**Introductory Neuroscience & Neuro-Instrumentation**
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**AIIMS Rishikesh**
**Lecture - 52**
**Epilepsy: Introduction to Epilepsy and Classification**

A very good morning and welcome to Introductory Neuroscience and Neuro-Instrumentation series, my lecture on Epilepsy. I am Professor Latika Mohan, Professor, and Head of Physiology AIIMS Rishikesh.

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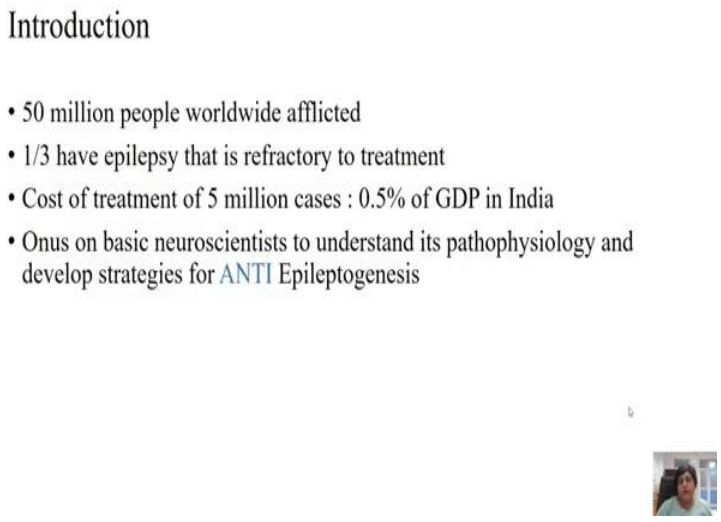


And, let us walk through one of the common disorders which creates a lot of morbidity amongst number of people. So it is a disease that afflicts almost 50 million people worldwide and many of them have epilepsy, which is refractory to treatment. So it creates a lot of discomforts and very poor lifestyle in these people.

It is a very expensive disease because it requires long-term treatment with medicines. There is no cure and upon it, that accounts, the treatment accounts to almost 0.5 percent of the GDP in India. The, once an epilepsy is established, a chronic epilepsy is diagnosed, we can only control it with various medications that are available in the market or maybe some surgery. But there is no definitive cure.

So the onus of responsibility on basic neuroscientists is to understand the pathophysiology of this epilepsy and to develop strategies to prevent the development of epilepsy in the first place or ANTI Epileptogenesis.

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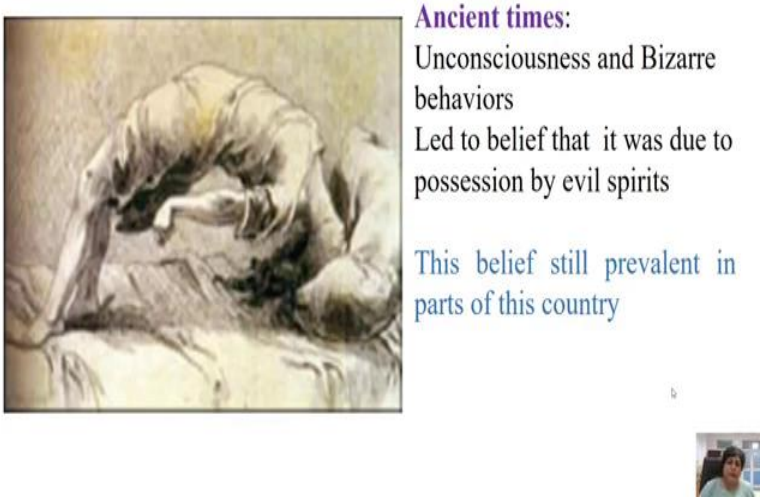


So since ancient times, because epilepsy manifests as bizarre behaviors, unconsciousness, and so forth, it was commonly believed that was due to possession by evil spirits and the treatment offered in those times was basically Jhad-Phunk and prayers and exorcism by various, you know, priests, and so forth.

And it is really sad and unfortunate that this belief is prevalent in parts of this country even today. And I, myself have had an experience where they had a 14-year-old boy, who was brought in for electro diagnostics, EEG and he had never got treatment for epilepsy, and he was from the village and he was having four seizures a day and suffering so much.

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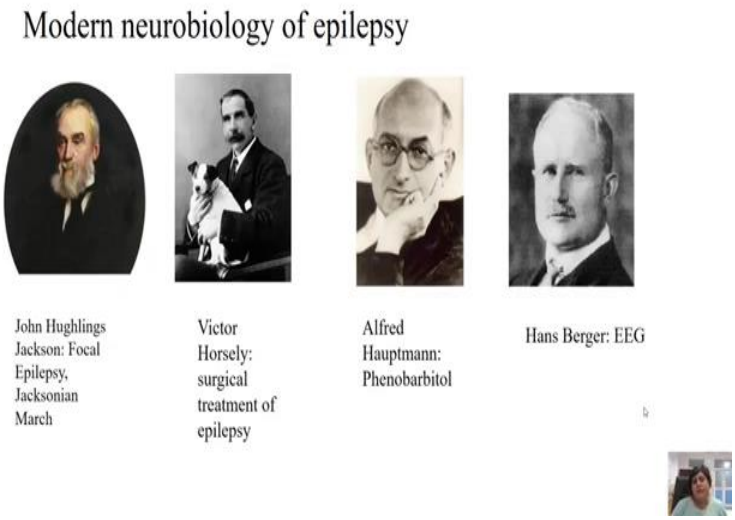


So to this era of darkness, light was brought by four good scientists, four scientists who worked in the field of epilepsy, and four different aspects of epilepsy that they shed light on. The first and foremost, he is the kind of father of neuroscience or clinical neurophysiology, John Hughlings Jackson.

He brought a scientific approach to all neurological diseases and he established a clinical neurophysiology. And he also was the first one to show that epilepsy could be due to a neurological disorder, not because of some kind of ghosts and so forth.

And he also brought in the concept of the focus of neurological illness, which may give rise to various kinds of symptoms. And this famous Jacksonian March, which we may come to later on is how this epilepsy progresses was, the name Jacksonian comes from his name and he is really the father of epilepsy, modern epilepsy as we know it.

Then, Victor Hoarsely was a surgeon and a physiologist and he worked on the surgical treatment of the physiology of epilepsy. And what he discovered was that some areas, which were sources of that abnormal electrical activity, which was giving rise to the epilepsy, could be removed, dissected from the brain, and some point of cure could be got.

Then till, say, about the early part of the 20th century, let us say about 1912 or so, there was no treatment for epilepsy available. It was a very difficult situation because many people were

having two to three seizures in a day and maybe more. And into this, light was brought by the discovery of Phenobarbital, which was the first drug where a medication could control the frequency of seizures.

And Alfred Hauptmann was a Jewish scientist who, actually he was a mathematician, and he, he basically worked on Maths and Chemistry and he discovered Phenobarbital and that was, that predated the discovery of other important anti-epileptics like Phenytoin and other modern drugs. So the first drug was basically discovered by him.

And then there is Hans Berger, who was active around 1930s actually and he discovered the technique for EEG. Now, EEG, his approach was, he was a psychiatrist. And he was trying to find reasons for psychiatric illness and how to pick up brain waves for psychiatric illness. And it was just fortunate that EEG became a very simple tool for diagnosis of epilepsy as a serve aside spin-off benefit.

So these are the four approaches one can even today take in the modern world as to how we can deal with epilepsy. It can be either through your basic physiological approach, with the surgical treatment, there are still so many things that need to be understood. Pharmacological treatment of epilepsy developing various models, and electro diagnostics and electrophysiology. These are still available as the approaches to research in epilepsy.

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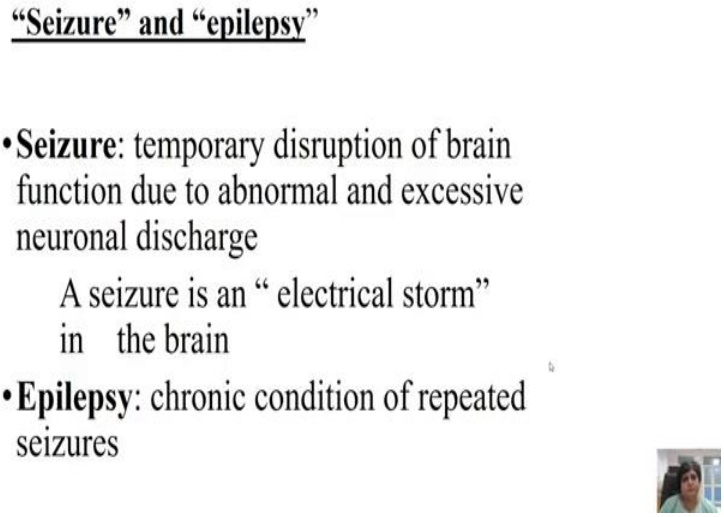

So at the outset, I would like to clarify what is the difference between use of the word seizure and what is epilepsy. So seizure is a one-time event that is a temporary disruption of brain function due to abnormal or excessive neuronal discharge. So it is a one event when a kind of electrical storm, tornado kind of takes over the whole brain. So there is an abnormal electrical discharge which completely takes over entire brain function.

In contrast, epilepsy is a series of seizures. So if you have a one-time seizure, it does not constitute epilepsy. Maybe due to various things; sometimes dehydration, sometimes you know, ill-health. So many things are, there are reasons for you know, the epilepsy kind of happening, the reasons for seizures happening. Whereas, epilepsy is when you keep on having chronic condition of seizures, two to three times a day and repeatedly having these symptoms.

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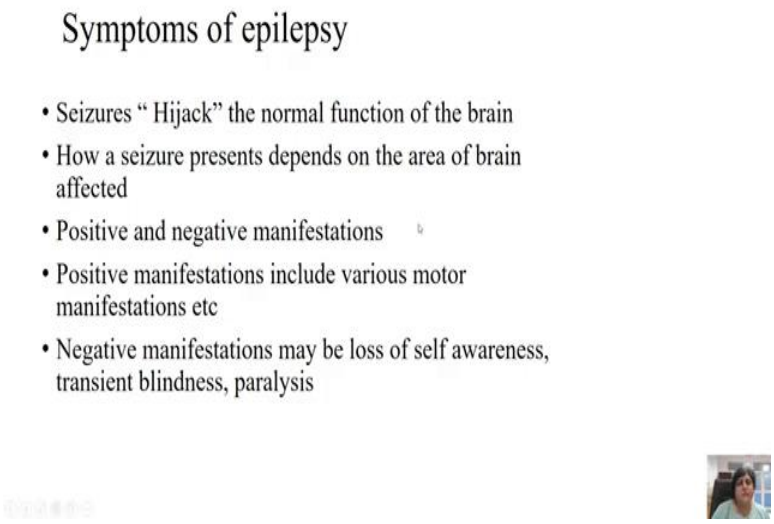


So what are the symptoms of epilepsy? Seizures hijack the normal function of the brain. So firstly, how a seizure presents itself depends on which area of the brain it is coming from. So, the, if it is a small focus somewhere, a small area somewhere from where there is injury or damage to the brain. It will start activating, increased number of electrical activity will start activating in that particular area.

And, as you know, the various areas of the brain subserve various functions. So, the frontal area is basically involved with thought process. The temporal area is associated with sound-hearing, the occipital area is associated with vision. So if there is a seizure, which is beginning from any

of these, like say, from the temporal area, the person will start hearing weird sounds, some different kind of sounds. Or if it is starting from the occipital area, he may see some lights or these things. So this episode is known as aura and this heralds the beginning of a seizure.

Then there are certain positive and negative manifestations. A positive manifestation which we all commonly known of is a severe muscular spasm, either person goes into an absolute kind of contraction, muscular contraction from head to toe and he falls down to the ground.

And after that, after this spasm is relieved, which may last few seconds, then there is alternating relaxation and contraction of the muscles, which is what we see, known as the tonic-clonic phase of the of the seizure. So these are the positive manifestations. So I would include the hearing of abnormal sounds, the seeing of abnormal visions, this acute and spasm of the body, and the tonic-clonic contractions of the body. These are all positive manifestations of the seizure.

The negative manifestations are the person may fall into unconsciousness. Now, what happens is that the seizures when they are hijacking the normal function of the brain, there is a huge and massive spread of electrical impulse throughout the cortex and the lower parts of the brain also.

And this basically uses up all the neurotransmitters, it uses up the ATP. It uses up everything you know the endocrines, the hormones, everything. And what results at the end of that is that everything is wiped out and the normal brain function takes a little time to come back. So the person goes into a period of unconsciousness.

And that, following that you may also have transient blindness, confusion, paralysis, and so many other features. So positive and negative are the various features or clinical manifestations or behavioral changes that you will see in a patient of epilepsy. And after that phase is passed, he may be absolutely normal for a longer period of time till he has another search seizure.

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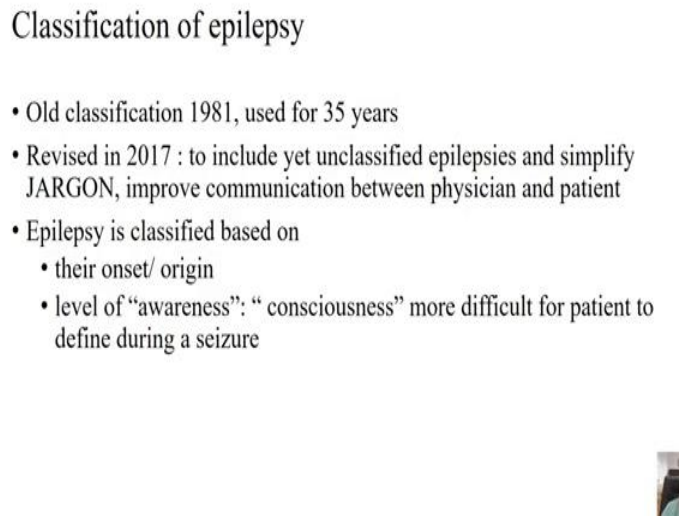


Now, classification of epilepsy. We had an old, very complex kind of classification which existed for almost 35 years. This was revised in 2017 by the International League against Epilepsy and it was simplified and made in such a way that it made communication between the physician and the patient easier.

So Epilepsy is being classified based on the onset of its origin and the level of awareness or consciousness which the patient experiences during that particular period of epilepsy.

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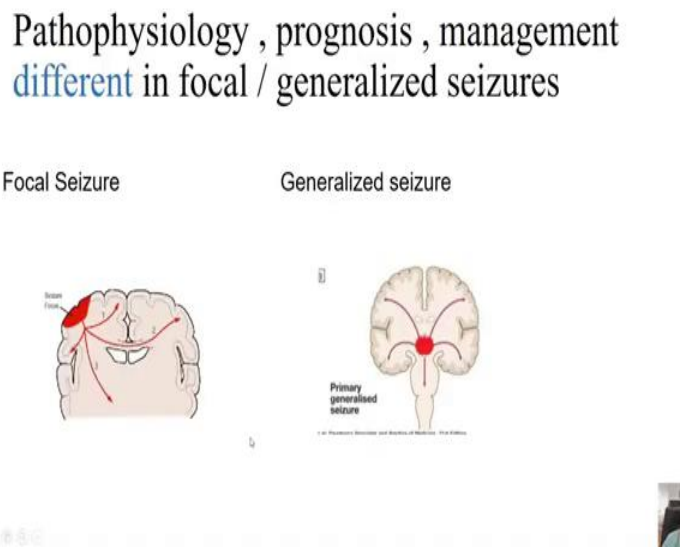

So broadly, there are two types of epilepsy. You have focal epilepsy and you have generalized epilepsy. Now, this shows the focal seizure and a generalized seizure, how it develops. A focal seizure will start at any area of the brain which may have any injury or any kind of a malfunction.

So it can be any, if you see, there is almost like a globe like a 360-degree thing of the brain. You can have a seizure focused at any particular point of any dimension. It may be 1 centimeter in diameter, it may be 20 centimeters in diameter; does not matter. It is basically, the size is not important but the area is having abnormal electrical discharges.

At some point, these discharges start to become excessive and they overcome the normal controls which are present, and then, they may track into the normal tissue. So this normal, when it starts tracking into the normal tissue when the normal tissue gets excited, you start having the initial features, that is, the aura of the seizure and then it spreads 360, there is the secondary generalization, it spreads in all direction; it can go in any direction. You cannot predict which way it will go. And you will get a, end result would be a focal seizure.

A general, generalized seizure, the activity which is abnormal lies somewhere in the sub-cortical areas, in one the nuclear, generally, is the thalamus. They may be some abnormal channels, you know, like some type of typical calcium channels, which may be the source of abnormal electrical activity.

And once they reach a certain degree of kindling and secondly, the cortex also is hyper-excitable for some various reasons, which I will tell you about later. There is a catastrophic one-time and complete spread from the center of the brain on all 360 direction and you get what is the generalized tonic-clonic kind of seizure. So this is the difference between, this is the broad classification.

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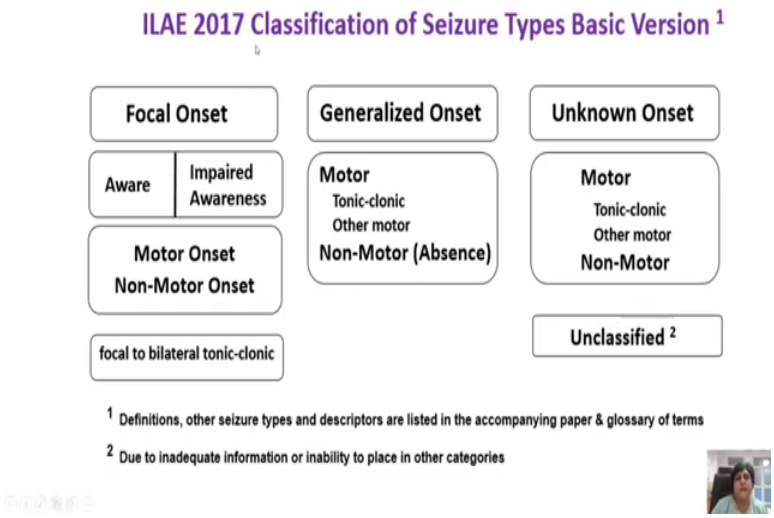


So let us see the classification, the ILAE Classification, 2017. You have Focal Onset, you have Generalized Onset, and you have Unknown Onset. So focal onset, I have explained now, we are talking about onset here now because that is where we expecting the seizure to start from.

So in focal onset, you may have two types; one is that person is completely aware of what is going around, on around him when he is having the seizure. He does not lose consciousness or he may have some altered consciousness. And you may have motor type of seizures and non-motor also.

An example of a non-motor seizure is that he may only have a thought disorder or he may just have hearing of certain sounds. Or he may have only some other, you know, symptoms depending on where that abnormal electrical activity has traveled, it may not travel to a motor area.

And it can have generalized, you know, where focal to bilateral tonic-clonic, it is what is called secondary generalization. That means from the focus it has started and it has spread in all directions and get to a generalized seizure.

When you talk about the generalized onset, basically here, there is no question of impaired awareness. There is always loss of consciousness and there is a motor kind of seizure where you can have tonic-clonic contractions or you may have a myoclonic kind of contraction.

Or you may have what is the absence seizure, where the person just loses his consciousness for a moment, may not have loss of muscle tone and may not fall to the ground, but he will just have a blank spell and that is what is known as absence seizures. It is very typical in young adolescent people who have this kind of condition.

And the dustbin diagnosis is your unknown onset seizure where maybe motor, non-motor, where you cannot specify where a, is coming from focal or its coming from generalized or it is having both kinds of episode. Certain clinical conditions, very difficult to classify and that is why we call it a seizure unknown onset.

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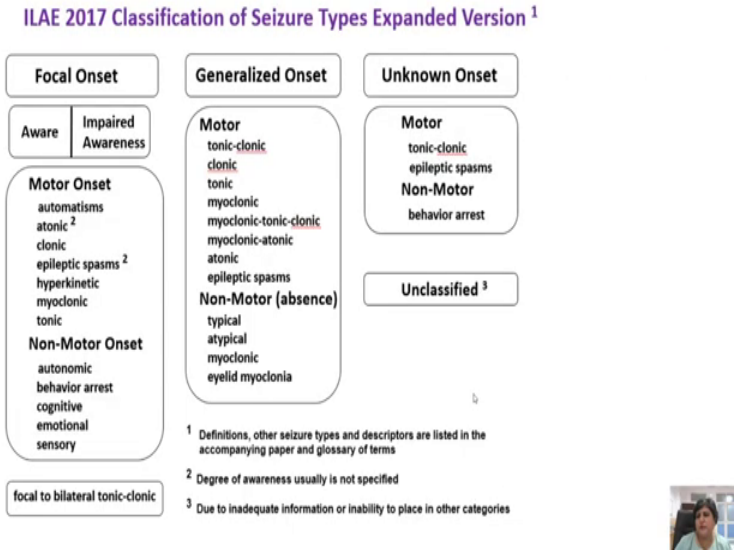


So this, there is a, you know, more detail sort of, you know, clinical details based on various typical type of features that you may have seen. It is, there is a more verigeneated kind of classification also. But broadly, it comes down to focal and generalized. And where you cannot figure out whether it is focal or generalized, unknown.

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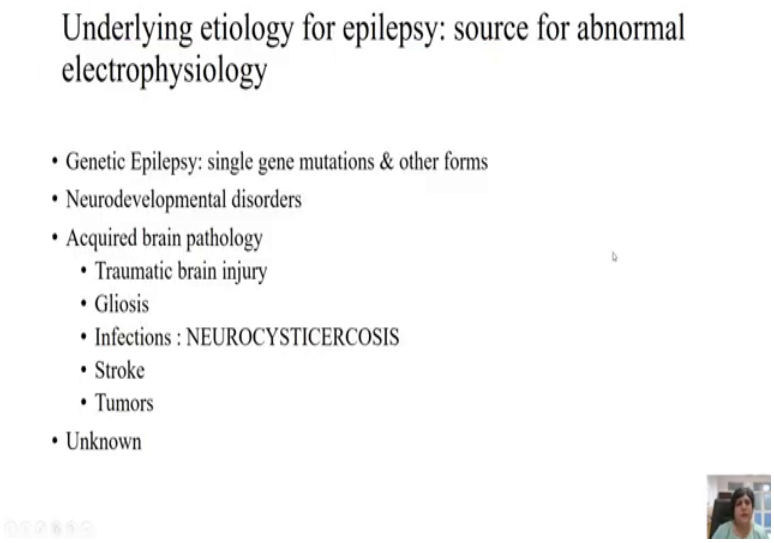


So let us understand what is the underlying etiology or what causes epilepsy and what is the source for this abnormal electrophysiology. So genetic is the first that there are certain genetic disorders, certain known syndromes where there are abnormal channels and there maybe, you know, presence of certain abnormal formations, which are may be due to various genetic mutations and other forms which lead to epilepsy.

Then certain neurodevelopmental disorders are there where there are abnormal brain formations. Then, these are person, the child will have seizures from birth more or less, and will present very early in life with various aspects of a seizure. The other is the acquired pathology, which we commonly see. Any trauma to the brain like a head injury; most head injuries, few patients are associated with some degree of seizures.

There may be a fib gliosis is a kind of fibrosis of the brain. So if there is like a scarring of the brain. So, suppose there is been a head injury and some portion gets scarred, that leads to the, you know the seizures persist and it becomes a kind of a permanent problem of epilepsy.

Certain infections, like neurocysticercosis. Now, cysticercosis is a kind of worm and this worm infestation basically takes place especially with people who are living in rural areas and with animals, so it is very common in my state of Uttarakhand.

And the problem is that this forms a kind of cyst or kind of a small round kind of a cavity in the brain and this becomes a source of your abnormal electrical activity and causes the establishment of seizures and epilepsy. Stroke also gives rise to epileptic symptoms and certain tumors maybe that manifest especially. The first time when they are present, it may be in the form of a seizure.

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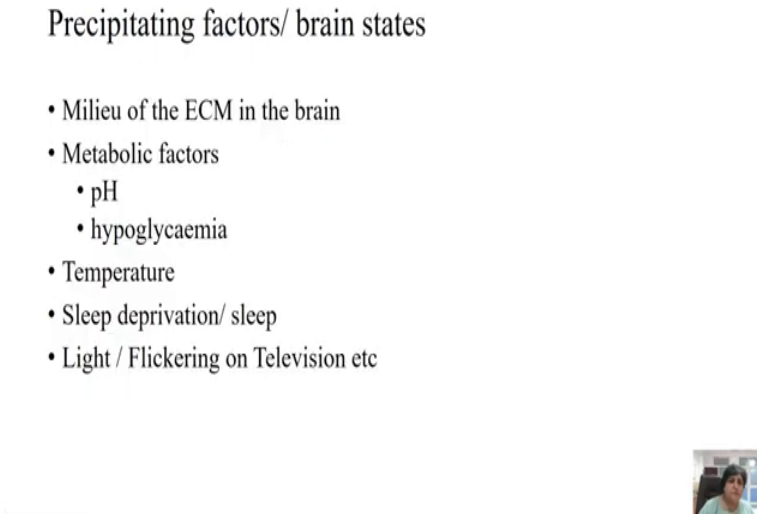


So those are the etiological factors, which I just covered that there are certain things which give rise to the epileptic state. However, each, when a person has a tumor or when he has a brain injury, there will be phases when he is not having a seizure, he is normal and there will be phases when he will be having the seizure. So what precipitates a seizure in a person who has the tendency to have it?

So it may be the extracellular fluid in the brain; what is the, what is the milieu, you know that may be certain, the pH may be altered or maybe he has a dehydration. Certain metabolic issues like hypoglycemia or low blood sugar may be there.

So these are when a person has a tendency to throw seizures because he is got the presence of any of those points that I brought out, either he has got some genetic reasons or he has got some traumatic brain injury or he has neurocysticercosis, cysticercosis. It maybe, not that he is having the seizures all the time because of that, there will be certain circumstances in which the seizures will get precipitated.

Fever, temperature; that is one of the, you know, person has a high fever, it will precipitate the seizure. If he does not have a good night sleep, sleep deprivation, very often will precipitate seizures or if you may sleep too much, certain seizures only show up in sleep and in some few rare cases, a flickering light on say like television, that may precipitate a seizure.

That is why we do a test called focal, we do this test called photic stimulation, and people who have a tendency to respond to this flickering light on television they have a convulsive response every time you show them that photic stimulation at a particular frequency. But this is not there in every patient of epilepsy.

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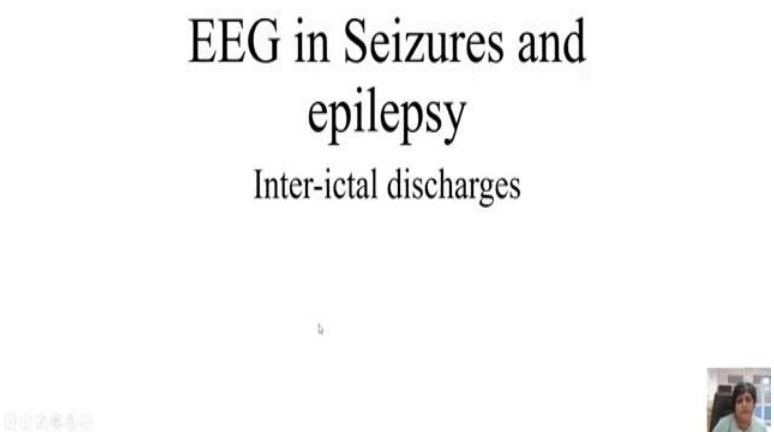


So this, how do we diagnose on EEG that a person has got epilepsy? We see something known as inter-ictal discharges. Now, inter-ictal means in between seizures. So person, if he is having a seizure and you try to record EEG, you will get nothing because there is so much of muscular movement. It is only in between that you are able to do the recording.

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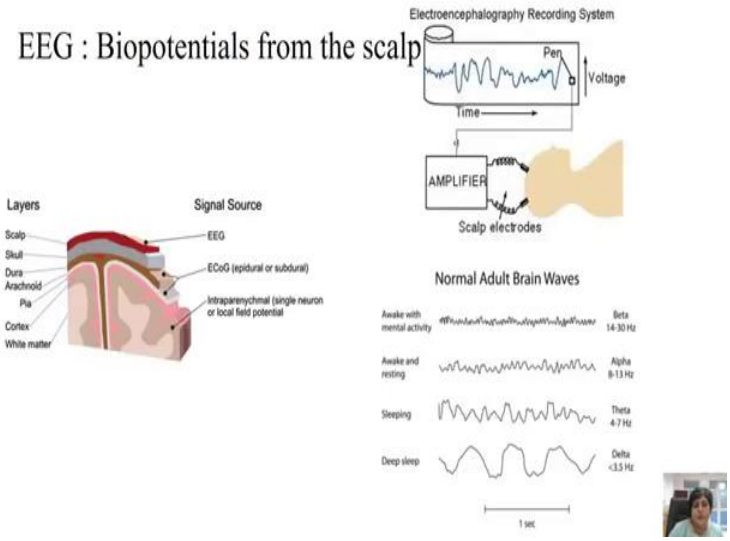


So how do we do an EEG recording? EEG is basically the recording of biopotentials from the scalp of the brain. So if you see this is a cross-section of the brain. And you can see that the signal is being, is going to come from the cortex. And it is coming through the various layers of the cortex and we are basically recording it with electrodes on the scalp in, and generally, it is recorded in microvolts.

So we have a, an (ampli) this, whatever recording of potentials we pick up, we put it through an amplifier, and then we are able to digitally record it now. This is an old diagram, so this shows it on a pen and paper but you record it digitally these days. And you get various types of frequency amplitude, this thing, recordings.

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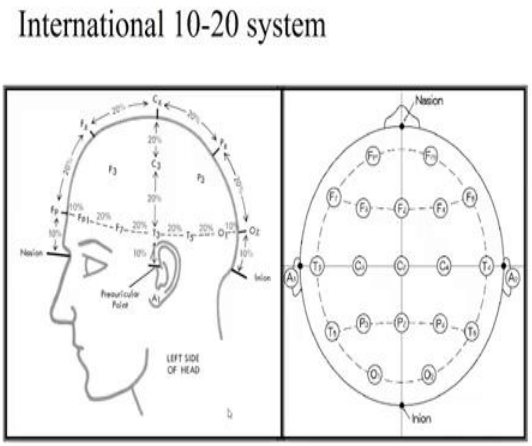


The electrodes are placed in what is known as the 10-20 system. It is like a grid, like a latitude and longitude on the globe. And you have these various points from which, which are, you know statics, standardized and they are, you know, kept in and you can make this as dense as you want, like even make variations where you have electrodes closer and closer to each other.

And so, basically, two types majorly of the records that you can take. One is that you connect one electrode to another in the scalp. Like F3 can be connected to FZ and the other is that this is connected to the recording electrodes on the ear, which is a reference electrode.

So you can have a bipolar or mono-polar record of the brain. And basically, in between these two, you are measuring the potentials in terms of amplitude and frequency.

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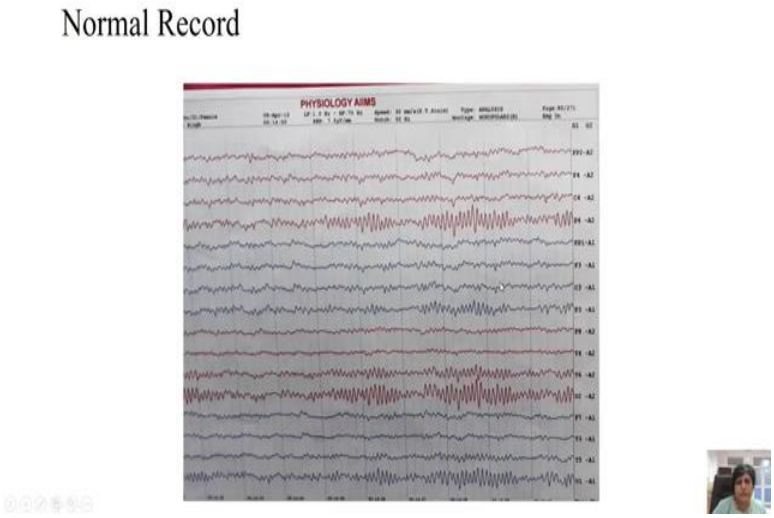


This is what a record looks like and you can see on this thing, right side you have this entire number of electrodes. This is basically all of them are to the referential, that is the various electrodes have to point it to the reference electrode, combined within the reference electrode and you are seeing this particular kind of recording.

This, if you see P4, parietal four to A2, you will see this waxing and waning kind of a record which is typical of alpha waves of the brain. So there are certain normal standardized, you know, waves that you see which are there in a normal brain. You will see certain abnormal artifacts also which is because of electrical discharge and all and they are not normal, which are not abnormal in terms of electrophysiology. But you are, there everything is up in the EEG, even an ECG can be picked up in an EEG.

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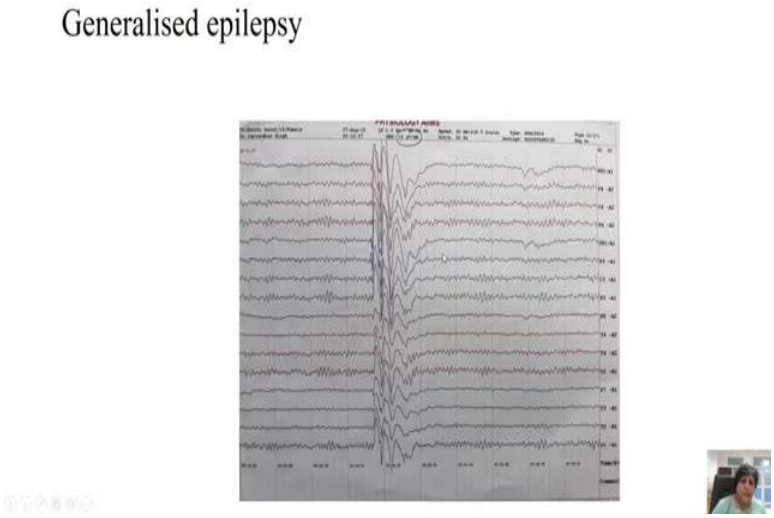


So this is what a generalized epilepsy will look like. So I think it is staring out at you in the face. You can very clearly see that this record is you know, the amplitude is the same in all the electrodes and it is, it is in the same place and it is strong.

And this is a typical record, good record for a generalized epilepsy with this broad-based, sharp wave which is there. You can 3, see 3 coming in phase of about 1 second. So the, it is about 3 hertz, this discharge.

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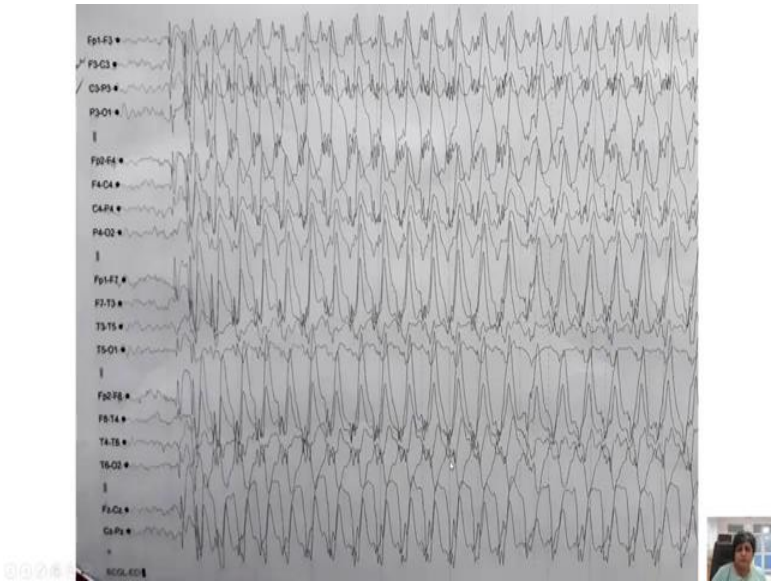

This is another recording of a generalized epilepsy. On the left side, you can see a bit of the normal discharge, and then you can see there is a, these high-amplitude sharp waves which are there persistent throughout.

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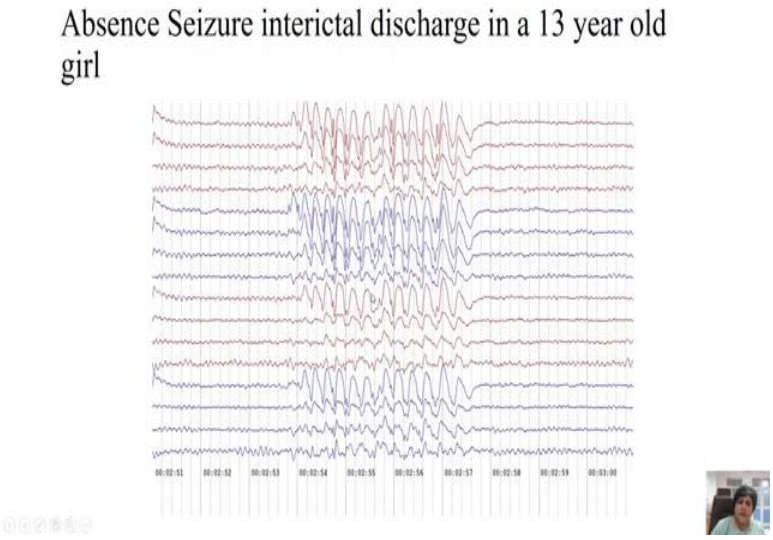


This record is of absence seizure in a 13-year-old child. Absence seizures are common, is a specific subset of generalized seizures, which are not accompanied by a loss of conscious or loss of motor or a tonic-clonic kind of activity.

There is loss of consciousness for a small period of time where the child does not remember where he was and he may have a blinking kind of action. And there is a typical wave and spike, wave and spike pattern which is recordable on the EEG.

So this is one of them, you know, standard epileptic signatures, which was and this was the first to be recognized and this is what established EEG as a tool, electrodiagnostic tool for epilepsy.

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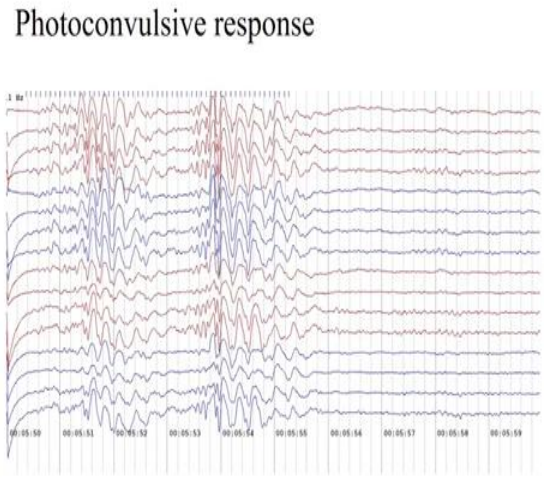


So, in this, I am showing a photo convulsive response. We have given a stimulus here, 0.1 hertz of repeated photic stimulus, and in response to this photic stimulus, the person is having the presence of a discharge. Whereas, you see the rest of the normal, thing is normal.

Now, what I were again, bring out here is that the patient is not having a convulsion. He is not having any behavioral effects. This is recorded only on the EEG in response to the light. So he is not having a seizure, he is having the electrical activity in the brain which is, we are able to pick up in a EEG and come to the diagnosis that this person has got the tendency to have seizures and he is a patient of epilepsy.

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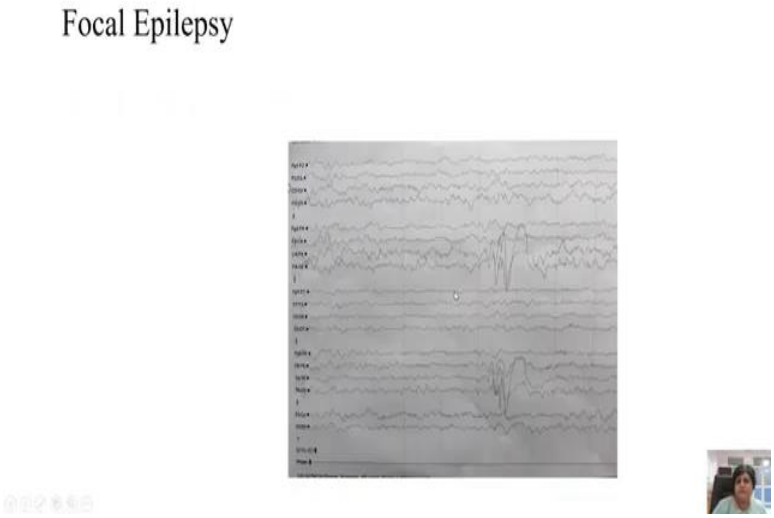


Focal epilepsy can be seen very clearly in this particular graph. If you see in this particular, that only in the right-sided electrodes are all labeled in even numbers and left-sided are labeled in odd numbers.

So if you see the electrical discharge, the abnormal electrical discharge is coming mainly from C4-P4 and it is coming from T4-T6. So it is basically coming only on the right side. It is not seen in the left-sided electrodes.

So it is coming from one side or one corner of the brain and it is not really spreading to the other aspects of the brain. It is very typically present in the central and parietal areas of the right side. So this is a typical record of a focal epilepsy or a focal, a focal discharge.

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Thank You

So with this, a little bit of introduction to what is epilepsy and how we are able to diagnose it. I will end today's lecture and I will give deeper into the various insights of what is the pathophysiology of epilepsy, how it develops in my next lecture. Thank you very much for a patient hearing.