first time, two characters are coming for the first time. These dark blue cells, they are called as ECL cells or enterochromaffin cells. What do you call them as? Entero- say that again, enterochromaffin cells. What did I say? Enterochromaffin cells. Enterochromaffin cells, they are there, they are there in both.

Enterochromaffin cells are there in both. Now what are these enterochromaffin cells? These are, I tell you, it has to fit there. They are histamine secreting cells. What are they? Histamine secreting cells which act locally. Locally, locally means what? The histamine secreting cells, what is the immediate neighborhood of the histamine secreting

cell there? Look at there and tell me.

Parietal cell. It is in the vicinity of what? Parietal cell. So enterochromaffin cell. I will make a statement. Enterochromaffin cell by secreting histamine, it stimulates the parietal cells. So the control is there only.

Are you with me so far? So who is talking to whom? Parietal cell. He is talking to parietal cell. What is the medium of communication? Histamine. Medium of communication, histamine, good. Then yet another major difference is the occurrence of these red cells.

Here, they are not here. So where do you get the G cells and where you don't get the G cells? In fundus we will not get the G cells. Very good. And where will you find them? Antrum.

Find them in the antrum. G cells are responsible for secretion of a hormone. So stomach is an endocrine gland and the hormone is gastrin. And why gastrin is called as a gastrin? Because it comes from stomach and it is a protein hormone. Gastrin comes from where? It comes from these cells located where? In the fundus or in the antrum part? Antrum part. Okay, I said gastric glands.

Author has used here the oxyntic gland for this. Can you guess why author has used the word oxyntic glands for this? Parietal. Parietal - these are oxyntic cells. Antral gland cells is rich antrum and also in the G cells or the gastrin secreting cells. Yes please. Why are there gastrin cells in the antrum part? Is there a more variable? Okay now let me tell you why.

Why this question is not very relevant. This is a highly simplified diagram okay. This phenomenon is far more complicated. There are at least half a dozen or more types of cells okay and at least a dozen and two dozen receptors known to be there about which I am not talking. So your question is bona fide. Within the framework of what we have done your question is justified - but your question cannot be really answered unless I go to the broader picture to which I am not going. But you are your question I respect the question but I am not going to answer it okay.

Wait for two minutes I will go to the entire answer - this is just a small part okay. I put this slide I will answer your question in a minute. This is histological section through the stomach. Can you see this slightly lighter cell. This cell here can you see the pin here. Can you see the arrow here and lighter cell it is a histological section to show the parietal cell okay. Alright let us move on I am sure you know what this what we are talking about. In that image the outline is very clear and then I will draw your attention to the fundus part.

In the fundus part the author talks about what cells? We have seen abundance of what? Parietal cells and we also know that parietal cells are a very important source for what? HCl. HCl okay. Now you have absorbed these facts - absorb one more fact. Parietal cells are also a source for yet another protein which is called as intrinsic factor. What do you call it as? Say that again say that again intrinsic factor. It comes from where? Comes from where? Okay now you can of course ask a question what might be the rationale for or logic for having the intrinsic factor. We will talk about it in details but at the moment to satisfy your curiosity intrinsic factor plays a very important role in the absorption of vitamin B12. No intrinsic factor no matter how much vitamin B12 you take it would not be absorbed. It is very critical and it is coming from the same cell that secretes HCl. Same cell that secretes HCl and intrinsic factor - it is important for? For absorption of vitamin B12 we will see to that later okay. So this is the story here then of course all over there are cells which we call as in the chief cells - chief cells secrets pepsinogen which is a large protein molecule and in the antrum part - you have the G cells and of course the mucus is there everywhere.

Alright so, this tells us about - you can read about this - the tubular gland - how much of gastic acid is secreted and how much intrinsic factor etc. But I would rather go on - this is a beautiful slide. You can immediately identify the vertical section through the wall of the stomach. At the top somewhere there is the lumen. Are you with me? Can you see those fine gastric pits there hello. These are all gastric pits here those those those - this is a gastric pit they are all gastric pits there. They have taken a section okay a frozen section okay and they have stained it with antibodies against the protein and that protein is the hydrogen - potassium pump. We have seen 100 times - we have seen sodium potassium pump okay. Now this time author tells us about what hydrogen potassium pump. Hydrogen - potassium is nothing but the source of secreting hydrochloric acid. So this is a parietal cell. What are you looking at is a parietal cell so the author has labelled the parietal cell for us specifically. And what is the marker? He has used antibodies against the protein. Antibodies against the protein and we are using the immunocytochemistry technique. The author shows us this is a beautiful image. What is this image? You take a single cell - this is single dark cell - dark cell - each dark dot - there is a cell. What is that? It is a parietal cell. You take the plasma membrane of the cell okay, that cell plasma membrane on the apical side - because from the apical side the acid will come into the lumen okay. And in that is sitting this beautiful huge protein okay. This protein like sodium potassium pump also has alpha unit which is very big a beta unit is very small. Two proteins - what they have done is they have only taken the alpha unit and then purify it inject it in rabbit. The rabbit will generate antibodies - take the antibodies put it on the section of the stomach of the rat and stain it okay - develop a color and every cell that has the protein now looks dark brown to me. We are good so far and so now let us see what has been happening within a single cell. So where are we - we are attempting to find out how a single parietal cell secretes acid. Good so far okay. So here we have a single cell - a huge cell - a parietal cell has been drawn for us by the author. This is the lumen and this is the basal side. The moment I see basal side I start

looking for the pump and the pump is there, okay. And there is something interesting because there is another pump here and what is that pump called as - hydrogen potassium pump. And that hydrogen-potassium pump is on the luminal side or apical side or the basal side it is there on the apical side good.

So this pump keeps on working and this also like this pump - also it is the potassium ions and there is a potassium channel. It keeps on circulating but what it does is every time it goes through a cycle okay - there is antiport system. It will drive and it uses ATP it is a pump it will drive this hydrogen ions to the outside. Now where do the hydrogen ion come from. It comes from - author tells us that water splits into OH- and H+ ions okay. This OH ion will combine with carbon dioxide which is everywhere - it will give rise to what? It will give rise to what? It will give rise to this bicarbonate ion. Are you with me? The bicarbonate ion will be driven out by way of what you call as anion exchanger - means which is what the chloride is exchanged for now. By now we are very familiar with anion exchangers. This time you cannot give me a strange look okay. We know where anion exchangers are was. It was in the intercalated cell of the kidney - this time I am not lying right intercalated cell - right. So there is an anion exchanger and so the H+ ions go and there is a chloride channel there okay. Because the H ions go the H+ ions will draw the chloride ions - positive negative positive okay. And then you will have a build up of the huge amount of - so there are hundreds of cells - each cell will put on thousands and thousands of H+ ions thousands. And you know something - for every single H+ ion in the blood there are few million H ions in the stomach but here is the beauty - osmolality of the fluid is still 300 mill osmoles. I mean you are you are replacing one ion with another ion. I am talking about what osmolality of the blood 300 - osmolality everywhere is 300. Beauty of biology is amazing. I mean you have so much of so much of a particular ion species there okay but you still keep the osmolality is still 300 - amazing okay. Can I move on now okay. Hello it takes time to absorb I know. I know so I would suggest that you go home and spend 10 minutes just looking at this diagram. I mean how beautifully the cell is separating okay - separating the ions in one compartment and how for every H+ ion which - goes look at my hand - which goes in this direction there is one bicarbonate ion which goes in this direction. One to one. Are you okay so far? But I will say here that whereas the hydrogen ion is a product of my interest - why it is a product of my interest because the pepsin enzyme which will come from pepsinogen - which will come from chief cells - the pepsin can act at pH 2 2.5 okay. Actually the as a result of the secretion of the H ions it is so acidic that the pH is almost 0.8.

Just imagine - it is a very concentrated hydrochloric acid but it does not remain so acidic because it mixes the with the food that we have taken. And as a result - the food slightly buffers it and then the pH goes to about 2 2.5. So actual digestion is happening at about what 2 2 to 2.5 pH. What is the product of my interest - is H ion+ and bicarbonate ion is a by-product are you okay so far? Now an interesting question is coming. I want you to apply your mind a by-product is coming okay. So far in any good engineering system - forget about biology - any good engineering system is really good if you are going to

employ the by product to some use. Got the question - now let us see if understood the question. If you have appreciated then tell me in what way can you use this by product. Very good absolute brilliant – genius. She is right - why because when the food goes to duodenum you need to neutralize it - neutralize it with what? Bicarbonate. Those bicarbonate ions are transported from the wall of the stomach eventually to the duodenum okay and that it is released with the pancreatic as it is released into the duodenum - so that all those acids at the level of stomach - you separate them okay and then at the level of duodenum again with them it is neutralized. So the pH of this duodenum is about - actually it is slightly alkaline - 7.2 to 7.4 okay. Great. Very good I am very happy with that answer yes go ahead. Oh that is that is that that is a that's very low concentration. I don't know that we know you see this is an observation that hydrogen goes here but this is far less as compared to that - I am not answering your question because I don't know okay. But this is an electron photo micrograph of the parietal cell and what is a peculiarity of this cell is huge number of canaliculi. Now what are these canaliculi? Canaliculi is membranes they are all membranes okay and those membranes are intracellular in the parietal cells. They are intracellular and those membranes are loaded with thousands and thousands and thousands copies of the pump so can you see this pump here. Can you see this only pump can you see this membrane here hello hello hello can you see the membrane? can you see these pumps. These they are not pumps it's a membrane sitting on it - if I take a tiny bit of the membrane on that I may get a thousand copies of the pump molecule okay. Therefore in every cell there are thousands, thousands and thousands may be large number and how it works is, so this is a, this cell is more or less a complete closed cell and there is an extensive system of membranes, we call them as canaliculi, what do you call them as? Canaliculi.

Canaliculi and but after the arrival of the food and when the cell is stimulated, okay, suddenly can you see this, these membranes are exposed to the outside, okay. And suddenly those membranes on which the pump was sitting - which was intracellular, okay, now it is exposed to the outside, okay. And once it is exposed to the outside it can secrete the hydrogen ions and then the hydrogen ions and the chloride and then it can go into the lumen. The answer is actually here, this is the diagrammatic view. This is the resting stage of the parietal cell, can you see those vesicles - on each vesicle can you see the green dot there? What does the green dot represent? It represents a pump, okay and then you stimulate the cell, there are many ways to stimulate the cell. One of them could be by way of histamine, and then as a result of that, there is again traffic, the vesicles - they merge with the plasma membrane. And once they are here they start secreting hydrochloric acid. The hydrochloric acid will be released into the lumen of the stomach, are we good so far, hello, are you good? Okay, this tells us something. So some stem cells, the cells give rise to these cells and they migrate. As they migrate they will specialise into different kinds of cells and the green ones are the parietal cells and what the blue ones are the enterochromaffin cells, parietal cells, mucus secreting cells, chief cells etc. and the author has abbreviated the function of each for us, we have already done that. Maybe what is the, we have already done this, this slide is interesting because it

tells us what, what molecule are we talking about, histamine, what is the source here, ECL, enterochromaffin, enterochromaffin cell and in the plasma membrane on the basal side of the plasma membrane of the parietal cell - you are going to get this receptor, it is again a G protein coupled receptor. Are you with me? Look at the receptor, look at the receptor which goes up and down, so somewhere here is the site where, histamine can combine and once it combine - it excites the cell and cell will start, cell will start secreting. So patient comes to you and says that I have a acidity problem, okay. Look at this image and give me a solution, anti-histaminic okay. You can use anti-histaminic. For a very long time, when I say for a very long time I mean 1990, 1995, almost 2000 till 2005, one of the most widely drug for controlling acidity was cimetidine, what was cimetidine, what? You said, it was H2 receptor, this receptor is H2 type, H1, H2 are system is H2 type - which are involved here. You could block the receptors and you could do it, are you with me? Now you did not ask me very interesting question - what happened after 2005? I will come to that because that answer is very exciting. But before you come to that let us see, what are we looking at, okay. So the major problem - you are secreting so much acid and then why does not it digest the stomach, okay. Why does not acidity eat up the stomach? Well it will if you damage the mucus layer, okay. Therefore there is a very thick mucus layer, very thick mucus layer and that mucus layer actually in the lumen of the stomach, it is almost 1 mm thick, okay. And as we know it, so here we have a very, very funny, I mean this is biology again, you are, this is the pH here is almost 7, this 1 mm thick layer has pH as about how much, 7 - it is coming in contact with the fluid where the pH is how much, pH is neutralization of course it is happening here, okay. But the only solution to that problem you know something, we have addressed this problem with reference to the high osmolality in the medulla, high osmolality in the medulla. I mean you have to completely keep on doing it, okay, because the natural forces, the laws of physical chemistry will bring about equilibrium. So what is your solution? Your solution is to keep on let these cells keep on generating bicarbonate, okay. So the parietal cells - let them keep on pouring in hydrochloric acid, so that pH remains at about 2 as long as the food is there, okay and this remains at about 7, you get the argument. Is there a partition separating the two pH's, no, so is some titration is going to happen, it is going to happen, okay. But you know what happens is in the case of the people who have a gastric ulcer - it is inevitably because there is a bacteria called *H. pylori* or something, *Helicobacter pylori*, am I right there, okay. That bacteria can damage this layer and once this layer is damaged then the mucus layer of the stomach proper is exposed and then the acid can start acting and then it can damage, okay. Very interesting slide, let us understand this, this is another slide on which I want you to spend some time, okay. So here we have the mucus, and this all pH here is 7 and pH here is 2 and here are our parietal cell and you know something as you go, as you go deeper into the gastric pit - the mucus layer becomes very thin, as you go deeper and deeper it becomes thin. It is very narrow that, it is very, it is 1 mm, it is 1 mm thickness when you go into the lumen of the stomach, okay. From the lumen of the stomach if you enter into the gastric pit the layer becomes very thin, it goes on becoming thin and thin and thin, okay. It is very thin by the time you reach the deep in the gastric pit. There is a

parietal cell and this parietal cell is secreting the H+ ions, is H ions coming in contact with the mucus layer, okay, the answer to that question is in strict sense yes but the layer is extremely thin, okay. So when the large amount of H ions can come, okay, they can still pass through it because the mucus layer is extremely thin, had the mucus layer been thin all H ions will be neutralized there only, they can still go through and look at the arrow H ions, H ions and then H ions goes through this, as if they go through a tunnel. And that tunnel is made up of what? Mucus and that layer becomes thicker and thicker and thicker, okay. And then you enter into the lumen of the stomach, there is mucus layer on both the sides There is no mucus and that is where the food will come and that is where the H+ ions will go and hydrochloric acid will go and these are the sensory fibers, the brain wants to know what is happening in the stomach. And at the same time just as the H ions are going here I want to draw your attention to the point number 4 which author is showing us. What is the point number 4? Bicarbonate ions, okay, so as you take your food and as the stomach is releasing hydrochloric acid on the other side, on the basal side the cell is releasing equal amount of, equal amount of bicarbonate and this phenomena is called as beautiful word, you will appreciate the word, love the word, what is the word? Very nice word, isn't it? What is the word? Alkaline tide.

What does the tide mean? Sudden, sudden, as much as H+ ions are going on that side, sudden increase. So if you literally keep on monitoring blood samples, okay from the stomach when you are fasting and when you are having food, okay you will suddenly find that there is too many H+ ions and accordingly the pH also slightly varies in the blood, okay. So you can read about the alkaline tide.