Overview and Integration of Cellular Metabolism

Prof. Aritri Bir

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

Indian Institute of Technology Kharagpur

Week 12

Lecture 57: Obesity, Metabolic Syndrome and Role of Adipokines

Hello everyone. So, we are back to our NPTEL lecture series of Overview and Integration of Cellular Metabolism. Today we are going to discuss obesity, metabolic syndrome and role of adipokines. So, obesity these days is one very vividly discussed and well concerned topic in healthcare sector. And general public not only the healthcare sector general public are also their concerns are also rising in this regard. People are more health conscious, more cautious about maintaining the proper metabolic health and metabolic status.

So, this is one very important topic for today. And here we are going to discuss obesity in terms of BMI and different risk factors. Different anatomical and biochemical perspective of fat deposition, then we are going to discuss the role of adipocyte in this regard. Hormonal control also different adipokines like leptin adiponectin and other hormones.

Finally, we are going to discuss obesity associated dyslipidemia and one other perspective of obesity which is known as metabolic syndrome. So, let us proceed. So, obesity is basically if you see biochemically, this is the result of excess calorie intake or excess calorie storage in comparison to the expenditure of the energy by different activities of body which actually utilizes energy. And if you see from the dietary perspective, if the dietary energy is excess what are the fate of that excess energy that can be stored in the form of fat in adipose tissue for future use as fuel, then it can be burned doing different physical activity or exercise or it can simply be wasted through thermogenesis heat production and where it occurs in mitochondria via uncoupling. What happens when the oxidative phosphorylation is not coupled to the sorry the oxidation the electron transfer through electron transport chain, if it is not coupled to the phosphorylation of ADP that is formation of ATP, the energy is released at heat and that is uncoupling causing thermogenesis.

Now, in humans or in mammals this energy expenditure or energy storage which is

finally, related to obesity are basically a conglomerate action of different hormones and different neuronal signaling which tries to keep balance between the fuel intake and energy expenditure and deviation from these homeostasis is actually causing obesity. Now, if you see the statistics what is projected that by the year 2033 there will be an overwhelming increase of obesity and obesity associated disorders. The prevalence of overweight and obesity is supposed to be raised 89 percent in male 85 percent in female that is huge and that is associated with different health condition like increase in coronary heart disease by around 97 percent cancers will be raised by 61 percent the surge of type 2 diabetes will be around 21 percent. So, that is a huge burden over the healthcare sector and its expenditure whereas, minimal interventions like maintaining the body mass doing proper exercise going through different proper diet formulation that if those modifications along with proper treatments are increased just by 5 percent there can be notable change. So, you can see these things are basically reversible, but of, but of course, of a great concern.

So, obesity mostly how it is diagnosed there are different indices to diagnose obesity different markers of obesity one very important marker of obesity is BMI or body mass index and it includes the parameters like height weight and the amount of body fat in individual is calculated by this. So, what is the formula you can see? BMI is represented as weight in kg importantly weight in kg divided by height in square and the height is in meter. So, this is the calculation of body mass index. Now, based on that the gradation of the metabolic status is represented as if the BMI is equal or less than 18.5 they are underweight.

So, basically what is the normal range of BMI? It is represented as 18.5 to 24.9 below that we consider it as underweight and if the BMI is raised above 24.9 it is basically going towards the overweight and obesity profile. So, what is overweight? It is 25 to 29.

9 then 30 onwards BMI 30 onwards we consider it obeys that is grade 1 obesity there is grade 2 obesity and grade 3 obesity. So, based on the BMI different obeys obesity is basically classified in different status and now if you if we talk about nutritional status of human body remember over nutrition is also one nutritional deficiency actually nutritional disorder sorry. So, when we say there is nutritional deficiency that is underweight whereas, overweight is also one nutritional disorder. Now, BMI is a surrogate marker is an indirect measurement of obesity why so? So, basically we are talking about weight now consider if a person a well built person who is having good muscle mass like body builders. Now, muscles are the weight of muscle per kg or weight sorry weight of muscle density it is much much higher than fat.

So, for a well built body or a body builder their weight will be very high whereas, the fat

content will be very low. So, their BMI will be high, but they are not obeys. So, if solely we depend on body mass index to identify obesity that will be misleading. So, there are multiple other parameters or indices which are utilized to diagnose BMI. So, if we define in terms of actual body fat what is the total percent body fat.

So, we define as 25 percent or greater in case of men or 35 percent or greater in case of women and how those are measured by measuring skin fold thickness bio electrical impedance underwater weighing these are the different methods to measure the percent total body fat and represented as the percent in the whole with comparison to the whole mass. But problem is the method is these may all of these methods are actually inconvenient and as well as costly. So, mostly these are not practiced, but in clinical practice very common parameter which is used to check the obesity is waist circumference the circumference total circumference of our waist. Now, how it is relevant remember abdominal fat abdominal fat is a very good reflector of obesity very good reflector of accumulation of fat and mostly they are very much this increased abdominal fat is very much related to different cardio metabolic risk. So, measuring the abdominal fat in terms of waist circumference are very helpful in clinical practice and the measurement technique is very easy just you need a measuring tape to measure the waist circumference.

Now, there are different types of fat depot in our body that can be and those depot are actually divided into two types one is subcutaneous fat another is visceral fat. Now, subcutaneous fat as it is evident by the name those are under skin of body, truncal fat, abdominal fat or gluteal femoral regions. So, in these regions underneath the skin there is accumulation of fat and those are subcutaneous fat and it comprises around 80 to 90 percent of the total body fat. Whereas, visceral fats are mostly surrounding the viscera and associated with digestive tract. So, they are mostly located in omental and mesentery region and this visceral fat is basically very highly related to different cardio metabolic risk factors that is why these days instead of obesity if we talk about cardio metabolic risks or metabolic metabolically unhealthy obesity.

So, we talk most about visceral obesity and these visceral fats are actually very much tough to lose in comparison to the subcutaneous fat. So, you can see surrounding the viscera is the visceral fat whereas, under the skin this is our subcutaneous fat. Also this abdominal fat and gluteal fat they have some biochemical differences like the fat cells in abdominal fat are of smaller size whereas, gluteal fat cells are larger in size. So, gluteal fat cells have the greater capacity to store fats fats in terms of triacylglycerol. Now, abdominal fat is more responsive to hormonal changes even to different drugs as well whereas, this gluteal region fats in gluteal regions are basically less responsive.

So, if you see if we compare between males and females, females are having more tendency to accumulate fat in gluteal region whereas, males are having greater tendency to accumulate fat in abdominal region. But again if you see the fat losing effort in both of them because the abdominal fat is much more much more responsive to the availability of fat exercise and these are causing different hormone release. So, the abdominal fat is basically much more responsive. So, for males losing weight is very easy, losing weight from the abdominal fat region in comparison to the gluteal fat region. But then you need to notice that abdominal fat in terms of its effect over health status it is much more harmful because when there is lipolysis free fatty acids or different substances which are released from abdominal fat they comes directly to liver via portal vein and the it these released substances have effect over the metabolism of liver which is not in case of gluteal fat.

So, the harm from gluteal fat is much low. Now, obesity if we discuss from the perspective of the fat cells or adipocytes. So, obesity can be increase in number of adipocyte or increase in the size of adipocyte or both. So, basically there can be hypertrophy which is increase in size or hyperplasia which is increase in number or both. Now, suppose the condition where triacylglycerol accumulation is increased via different diseases or via different diet increase calorie intake.

If there is increase triacylglycerol flow those are stored in adipose tissue and adipose tissue is in influenced to in to be increased in size. So, initially there is hypertrophy. Now, what happens when these adipocytes are actually filled with fat totally triacylglycerol they do not have the capacity to expand. So, what happens this is the time when few stem cells pre adipocytes those are actually in store in reserve in human body they get activated. So, this pre adipocytes starts to differentiate and form adipocytes.

So, there is increase in number of adipocyte. So, you here you can see pre adipocytes now are coming in function before that there is just increase in size that is hypertrophy after that not only hypertrophy there is also hyperplasia. Now, when there is hyperplasia losing of weight becomes more harder because majority of the time mostly losing the number of adipocytes are actually very very tough next to impossible. So, what happens only when there is both hypertrophy and hyperplasia if we go for weight reduction or treatment for obesity mostly what happens there is shrinkage of the size of the fat cells. So, these reverses, but once again there are those fat cells which are increased in number.

So, if there is greater flow of triacylglycerol once again they will undergo hypertrophy and more in stress underglow undergo hyperplasia. So, this is about obesity's biochemical perspective. Now, there are different risk factor which predisposes to obesity like first very important is poor diet in terms of intake of calorie, dense food,

refined sugar, fast food and mostly these type of diets are actually having very low essential nutrients they are rich in unhealthy fats. So, apart from that this poor diet it can also be triggered by sedentary lifestyle, lack of physical activity basically there is decreased energy expenditure. Then there is a obviously, there is genetic factors also that obesity can be familial can be induced by different environmental and socio economic factors like environmental factors where you live in a condition where you are exposed to the sedentary lifestyle there are many work pattern .

Even in working condition daily a person is working, but the pattern of work is sedentary in those cases that is some environmental influence as well as socio economic influence where underprivileged people who cannot obtain or who cannot opt for the nutrient rich food they go for poor dietary pattern. There is psychological factors stress, induced stress hormones sometimes can induce obesity, sleep deprivation one very important topic one very important point mentioned these days that lack of adequate sleep induces obesity because basically poor sleep pattern affect the hormonal regulation. There is a homeostasis in hormonal release related to energy expenditure and energy gain these balance is basically disorganized if there is poor sleep pattern. And finally, there are different secondary cause of medical obesity like different medical conditions like hypothyroidism, polycystic ovarian disease they can contribute to weight gain and obesity. Now, I am coming to one very important topic that is adipokines.

Now, adipokines as it is very much similar to adipo and kine if you break this there is kines means cytokines. So, cytokines which are released from adipose tissue those are actually termed as adipokines. These days adipose tissue are not only the organ for fat storage rather adipose tissue these days are coined as endocrine organ because it releases different bioactive molecules which regulate the energy homeostasis metabolic status of the body takes part in inflammation and their dysregulation are related to different cardio metabolic diseases like obesity metabolic syndrome cardiovascular diseases like that. That is why adipose tissue these days are termed as endocrine organ. Now, amongst this adipokines the important ones are leptin, then adiponectin, resisitin as well as different cytokines like interleukin 6 tissue necrotic factor TNF.

So, these are also released from adipose tissue. Now, apart from if we say adipocytes or pre adipocytes apart from this adipocytes and pre adipocytes other cells which are located in adipose tissue they are also able to secrete this adipokines like those immune cells which infiltrates adipose tissue they are also capable to secrete adipokines. Now, adipokines can be pro inflammatory as well as anti inflammatory obesity these days are considered as chronic sub inflammatory state. So, basically there is increased production of pro inflammatory cytokines which are causing inflammation and there is inhibition of anti inflammatory cytokines. Now, they are also relevant to different disease

development like insulin resistance type 2 diabetes mellitus cardiovascular diseases those are associated with obesity.

Now, there are list of novel adipokines these days which have been vastly studied, but today we are going to discuss about these 3 leptin adiponectin and resisitin which play immense role in pathogenesis of obesity and various studies also have confirmed their serum differences in their serum levels in this regard. So, coming to leptin, leptin is basically the name leptose is a Greek word which means thin. Now, it has been first identified as a product of gene OB which stands for OBS and it is one peptide hormone or peptide biochemical nature is a proteinaceous nature which consists 167 amino acids. The receptors of leptin are mostly located to hypothalamus the region of hypothalamus which is related to the feeding pattern that is arcuate nucleus and it plays very important role in energy homeostasis how it basically decreases the appetite and induces satiety. And also leptin stimulates sympathetic nervous system and regulates the sympathetic nervous system related physiological things like blood pressure heart rate thermogenesis .

You can see when there is release of leptin from adipose tissue it works over the receptors which are located in the arcuate nucleus causes different neuronal signal release via sympathetic nervous system which induces or rather works through the beta 3 adrenergic receptors and releases norepinephrine. Now, norepinephrine is related to release of protein kinase A which actually phosphorylates different relevant enzymes like you can see here this adipokines are related to lipolysis via phosphorylation of perylepin also phosphorylation of HSL hormone sensitive lipase which is the hormone here is norepinephrine. So, this is how energy homeostasis is maintained or influenced by leptin. Now, a bit discussion about the arcuate nucleus arcuate nucleus is actually related to the status of the body where whether body is not satisfied wants to eat or it is satisfied.

So, no eating is required. So, there are 2 types of neurons one is orexigenic neurons orexigenic stands for appetite stimulating neurons whereas, anorexigenic neurons is related to anorexia or appetite suppressing or even it is related to satiety produces or signals for satiety. Now, what happens orexigenic neurons are actually releasing the neuropeptide Y here you can see it releases neuropeptide Y which signals to the brain for reading for eating more. So, it induces appetite whereas, anorexigenic neurons releases alpha melanocyte stimulating hormone it is also known as melanocortin. Now, if you can see adipose tissue releases leptin and these leptin actually induces anorexigenic neurons releasing MSH. So, it releases signals for eat less and mobilize more whereas, it inhibits the appetite or food intake.

Now, similarly there are different other hormones gut hormones like ghrelin or pyridyl 336 they are related to controlling the food intake. Now, you can see another hormone very important insulin is also related to this satiety or appetite stimulation we will discuss more regarding this later. So, leptin is basically stimulating anorexia by inducing satiety, but what is the signaling cascade? The signaling cascade of leptin is actually JAKSTAT system what is JAKSTAT system? Now, leptin receptor are actually one single transmembrane receptor. So, this is our leptin receptor transmembrane receptor because it is one side is exposed outside the cell whereas, one side is in located inside the cell. Now, what happens when this receptor binds to the ligand who the ligand is here definitely leptin.

Now, when leptin binds there is dimerization of these 2 receptor. So, there are 2 receptors which basically dimerizes 2 leptin receptor which basically dimerizes with one molecule of leptin. This leptin receptor binding activates phosphorylation via one enzyme genus kinase. So, for JAK is actually genus kinase. So, this is actually each monomer each receptor has genus kinase JAK which is activated causes the receptors phosphorylation.

Now, this phosphorylated receptors are actually acting as a docking system who docs here STAT stands for signal transducers and activators of transcription. Now, there are 3 different types of STATs 3 5 6 3 of them can bind to the phosphorylated leptin docking part that is also known as FAT STATs. Now, this docked STATs docked means which is attached to this phosphorylated JAK they are now this STATs also are now getting phosphorylated by the same genus kinase and undergoes dimerization. So, you can say leptin receptor is phosphorylated where STAT binds then this bound STATs are also phosphorylated and they also dimerize. Now, this dimerized STATs they access transcription factor how they enter the nucleus in the nucleus they bind to the regions of over the DNA some coding regions over DNA which codes for the hormones like neuropeptides then POMC is basically pro opioid melanocortin which is the precursor of melanocortin or alpha MSH and thus it induces the satiety.

Now, leptin as I told it acts to beta adrenergic receptors as well via releasing norepinephrine and it increases thermogenesis. Now, thermogenesis is related to one very important protein thermogenin mitochondrial protein which is the transcribed product of the gene UCP1. Now, this UCP1 synthesis is also increased via this process. Now coming to how leptin is leptin response towards starvation now remember though leptin induces appetite it modulates in function when there is starvation how definitely there is leptin reduction when there is nutritional deficiency and all these thermogenic or energy expense these processes are actually stopped and body is induced towards fuel conservation. Now, leptin triggers TSH decreased thyroid stimulating hormone.

So, basal metabolism is decreased now basal metabolism is one energy expenditure. So, that is decreased as well as energy expenditure in reproduction is decreased by LHFSH hormone decreased, but it increases the glucocorticoid which is related to lipolysis. So, basically leptin is important in combating severe nutritional deprivation and it is also leptin also triggers one important kinase AMPK AMP activated protein kinase how it acts we will discuss soon. So, as we are discussing about the arcuate nucleus you can see insulin is one very important hormone which also stimulates or regulates appetite and satiety. So, insulin is not only the reflection of adiposity it also the reflection of blood glucose level.

Now this action of insulin and leptin they are somehow related basically leptin is it is seen that leptin increases insulin's function it increases insulin sensitivity and definitely there is a crosstalk in their signaling how this auto phosphorylation receptors are phosphorylated by ligand binding. This auto phosphorylated pathway are actually having some common substrates like IRS 2 insulin responsive substrates 2 these are actually phosphorylated and via downstream pathway it inhibits the foot intake. So, basically there is a crosstalk the tyrosine kinase which causes the phosphorylation they can be common as well as the substrate for this tyrosine kinases are also common. So, that can be a link between leptin and insulin's function. Then coming to another important adipokine that is adiponectin which is also one peptide hormone and it is known as insulin sensitizer protects again atherosclerosis or cardiovascular events inhibits inflammatory response as we told that obesity is one sub inflammatory condition considered these days.

So, basically it is helpful in combating the inflammatory response. What are the metabolic roles definitely it energy storage related metabolism are actually inhibited whereas, energy expenditures are increased like fatty acid uptake and their beta oxidation then glucose uptake and their catabolism they are increased whereas, energy storage in terms of fatty acid synthesis, neo glucosinases they are inhibited and adiponectin also imparts in action by activating AMPK. Now, let us see how AMPK actually works. So, AMPK is AMP activated protein kinase. Now, what happens when there is decrease of the triacylglycerol content in adipose tissue it causes release of adiponectin and adiponectin activates AMPK also exercises can release can activate AMPK.

So, this is the effect and what is the fate when AMPK is activated AMPK is a protein kinase. So, it basically phosphorylates different enzymes related to different metabolic pathway. So, it is imparting effects like it is inhibiting energy consuming processes and stimulating energy producing processes. Now, let us see when there is activation of AMPK inhibition of lipolysis is there because there is inactivation of hormone sensitive

lipase cholesterol synthesis is inhibited because HMG coenzyme A reductase is inhibited triacylglycerol synthesis is inhibited acyl transferase G-PAT transfer acyl transferase is inhibited glycogen synthesis is inhibited. Then synthesis of protein inhibited because it causes phosphorylation of elongation factor 2 elongation factor 2 is one very important factor related to protein synthesis or translation we call the process of protein synthesis from mRNA it is known as translation.

So, it inhibits translation as well as it inhibits the M-2 or pathway M-tor stands for mammalian target of rapamycin this is one signaling pathway which is related to protein synthesis and that is inhibited. Now, who is induced breakdown of lipid breakdown of carbohydrate also glycolysis then carbohydrate uptake is increased breakdown of lipid fatty acid oxidation in increase. So, these are the effect of AMPK. Now, AMPK in adipose tissue actually inhibits the fatty acid synthesis and in brain it signals for feeding behavior it more whereas, energy expenses are actually decreased. So, this is the vivid effect of adiponectin over body which is activated by adiponectin which is activated via AMPK as well as exercise also can stimulate this AMPK pathway.

Now, another adipokine resistin which has been invented in mice and the naming is the name is related to insulin resistance because it induces insulin resistance then it is secreted in humans it is secreted from mostly adipose tissue apart from that there are other tissues as well like bone marrow, lung, placental tissue, pancreatic islet cells they are they can also release resistin. Now, it has been seen that in obesity resistin level is actually increased basically increase resistin level is related to visceral adiposity and also studies have confirmed is contribution in different diseases like insulin resistance, metabolic syndrome, type 2 diabetes mellitus. So, if we talk about the mechanism it is basically related to adipocyte differentiation and also lipid metabolism, but the functions are not vividly established yet. So, these are the adipokines or cytokines related from adipose tissue which are very much related to eating pattern, feeding pattern then metabolic status or energy expenditure or energy storage of the body. Now, diet also have some effect over gene expression genes which actually related to increasing or decreasing the body mass.

Now, what is that signaling pathway there are a there is a protein a protein of ligand activated transcription factor family which is known as PPAR, peroxisome proliferator activated receptors and these receptors their ligands are basically dietary lipid. So, dietary lipid activates this receptors and alters the expression of the genes which are related to fat and carbohydrate metabolism. Now, as it is evident by the name the it was first recognized for synthesis of peroxisome. So, that is why it is known as peroxisome proliferator activated receptor, who are the ligands I already told fatty acids or fatty acid derivatives lipids, but apart from that there are different drugs or synthetic agonist which

can be which can be used in treating or modulating the energy expenditure or metabolic status of body they are also activating the PPRS signaling pathway. There are 3 types PPR gamma, PPR delta and alpha and here you can see the signaling pathway.

So, basically ligand which is fatty acids or its derivative it reacts with this transcription factor PPAR and it forms heterodimer. Heterodimer because along with PPAR receptor there is binding of one different types of different type of receptor which is known as retinoid X receptor this dimerization of receptor PPAR and RXR they together actually influences the transcription of different genes related to fatty acid and carbohydrate metabolism different enzymes basically. Now PPAR gamma is primarily activated in liver and adipose tissue and their activation is related to differentiation of fibroblast in adipose tissue and encodes for protein required for lipid and synthesis and storage. Now, here you can see PPAR gamma actually causes fat synthesis and storage in liver and also fat synthesis storage and adipocoin production from adipose tissue whereas, it renders insulin sensitivity towards muscle. Alpha variety is located in liver, kidney, heart, skeletal muscle, brown adipose tissue and their ligands apart from the free fatty acids eicosanoids type of fatty acid lipid can be the ligand of PPAR alpha.

Apart from that one drug which is basically used for treating obesity as well as coronary heart disease because it causes raising of HDL and lowering of triacylglycerol the group of drugs fibroblasts can also act through PPAR alpha. And it basically turns on the gene which are related to beta oxidation energy expenditure. So, it causes beta oxidation in muscle, beta oxidation in liver and is actually activated in response to starvation causing beta oxidation. Then delta, delta is actually related to not only fatty acid oxidation, but it also causes thermogenesis and causes fat depletion definitely. Now, we are coming to lipid burden hypothesis which talks about how the metabolic profile changes when there is increased calorie intake.

So, what happens normally the adipocytes are actually quite able to store triacylglycerol and also synthesizing triacylglycerol and they are much sensitive to insulin and produces leptin. But in case of obesity the storage of triacylglycerol is hugely increased so much so that there is over filling of adipocyte and also these adipocytes are rendered insensitive to insulin. So, basically the adipocytes are not able to store more triacylglycerol. Now, what happens different transcription factors actually activates different genes which causes development of new adipocyte synthesis apart from the existing adipocytes. But this adipocyte synthesis is actually down regulated in adipose tissue, but not in other regions rather up regulated in other regions like skeletal muscle and liver.

So, basically now there is adipocytes in skeletal muscle and liver in obesity and they are

able to store lipid. That is why obesity is actually characterized by not only storage of fat in adipocytes, but also there is ectopic lipid droplets accumulation. In ectopic regions like skeletal muscle liver there is lipid accumulation and this ectopic lipid accumulation everyone is not able to handle. There are few people genetic predisposition or familial disposition predisposition which makes them susceptible to develop different metabolic diseases raising from that. So, insulin resistance is also manifested from that because there is changing in the signaling pattern related to different enzyme there is release of different adipokines changes in release of adipokines also they are triggering is there because obesity is defined as one sub inflammatory status which is triggered in case of much more fat storage.

And that causes activation of different macrophages releases of different cytokines and finally, this lipid filled adipocytes they undergo lipo apoptosis a programmed cell death of this lipid. So, this is how obesity can proceed to different metabolic diseases if kept for prolonged time. Now, obesity related dyslipidemia how it causes obesity can cause dyslipidemia. So, you can see in obesity there is basically impairment in lipolysis. So, it is characterized by increased plasma free fatty acid level and triacylglycerol from increased lipolysis and it goes uncontrolled.

Now those free fatty acids which are released in circulation they reaches liver this free fatty acids from adipose tissue basically reaches liver from liver it is secreted as VLDL. So, basically there is increased VLDL in circulation. Now this VLDL it actually competes VLDL is hydrolyzed by lipoprotein lipase which is located in the endothelium. Now there is so, increased in VLDL that it actually competes for lipoprotein with chylomicron.

So, chylomicron breakdown is actually decreased. So, that causes hyper triglyceridemia circulating chylomicron has huge amount of triacylglycerol in it. So, there is hyper triglyceridemia. Then free fatty acids which are released in circulation they also causes causes changes in expression or activity of lipoprotein lipase. So, basically hydrolysis of triacylglycerol is also hampered. Then we all know CETP which is cholesterol ester transfer protein cholesterol transfer protein what it does it actually exchanges triacylglycerol from with cholesterol ester there is an exchange of TG and cholesterol ester between triacylglycerol rich lipoprotein and triacylglycerol poor lipoprotein.

Now who are triacylglycerol rich lipoprotein VLDL ideal and who are poor in triacylglycerol LDL and importantly HDL. So, what happens when there is CETP induced transfer of triacylglycerol from VLDL to HDL there is definitely decreased of HDL and decreased of HDL you know it is related to it is very much associated with increasing cardiovascular diseases or myocardial infarction or atherosclerosis. And apart

from that these triacylglycerol in LDL which actually transfer through CETP those are I mean triacylglycerol rich LDL when they are digested in liver hepatic lipase they form small dense LDL and this L small dense LDL is also very much related to higher risk of cardiovascular disease. So, this is the dyslipidemia arising from obesity which is characterized by hypertriglyceridemia increased VLDL in circulation and low HDL in blood. Now coming to one important topic metabolic syndrome, metabolic syndrome obesity type 2 diabetes mellitus insulin resistance these profile these days are very much discussed and this metabolic comprising or combination a clustering of metabolic abnormalities was first noted by Gerald G.

D. Raven, but he named this as syndrome X initially the name was not metabolic syndrome, but later on international acceptance were given to this term and international classification of disease coding has included metabolic syndrome in the disease list. Now metabolic syndrome is diagnosed by there are different criteria proposed by WHO EGIR NCEP, IDF, American Heart Association, but the widely accepted one are NCEP and IDF criteria NCEP stands for National Cholesterol Education Program and IDF stands for International Diabetes Federation. So, what are the criteria NCEP cause says that either of these 3 if present the person is having metabolic syndrome. What are the parameters? Waste circumference, serum triacylglycerol level, serum HDL level, blood pressure and blood glucose level.

So, either of these is altered. So, if there is large waste circumference or increased triacylglycerol level, increased blood fasting blood glucose level, low HDL level or days blood pressure I any of the 3 if present the person is coined as metabolic syndrome and there are different cut offs given by either NCEP or IDF. Now, importantly there are 2 factors which actually decides whether there is whether there will be metabolic syndrome or not. One is adult weight gain means fat accumulation and not only fat accumulation predisposition of ectopic fat accumulation. So, fat accumulation and predisposition to the ectopic region are actually deciding whether person will proceed to metabolic syndrome or not, but once again there are different other factors which influences which influence metabolic syndrome like lifestyle factor, sedentary lifestyle, poor diet, then socioeconomic factor apart from that there is genetic and epigenetic factors.

So, these are all actually influencing the metabolic syndromes occurrence. Now, remember in one important thing that thing a person is obese does not mean he is metabolically unhealthy. As I told you only considering obesity in terms of BMI will not be helpful to check their metabolic status. So, these days obesity is actually distinguished in 2 different types. One is metabolically healthy obesity another is metabolically unhealthy obesity. So, let us see who are metabolically healthy? Obese person obesity

which is diagnosed by BMI those obese person who are having metabolically healthy profile.

What is that metabolically healthy profile? So, basically they are not having any dyslipidemia, frier cell visceral level is low, HDL level is high, they are not having any carbohydrate metabolism, alterations or insulin resistance, insulin sensitivity is high, insulin sensitivity is proper as well as carbohydrate metabolism is under control also inflammatory status as I told obesity is one sub inflammatory condition. So, in those obese patient the inflammatory status is also under control. So, different inflammatory markers c reactive protein interleukin 6 they are low. So, basically they are metabolically healthy whereas, metabolically unhealthy obesity metabolic derangement is there obeys as well as metabolic derangement in terms of insulin resistance, in terms of the dyslipidemia, chronic inflammation in inflammatory markers are increased in them.

So, that is why they are known as metabolically unhealthy. Why? Because finally, it has been seen metabolically unhealthy obesity quickly these persons if they are not treated or not no interventions are given in those cases they proceed to develop insulin resistance, hypertension, cardiovascular risk, type 2 diabetes mellitus like that. But remember person metabolically healthy metabolically healthy obeys does not mean they are actually free from developing these disease. So, even prolonged phase of metabolically healthy obesity though the rate of development is much much slower than metabolically unhealthy obesity they also can develop these diseases these metabolic abnormalities if super added triggers are there or these obesity remains increasing for long time. So, we have discussed metabolically healthy obesity metabolically unhealthy obesity as well as metabolic syndrome.

So, this is all about the class let us see the key points. So, we have discussed what obesity is the imbalance rather excess calorie intake with in comparison to the energy expenditure which is tightly regulated by different hormonal and neural control and the different parameters of measuring obesity from body mass index to body fat percentage weight circumference. Then we have discussed different fat depot in our body visceral fat subcutaneous fat as well as gluteal fan and abdominal fat. Then adipokines we have discussed leptin adiponectin and resistance and peroxisome proliferator activated receptors how they are contributing in energy imbalance and obesity and finally, different effects of obesity as well as metabolic syndrome we have discussed. So, these are the targets and greater concern these days for healthcare cost and morbidity control. So, these are my references. Thank you all.