Course: Electrophysiology of Heart

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Week :01

Lecture 1: Ionic basis of membrane potential

Hello everybody. So, today we will start our first topic that is ionic bases. So, we will discuss the basis of membrane potential. So, in this topic electrophysiology of heart this is the basis after which you will understand the principles of electrocardiography mainly ECG. So, we need to understand the concepts behind resting membrane potentials or the membrane potentials and what are the factors which results in the generation of resting membrane potential. So, we will cover resting membrane potential and factors contributing to resting membrane potential.

Now, what do we understand by membrane potential. Now, membrane potential is an electrical potential difference which exists across the membrane of all living cells. Now, at rest when there is no stimulation to the cells given that is known as the resting membrane potential. Now, for example, if there is a cell generally in a cell in the middle portion of the cell there are charges equal number of positive charges equal number of negative charges.

So, usually we consider the center of the cell as electro neutral again extracellularly we have charges similar kind of equal charges both cations and anions. So, that we also consider as electro neutral, but at the surface of the membrane and just below the membrane there are difference of charges. So, as we can see there are difference of the charges at the surface of the membrane and just below the membrane which gives rise to a potential difference and this potential difference is known as the resting membrane potential when we are according it at rest. That means, when we are not giving any stimulation to the cell. So, how we record this membrane potential generally we record this membrane potential with the help of micro electrodes.

We have numerical method also where we can calculate the potential, but we can use micro electrodes like two micro electrodes as we can see over here. In a similar cell if I draw. So, we have the charge differences across the surface. So, center is electro neutral. So, we have to put a micro electrode over here and just beneath the membrane another micro electrodes.

So, two micro electrodes we have to put and this micro electrodes will be connected to a galvanometer. So, that will give rise to the recording of your potential difference. Now, usually the most important question comes around is the micro electrode diameter what is the micro electrode tip diameter as the name suggest the tip will be very fine because we want to just pierce the cell membrane not go into the center because center is anyway electro neutral. So, the diameter of this tip of the micro electrode should be less than 0.5 micro meter and this micro electrodes are made up of glass.

So, two micro electrodes usually we connect and we measure with the help of a galvanometer. We have a solution in that usually it is silver chloride in 3 molar KCL or potassium chloride solution if you could remember this it is well and good. So, with the help of this micro electrodes we could calculate the potential difference that is resting membrane potential in a membrane. So, in this way we have various tissues or cells in our body which give rise to various resting membrane potentials. Now, we see neuron or the nerve cell it has got a resting membrane potential of minus 70 milli volt very important.

The skeletal muscles has got a resting membrane potential of minus 90 milli volt. Similarly, a cardiac muscle has got resting membrane potential of minus 90 milli volt. We have smooth muscles also smooth muscles giving rise to a resting membrane potential of around minus 60 milli volt. So, these are the various tissues and cells in our body which has got different types of membrane potentials because of different ions permeability. So, next we come to the genesis of resting membrane potential.

Now, membrane potential is mainly due to the selective permeability of the cell membrane. As we know we have a phospholipid bilayer cell membrane in our body and this plasma membrane is selectively permeable. So, it is permeable not to all ions. So, it is mainly permeable to specific ions. So, what are these ions and what is the permeability coefficient of these ions we will see.

Besides that there are other added factors also like the equilibrium potential of a particular ion which we can calculate with the by using the Nernst equation. When we consider too many ions then we do not use Nernst equation. Nernst equation is of only for one single ion. We have other equations also then we have donnan effect also. And also we have the regulating pump or the primary transport mechanism that is sodium potassium ATPS.

So, these are the other factors, but before that what we have to remember is the most important is the permeability depends on the diffusion of ions or the resting membrane potential is mainly dependent on the diffusion of ions through leak channels. Now in our body we have number of channels like we have ligand gated channels, we have voltage gated channels, but there are leak channels also which will remain open even at rest. So, that usually contribute to the resting membrane potential. So, as it has been discussed that there is selective permeability Gibbs Donnan effect Nernst equation and Goldman Hodgkin equations which we will discuss with further slides. Now selective permeability of the membrane is some ions are very highly permeable while some are less and some are not.

The ions which are not at all permeable to the cell membrane they those are mainly the proteins the macro molecules the anions. The permeability mainly depends on the molecular weight and the radius of the ions in the hydrated form this is very important. The molecular weight if the molecular weight is very much which is seen in case of protein. So, they are not permeable through the cell membrane and also if the ion is in the hydrated form or not. For example, potassium ions in hydrated form has got the effective radius very less.

So, that is why the potassium permeability is very high as compared to other ions. So, if we are asked what is the permeability of potassium with respect to chloride or sodium ions. One should remember that our cell membrane generally all mammalian cells is permeable to potassium chloride ions and sodium ions mainly. So, the permeability coefficient is in the order of potassium to the very high extent compared to chloride compared to sodium. So, potassium is highly permeable through the cell membranes the permeability coefficient is very much high.

It is 500 to 1000 times greater that compared to the other ions mainly that compared to the sodium. So, this mainly constitutes that the resting membrane potential of any cell will be close to the equilibrium potential of potassium ions. Now, what is equilibrium potential I will come that to later, but this you have to remember that the resting membrane potential of generally all the mammalian cells should be close to the equilibrium potential of potassium ions because of the high permeability and the high permeability coefficient of the potassium ions. Now, this already we know there is an unequal distribution of the ions intracellularly as well as extracellularly. We have sodium ions which is present in huge number extracellularly and intracellularly we have the potassium ions.

So, the potassium ion concentration is very much in high concentration in intracellularly whereas, ECF or the extracellular fluid consist more or less of the more concentrations of sodium ions. And as I told you the macromolecules or the proteins or larger anions are present in the inside the cell that is intracellularly. So, we come to the Gibbs Donnan equilibrium what does this Gibbs Donnan equilibrium tell. Now, the two solutions when they are separated by a semi permeable membrane they should be at equilibrium when each solution will be electrically neutral. Now, how to say that the solution both the solutions A or B when it is separated by selective permeable membrane they are at equilibrium.

The quantity the total quantity of cations will be equal to the total quantity of anions. Firstly, the second thing is the product of the diffusible ions the term is very important diffusible ions we are not considering the ions which are not diffusible. So, the product of the diffusible ions on one side of the solution or one on one side of the membrane should be equal to the product of the diffusible ions on the other side of the membrane. So, when we take the two solutions which are separated by a semi permeable membrane. So, if we take this two solutions suppose this is solution A and this is solution B.

So, in solution A suppose we have x number of sodium ions in solution A we have y numbers of chloride ions. In the other solution B we have m number of sodium ions and n number of chloride ions. So, as per the rule to make the solution to be in equilibrium the x number of sodium ions at solution A should be equal to the y numbers of chloride ions of solution B. That means, the cations will be equal of solution A sorry the cations number of cations of one solution should be equal to that of the number of anions of the same solution. Similarly, in solution B the n the m of sodium ions should be equal to the n number of chloride ions in solution B.

The second rule is x and y the product of that since sodium and chloride are both diffusible the product of this x and y should be equal to the product of m and n. Now, this is in solution A and this is in solution B. So, you can see this x y and m and n products these are of the diffusible ions. Now, the problem comes whenever we get a non diffusible ion the same if I draw two solutions which is separated by a semi permeable membrane this is solution A and solution B. We consider suppose there are sodium ions 150 sodium ions there are 150 chloride ions in solution A.

In solution B suppose there are 150 sodium ions there are 0 chloride ions, but there are 150 y ions say proteins or larger anions which are non diffusible. So, in this case though we can see that the number of cations and anions of each solutions are equal, but the product the diffusible ions product are not equal because we are not considering this y because y is an non diffusible ion. So, we would not consider the product of the non diffusible ions. So, at this point of time after sometime this solutions will undergo certain changes what changes it will undergo usually what will happen there will be transfer of or there will be permeation of ions from A to B. Since, we can see that the chloride ions are not present in B that means there is deficit of negative charges.

So, the chloride ions will move from A to B. So, suppose in B the chloride ions have moved 50 chloride ions and already we can see there is 150 negative ions by this we are anyway these are non diffusible ions. And here we get in A 100 chloride ions therefore, because since it is 50 chloride ions has already passed to solution B. Now what will happen since the more number of anions are present in solution B now sodium will tend to get transferred from solution A to B. So, there will be 100 sodium ions in solution A and another 50 sodium ions will get transferred to solution B which will result in 200 sodium ions in solution B.

So, now you can see the cations 100 it is present in solution A number of anions in case of solution B number of anions that is 150 and 250 200 and cations 200 sodium this is already according to the rule. The second part of the rule is the product. So, 100 into 100 of solution A is equal to 200 into 50 of solution B this is the product of the diffusible ions. So, Donnan effect is mainly due to the presence of this non diffusible ion which states that because of the non diffusible ion since it is not permeable to the semi permeable membrane. So, there will be asymmetrical distribution of the diffusible ions across the semi permeable membrane which again gives rise to the resting membrane potential or to maintain a final equilibrium.

So, the presence of non diffusible ion on one side of the membrane affects the distribution of the other ions to which the membrane is permeable. So, that results in the asymmetrical distribution of ions across the cell membrane. So, this is called the Donnan effect. Now second we come to the Nernst equation. Now apart from Nernst Gibbs Donnan effect Nernst equation is mainly because of the one single ion.

Now how one single ion contributes to equilibrium potential across the cell membrane that we will see. Suppose we consider here we are consider a cell we are considering a glial cell. Glial cell of nervous system is very specific because it consists of one type of leaky channels usually that is potassium right. So, they do not have usually other types of channels. So, when it is when we are considering only one ion channel.

So, we calculate Nernst equation. So, here these are leaky channel of potassium. As we know intracellularly we have potassium concentration more and extracellularly we have potassium concentration less. And this gradient is maintained by none other than sodium potassium ATPS pump which is a primary proton which is a primary transport pump. Now what it does it usually throws away sodium outside 3 sodium outside and influx of 2 potassium occurs. So, in this way the potassium concentration inside the cell is more compared to the extracellular fluid.

So, what this cell will try to do. So, this cell will try to push potassium outside. So, the potassium when it will try to get outside from inside to outside this is mainly because of the chemical gradient. And when the potassium is going outside at the extracellular fluid there is also accumulation of positive charges. Now, this positive charges will cause the potassium to go back into the intracellular fluid. That means, the positive charges will again hinder the flow of this or oppose the flow of the potassium ions from inside to outside.

So, this opposite force is nothing but electrical gradient. So, this opposing forces electrical gradient which will cause the movement of ions from outside to inside. And chemical gradient which causes movement of ions from inside to outside this will continue. This will continue till there is an equilibrium reached. At equilibrium what will happen at equilibrium there would not be any net flow of the potassium ions.

Net flow of the potassium ions means that suppose there are 5 potassium ions which are going out the equal number of 5 potassium ions will go inside. So, the net flow will be 0. So, at this stage of equilibrium if we calculate the voltage across this cell membrane this voltage is known as equilibrium potential. Now, this equilibrium potential since we are considering of potassium ion. So, obviously this equilibrium potential is of potassium ion or the Nernst potential of potassium.

So, this equilibrium potential or Nernst potential of potassium usually we can record with the help of micro electrodes. But if we do not have the micro electrodes we can calculate by using the Nernst equation. Nernst equation states e x x is the ion whichever ion whether it is potassium or sodium at one time you can only calculate one ion. It states e is equal to that is the potential difference is equal to R T by Z F log e concentration of the ion outside by concentration of the ion inside. Now, if we do not consider if we just convert log e to log 10.

So, this equation will be R T by Z F the value 2.3 we get since we consider we have converted log e to log 10 that is concentration of the ion outside by concentration of the ion inside. Now, you do not have to remember all this factors R T F Z is mainly for the valency F is the Faraday's constant R is the universal gas constant and T is the temperature. So, at 37 degree centigrade core body temperature this factor R T by F is equivalent to 26.7. So, generally if we put this factor over here we get 61 by Z it is the valency log 10 of concentration of the ion outside concentration of the ion inside.

Now, depending on the valency of the ion if you want to calculate the equilibrium potential of potassium you will consider it as plus 1. If you want to calculate the equilibrium potential of chloride ion you will take it as minus 1. So, that will give the result of this Nernst potential or the equilibrium potential of each ion. So, in this way the equilibrium potential of or the Nernst potential across the cell membrane of each ion is determined. And already I have told you how Nernst equation helps in the calculating of equilibrium potential for each ion individually.

Now, this is for the individual ion like for example, in glial cells, but ours in our body we do not have only glial cells we have so many cells. So, those cells consist of various number of ion channels like potassium as I told you they are permeable to sodium ions also they are permeable to chloride ions also. So, at that point of time we use Goldman-Hodgkin-Katz equation or constant field equation. This is also known as constant field equation where we take into consideration of not only one ions what other ions also mainly sodium potassium chloride. So, you do not have to remember this formula as a whole, but what is very important is the Nernst potential or the Nernst equation you have to remember.

Now, similarly the constant has already been told what is B, what is R, what is T and the Faraday's constant. The importance of Goldman constant field equation is the voltage of the membrane potential is strongly dependent on the concentration gradient of each of this ions. The and also it depends on the permeability the membrane permeability of the individual ions. As I had already told you the potassium ions has got more permeability because of the effective radius size of its ion hydrated ion. And due to the concentration gradient the cations diffuse to outside of the cell leaving the non diffusible ions inside the cell.

Now, what is the role of sodium potassium ETPS pump as I told you sodium potassium ETPS pump it is very important not in genesis of the resting membrane potential, but rather regulation or maintaining the maintenance of the gradient of the resting membrane potential. It is very important in putting the material maintaining the gradient or the regulation of the resting membrane potential. The genesis already done by the diffusion of the ions to the leak channels and the Nernst potentials and the constant field equation. So, the role of sodium potassium pump is to maintain the resting membrane potential than generation of the resting membrane potential. And its contribution is around minus 4 milli volt and it is an electrogenic pump as it is already told you that it pumps out sodium 3 sodium ions with 2 potassium ions inside.

So, few electrophysiological terms after this it is very important the first thing is suppose this is the axis we are drawing. And here suppose this is minus 70 milli volt as I told you the resting membrane potential is usually close to the potassium ions. So, we will take it as minus 70 milli volt and here it is 0 and there we have plus 5 plus 10. So, whenever the potential is moving towards 0 that means from negative to negative it is moving towards negative towards the positive side this is known as depolarization. That means the resting membrane potential is moving from negative towards positive side that means from minus 70 milli volt it is moving towards 0 it is minus 60 minus 50 minus 40 minus 30 and it will move towards 0.

Now, 0 is usually considered the isoelectric voltage or the threshold voltage usually at this point the depolarization is at its peak and more influx of cations will result in further depolarization. And on further depolarization this peak will go up and it will reach around plus 10 or plus 20 or plus 30 milli volt and this is known as overshoot. Because anyway it is moving further away from the resting membrane potential that is from negative to highly positive voltage. So, this is overshoot. Now, again from this if it comes down towards the resting membrane potential or from positive to minus 70 milli volt resting membrane potential means the membrane potential at rest this is known as repolarization which means again the values are from positive to negative.

Further from this negative if it is further decreasing it is becoming again negative more negative this is known as hyperpolarization. So, this four few terms electrophysiological terms you have to remember that is depolarization, repolarization and hyperpolarization. Depolarization means whenever the resting membrane potential is moving towards the positive side that is it is decrease in the RMP. Usually we say it as decrease in the RMP and repolarization means the potential is already coming back to the resting membrane potential. And hyperpolarization means increase in the resting membrane potential that means it is becoming further negative the membrane is becoming more and more negative.

Now, this is very important in case of hyperpolarization hyperkalemia few conditions are there say hyperkalemia, hypokalemia or hypercalcemia. So, these are the conditions often it is asked what is the condition of the or what is the state of the resting membrane potential whether it will decrease or increase. So, hyperkalemia usually it is a conditions where the potassium ion concentration gets increased in the extracellular fluid. So, at that time you have to think suppose this is a cell and it is having this leaky potassium channels through which usually potassium will go outside. Because inside potassium the tendency of the potassium is always to move from inside to outside because intracellularly potassium is more.

But in case of hyperkalemia already the potassium concentration is more extracellularly. So, when my positive ions or the cations or the potassium concentration is more extracellularly it will hinder the potassium ions which is coming from the cell which means it will prevent the flow of the potassium ions from inside to outside which means the potassium concentration in the cell it is cell gets increased. So, or we can say the potassium will stay back in the cell. Now, when the potassium ions are staying back in the cell which means there will be positive ions or cations developing in the cell which means it is getting depolarized. The cell is getting depolarized or depolarization is occurring which means there is decrease in the resting membrane potential.

So, in hyperkalemia there is decrease in the resting membrane potential because of the accumulation of the potassium ions. The similar thing exactly the opposite pathway occurs in the hypokalemia when there will be less concentration of potassiums in the extracellular fluid and that will give rise to the increase in the resting membrane potential. Now, the question comes what happens in case of hypernatremia or hyponatremia that means when the sodium concentration gets changed extracellularly the answer will be there would not be any change in resting membrane potential. The RMP will not change at all why the RMP because as you can see in the lecture the RMP genesis is mainly dependent on the diffusion of the ions through leak channels. And in our body there are number of potassium leak channels as compared to the sodium channels there are very less.

So, generally that sodium ions do not contribute to the resting membrane potential. So, whether it is hyponatremia or hyponatremia that will not give any rise to any changes in the resting membrane potential. But definitely any change in the potassium concentration extracellularly will give rise to the resting membrane potential change. So, in case of hyponatremia or hyponatremia the RMP will not change. So, with this we come to the concluding part of the chapter where we have discussed what is membrane potential the resting membrane potential and how the resting membrane potential is generated.

The most important thing is to remember the permeability is highest for the potassium ions which gives rise to the resting membrane potential in most of the cells the resting membrane potential lies close to the potassium ions. But if a question is asked suppose the resting membrane potential is of a particular cell say neuron it is minus 70 milli volt. Then it is corresponding to which ion at that time it is the answer will be chloride ion because the chloride ion equilibrium potential is minus 70 milli volt. The question what is asked that has to be very specific if it is asked the resting membrane potential of all the cells is close to which ion then it is potassium. If a particular ion is given if a particular resting membrane potential is given and asked it is close to which ion.

Then you have to write you have to give the equilibrium potential of that particular ion. For example, in case of neuron minus 70 milli volt is corresponding to equilibrium potential of chloride. So, with this I would like to conclude today's topic. Thank you.