Overview and Integration of Cellular Metabolism

Prof. Arindam Ghosh

Dr. B.C. Roy Multi-Speciality Medical Research Centre

Indian Institute of Technology Kharagpur

Week 01

Lecture 03: Digestion and Absorption of Carbohydrates

Hello everyone, welcome to your lecture series on Overview on Integration of Cellular Metabolism. The first two lectures were on very fundamental topics. Today, we will be starting with the metabolism proper and we will be going into carbohydrate metabolism and our lecture will start with digestion and absorption of carbohydrates where the concept that will be covered is how carbohydrates are digested, how glucose is absorbed and how glucose transporters play a key role in absorption of glucose. So, very basic thing to understand is the digestion of carbohydrates actually starts outside your body only how by cooking. See carbohydrate are actually made of units of glucose right of course, glucose is a carbohydrate is very fundamental it does not need digestion. Demention means breaking of a complex molecule into simpler forms so that we can absorb the whole thing right.

So, this carbohydrate molecules are connected by something that are known as glycosidic bonds. If we break this glycosidic bond we can break carbohydrate. So, cooking is one such phenomena where the heat and the mainly the heat actually helps in pre digesting your food even before you take it ok. So, it is easier to digest a cooked food compared to a raw food because our biological system with evolution has adapted in such a way that we can easily digested cooked food.

But wild animals for example, a tiger can easily digest a raw food because there are mechanisms by which they can more efficiently digest any other raw material specially carbohydrate ok. Now, carbohydrates where they are found it can be found in diet as both polysaccharide and disaccharide. Polysaccharide means multiple single units multiple units of monosaccharides are connected examples are starch and glycogen. And disaccharide means two a monosaccharide unit is connected with the help of a single glycosidic bond. Example of disaccharide is sucrose and lactose right.

So, what happens in GI tract water breaks these down into monosaccharide unit as we go down the entire whether be it polysaccharide or be disaccharide it will be easily

broken down as it goes down our inter gastrointestinal tract or GI tract and we can then easily absorb them. So, the digestion starts with alpha amylase. So, any enzyme that digest glycosidic bond or carbohydrates are known as amylase right. So, alpha amylase right at the buccal cavity because it is present in mouth ok it helps in digestion right. However, one very important thing to notice gastric HCL we you might be aware that our stomach the pH is very low because of presence of gastric acid.

This inhibits salivary amylase what is the importance? Importance is when the food is in our mouth and we are chewing it a lot the alpha amylase is already digesting because once we deglute it it goes into the stomach the action of alpha amylase will be inhibited. Therefore right from very childhood our parents and grandparents used to say please chew your food very carefully and do not swallow the food just like that. We are all in a hurry we all just take gulps and we swallow and then we go out and we frequently find our self it in digestion or bloating this is the reason ok. So, very fundamental, but very important to know. So, stomach in stomach carbohydrate digestion does not happen.

So, it continues in pancreate pancreas where the pancreatic juice has got alpha amylase where it breaks down the alpha 1 4 glycosidic linkage. Again what is alpha 1 4? When we consider a polysaccharide or multiple carbohydrate units they are they look like this. They may be branching they look like branch of trees twigs whenever we are considering this trait bond these bond they are alpha 1 4 these are 1 4 and whenever a bond is at a right angle that is a branch point this is alpha 1 6. So, alpha amylase can easily digest or break down this alpha 1 4 glycosidic linkages. So, if it works on this compound it will break continue to break till it reaches here.

So, this ultimately one molecule will be left behind and the rest thing can be digested right you get my point. So, whenever it can reach up to the branch and then we need more enzymes ok and that will of course, be discussed when we are discussing about glycogen phosphorylation and breakdown everything will be very clear, but for now to understand the fundamental concept of digestion you should know that alpha amylase digests or breaks down alpha 1 4 glycosidic linkages which will lead to production of compounds like maltose, isomaltose, dextrin it may be branched or unbranched oligosaccharides depending on how complex our food was. Then the specific enzymes that are present in the intestinal brush bordered cells or succus entericus in small intestine that is sucrose, maltase, isomaltase and lactase they will act on those disaccharides that will be converted to monosaccharides and then they will be absorbed all right. So, this is an overview how the carbohydrates are digested. So, this is the this is the thing that I drew in the previous slide right.

So, glucose unit these are individual units of glucose that are connected by alpha 1 4 or

alpha 1 6 linkages. So, this is the big starch molecule for example, starch is a polysaccharide that we get in potato or rice right plant source. So, this can be broken down. So, for example, alpha amylase can only break it down till the branching point. So, this with a so, few more than 2 or 3 units of glucose when it is connected it is known as oligosaccharide ok.

So, this oligosaccharide can be converted to disaccharide or this alpha amylase can directly break these 2 bonds and can be converted to disaccharide. Now, the enzymes in the intestinal brush border cells will again act on this disaccharide and then it will be converted to monosaccharide and it will be digested. So, the question is if everything is digested what remains of course, it is not digested right I told you in the intestine it can only reach up to a branching point and of course, something will always be there which is undigested. And this undigested part is actually the fibre component of our diet which actually contributes to the stool volume and this is actually good for our diet. Dietary fibres are essential for our diet the role of dietary fibres will be explained in detail in later lectures, but for now this picture illustrates the whole thing the digestion starts in the saliva it inhibit it is gets it it does not happen in the stomach ok in the pH no.

Next pancreas from pancreas amylase secreted which acts on small intestine because in small intestine the mechanism of action or the favourable environment of these enzymes to act is alkaline pH. So, pH should be high. So, our in our oral cavity and specially the in enzymes are small intestine they need alkaline pH and intestinal juice has got alkaline pH. So, then the enzyme now will become active they will convert the polysaccharide into whatever was digested from mouth they will pass through stomach they will be the small intestine they will be digested or converted to small disaccharides and then the disaccharide digesting enzymes are present in the brush border cells they will be converted to monosaccharide for example, glucose and fructose and then they will be absorbed through the intestinal brush border cells. Do not worry we will be highlighting we will be magnifying this whole thing very soon I will be seeing what happens after they are digested.

So, this is a chart for example, this is a chart which shows what are the essential enzymes that can act on the foods and what are what is the location and what are the ultimate end products you can get multiple choice question from each and every slide ok each and every point. So, be very careful that you do remember each and every one of them because remembering them will not only help you in the exam that is one of the goals, but it will help you to understand how you formulate a diet because diet planning is also one advantage as I told you of doing this course being a nutritionist ok. So, again this is a these are the two charts. So, this is the first table and this is the second table where I have shown how all the enzymes act on the substrate and what is the location of

action and what are the end product. Mind it for dietary fibers like cellulose hemicellulose and plant polysaccharide there is no digestion.

So, what do they do? They actually contribute to the stool the bowel movement increase the bulk of stool and improves constipation and that are actually fermented by intestinal bacteria. So, a lot of dietary fibers can actually lead to formation of gas passage of frequent gas bouts that is called a flatulence ok. In here there lies a applied clinical importance. There is an enzyme lactase ok did you overlook it? No it is very important. So, lactase what does it do? It breaks down lactose into glucose and galactose.

Lactose is a disaccharide consisting of a one unit of glucose and one unit of galactose and lactase is present in the brush border cell. If lactase is absent lactose cannot be digested and this is known as lactose intolerance. What is the symptom? Lactose generally is milk ok milk product. So, whenever an individual who is affected with lactose intolerance takes any milk or dairy product instant diarrhea happens flatulence there is projection of gas there is bloating in the stomach there is watery diarrhea. Why? Because the thing cannot be digested right and it contributes to the undigested product it contributes to the dietary fiber that will get fermented intentionally that will increase the osmotic tension that will lead to diarrhea.

So, these are the reasons why if something is excess undigested it will lead to diarrhea and flatulence and in this case when it is digested for everyone in person or in patients with lactose intolerance where there is lactase deficiency this will be a problem. What is the treatment? It is very easy we can simply use specialized formula or you can simply remove all milk products from diet ok. Now this lactase deficiency may be primary primary or secondary means this lactose intolerance can be congenital from birth because these enzymes are produced by genes that are developed in utero ok. So, if a baby is born with lactose intolerance what will happen? It cannot thrive on mother's milk there will be instant vomiting baby will cry interactively there will be swelling of abdomen and that is the very first sign of lactose intolerance in which clinicians and specially junior doctors who are attending the patient on bedside or even family members who are having a newborn baby should be aware. If a baby is rejecting breast milk excess swelling of abdomen is happening excess crying might be a case of lactose intolerance or it can be secondary where the lactose or lactase deficiency is acquired.

Why? Basically we have seen it is has been found that the lactase enzyme activity decreases with age. So, as we age the ability to digest milk product is lost. So, it can or cannot happen to anybody right mind it any phenomena of aging is individual specific you can say ok my grandmom always has milk and milk in diet and roti chapati it is fine it is she is blessed with a good lactase enzyme. Someone else might not be someone else

might develop lactose intolerance in early 50s or 60 years of age it varies right. So, acquired lactose intolerance can be treated how? We need to provide lactase from outside who can provide lactase from outside by tweaking the diet ok.

It advice him or her not to take raw milk ok just advice him to take curd we can add yeast also because these are very good sources of lactase why? Because it comes from the lactobacillus that is present in the curd or yeast ok. So, curd contains lactobacillus that will provide lactase it will help in easy digestion of the milk also yeast can be used in the treatment because it is available in sachet it can be prestripe if present in the gut it will provide the essential lactase enzyme. So, this alactasia will be cured ok. So, mind it there is a term known as hypolactasia hypo means less. So, this lactose lactase enzyme might be totally absent it is alactasia or it may be less ok.

It may develop with age and this is known as hypolactasia. So, now, after it is digested we are now concerned with absorption of carbohydrate mind it when we come to absorption only monosaccharides are absorbed excuse me. So, what are monosaccharides? Monosaccharides are compounds that are single unit of that are considered to be single carbon unit for example, glucose, fructose, mannose, galactose etcetera. And again for MCQ purpose the rate of absorption is of galactose is the most followed by the rate of absorption of glucose and then fructose. So, what if the final disaccharide is not digested to monosaccharide? Of course, they will not be absorbed minute quantities may be absorbed, but ultimately everything is eliminated through the kidneys because they are water soluble ok.

So, next we come to the absorption of glucose because this is most important glucose is the fundamental unit of carbohydrate all other catabolic pathway in carbohydrate metabolism will lead to production of glucose all also all biosynthetic pathways start with glucose right. So, we need glucose as a currency of readymade currency to form higher storage form of carbohydrate. So, it is very important that we get glucose absorbed through our gut right. So, the importance of glucose lies in carbohydrate metabolism and now we should focus on glucose absorption. Now, mind it our cell membrane since it is a protein lipid protein bilayer membrane unless the substance is lipid soluble it cannot freely diffuse and glucose is no exception.

So, since glucose is polar it cannot diffuse through the lipid bilayer membrane. So, we need someone to hand hold glucose so that it can pass through the closed gates of the cell membrane. These there are few transmembrane proteins that act as glucose transporters and various mechanism they actually help in carrying glucose across the brush bordered cell. One example is sodium dependent glucose transporter this is a co-transporter what do you mean by co-transporter? Co-transporter is someone or some form of gate in

which suppose I am waiting at the gate the gate would not open. Only if my parent is also at the gate then only the gate keeper will feel safe to open the gate and both of us can go in.

Later on after I am inside school my parent can easily sneak out of the back door this exactly what happens in the sodium dependent glucose co-transporter right. So, S G S glute it can also be termed as S G L T ok. So, what it does glucose alone not allowed only if when sodium is there both sodium and glucose attached to this transporter then the transporter simply turns it direction you have seen revolving doors when going into the shopping mall right. Once you are in the outside when the whole structure revolves you go inside right the whole gateway works in the same way. So, once glucose is inside our job is done the excess sodium is also inside it is later than pumped out with the help of sodium potassium ATPS pump this is very important pump which uses energy.

So, considering the whole phenomena when a sodium is going inside and later it is pumped out where energy is required energy is used indirectly, but considering the only sodium dependent glucose transporter S G L T energy is not required ok. Now there are two types of glucose transporter sodium dependent glucose transporter type 1 that is present in the intestine and type 2 is present in the kidneys. Type 1 is very important specially for see both are important, but type 1 is more important why because type 1 has led to the discovery of oral rehydration fluid is one of the very few miraculous discovery that has not been awarded a Nobel prize very ironical, but it has saved countless lives in diarrhea for example, in cholera there are loss of electrolytes and the ultimately diselectrolytemia leads to death. So, since we are talking about glucose transporters this is the applied importance where glucose is actually used for sodium transport. So, only if we drink sodium chloride it will not be absorbed, but if glucose is combined with sodium chloride in the solution then it will act as wonder drug glucose and sodium can get co transported and this prevents all the diselectrolytemia and this is the principle of ORS or oral rehydration salt oral rehydration fluid and this is the main stay of any form of diarrhea mind it.

So, next time due to any gastric upset if some of us are having constant watery diarrhea the only and only saving grace that will prevent loss of consciousness is oral rehydration salt and that acts on the principle of sodium dependent glucose transporter 1. Sodium dependent glucose transporter 2 is also is present in kidney and it is implicated in some form of diabrenal diabetes cause of diabetes specifically glycosuria, but that is not much important compared to the value biological value of sodium dependent glucose transporter 1 and its role in oral rehydration salt extremely important and it is a life saving emergency right. Next so, that was sodium dependent. So, so is there no way in which so, glucose can enter the system without its parent of course, there are there are

gates which will allow me to go to any party or club right. So, the glut that is glucose transporter acts in same way.

So, what it does? So, glucose transporter so, this is an illustration of glucose transporter that is present that is glut 2 it is present in blood stream from where glucose can be absorbed in the periphery. So, glucose in the intestinal cells it actually binds to the site of the glucose transporter ok what happens just like SGLT the mechanism is similar the whole thing flip flops into the inside the cell and ultimately the transporter when the transporter changes its direction glucose can be transferred inside ok and this thing is reversible depending on the need of glucose the glucose can go in and out through this transporter whether I mean from what suppose from site A to site B we need glucose absorption. Next when the site A needs more glucose glucose can go out in a similar fashion. So, considering the whole mechanism we have now magnified the intestinal brush border cell. So, what is happening? So, in the brush border cell sodium dependent glucose transporter now you know it is SGLT 1 SGLT 1 is happen is facilitating the entry of glucose into the luminal brush border cell with the help of sodium ok.

This sodium is pumped out of the cell by sodium potassium ATPase pump because the concentration of sodium and potassium inside and outside the cell is fixed ok and this is regulated by sodium potassium ATPase pump which uses energy and from the basolateral surface. So, here are the blood vessels. So, these are the blood vessels. So, intestine has got a lot of blood vessels whatever we eat it is ultimately absorbed in the blood. So, here the blood vessel in the blood vessel the interface of the brush border cell and the blood vessel that is the blood capillary GLUT 2 is present which is actually capturing the glucose and thus glucose can be absorbed via diet.

So, this was the enteric this is the mouth right very bad lip. So, we took down the glucose which you did we digested from oral cavity pancreas ultimately it has enter the brush border cells it has gone via sodium dependent glucose transporter one via GLUT 2 into the blood stream right. So, this GLUT 2 the activity of GLUT 2 is actually facilitated when in well fed state ok. So, in well fed state so, see there is a type of circulation that is known as portal circulation there if you are well versed in anatomy the blood the blood flow happens in reverse direction compared to the enteric blood vessel. So, just as a rule mind it GLUT 2 transports glucose into the cell when blood glucose is high right mind it here what we are seeing we are seeing GLUT 2 is transporting the blood glucose outside the cell we are hungry we need glucose.

So, glucose is getting absorbed in the blood right, but when we are in well fed state ok now glucose can be stored. So, this GLUT 2 the phenomena will be reversed, but this phenomena is not reversed in intestinal cells please do not think that when we have

excess blood glucose GLUT 2 will reverse the flow of glucose into the intestinal cells and then the whole glucose will be passed in the urine it does not happen that or stool it does not happen in that way because glucose actually cannot go out from this side if that was the scenario lot of glucose would be trapped. So, when we are considering inflow of glucose from blood to the cell we are talking about liver cells right. So, in liver the peripheral the glucose is being delivered to the cell where it can be taken up and stored as glycogen and this mechanism also helps to monitor the pancreas to regulate the level of insulin secretion because that is also another trigger the level of glucose whether the pancreas need to secrete more insulin or whether it needs to check on the secretion of insulin is a very important marker or very important phenomena in regulation of blood glucose which will also be discussing later. Next this is an example of another glucose transporter that is GLUT 4 ok.

So, in this type of transporter what happens this is like a flip flop mechanism where first the glucose will be captured and the mouth is opening outside the cell the glucose molecule is getting internalized at some point of time and then the mouth is opening at the inner side where glucose is entering into the cell. So, this type of cell is actually present in skeletal muscle, heart adipose tissue etcetera right very important because during exercise muscle actually accounts for 80 percent of total bodies glucose utilization. You must have seen all the if you have been to any aerobic exercise or gym or any yoga class or any hard work training center for example, energy drinks are provided that have got a lot of ready glucose because we need more and more glucose in muscle to increase those reps. So, that we can build our muscle right, but at basal metabolic rate brain utilizes 60 percent of glucose. So, mind it when we are not actively working basal metabolic rate means during sleep actually when nothing else is working the brain is the main source of glucose utilization and during exercise muscle is the main source of glucose utilization ok.

So, what is so special about GLUT4 compared to all other GLUT or I mean glucose transporter GLUT4 is under control of insulin whereas, all other glucose transporters are not this is again a very important multiple choice question very important concept in understanding how insulin can regulate blood glucose because it induces intracellular GLUT4 molecule to move the cell across the trans membrane and thus increase glucose uptake. So, when there is more insulin the blood the peripheral blood glucose will drastically reduce because all the glucose will get inside the cell and this thing is hampered in diabetes mellitus specially type 2 where there is insulin resistance that is seen in muscle and fat cells where mainly GLUT4 are present insulin cannot act on them therefore, cells cannot get inside and the level of blood glucose is very high and it leads to diabetes mellitus which will be again discussing in great details later. So, these are the overview of 3 types of glucose transporter sodium dependent glucose transporter GLUT2

at vascular site and GLUT4 in transport cell of heart and skeletal muscle and this is a chart again for MCQ where all the types of glucose transporters where they are located have been tabulated as I told you brain utilizes basally 60 percent of glucose what type of glucose transporters GLUT3 right. So, this is an MCQ question. So, the this is one example and mind it sodium dependent glucose transporter type 1 is present in intestine and type 2 is present in kidney and they help in co transporter.

See fructose transporter who does GLUT5. So, these are very small hidden MCQs that are present in the slide. So, you should pause them memorize make your own notes ok. So, to conclude this lecture session as covered mechanism of digestion of carbohydrate with various types of amylases in various areas of digestive tract we have also covered how glucose transporter help in absorption of glucose across different cellular environment. So, that is it for today these are my references and. Thank you for your attention.