

Bioengineering: An Interface with Biology and Medicine
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Lecture - 25
Clinician's Perspective-IV

Welcome to the MOOC-NPTEL course on Bioengineering an interface with biology and medicine. In our effort to have some clinician's perspective, for biology for engineers, today we have invited Dr. Kunal Sehgal. Dr. Sehgal is Director of Sehgal Path Lab.

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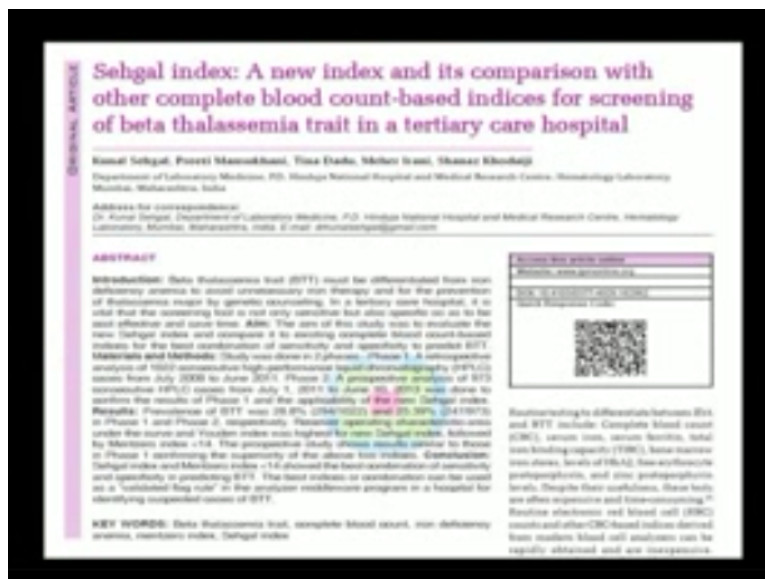
He is MD Pathology from Post-Graduate Institute of Medical Education and Research, Chandigarh, India in 2007. He finished the MBBS from St. GS Medical College and KEM Hospital, Parel in Mumbai in 2003.

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Dr. Sehgal was awarded Kataria Gold Medal for the best overall student of PGIMER 2008. The award was presented by the Prime Minister of India in 2009. He was also awarded Silver Medal in recognition of merit during the period of studies for MD Pathology at PGIMER. He was awarded the International Union Against Cancer, International Cancer Technology Transfer Fellowship at John Hopkins Hospital in Baltimore, USA.

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Dr. Kunal Sehgal has published over 50 papers in national and international PA review journals.

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Research Interests:

- Flow Cytometry - Instrument Setup and Standardisation
- Flow Cytometry based, Minimal Residual Disease Detection in ALL
- High sensitivity PNH assay using FLAER
- Research Parameters on CBC analysers

His research interest include flow cytometry – instrument setup and standardization, flow cytometry based minimal residual disease detection in ALL, high sensitivity PNH assay using FLAER, research parameters on CBS analysers.

It is our great pleasure to have Dr. Sehgal with us who is going to share you his clinical perspective and several examples where he is going to illustrate you how engineering discipline is so crucial for medicine and why clinicians still depend so much on various engineering devices, the data analysis tools and there is so much still gaps and unmet needs, which has to be fulfilled for the clinics. So let us welcome Dr. Sehgal for his lecture.

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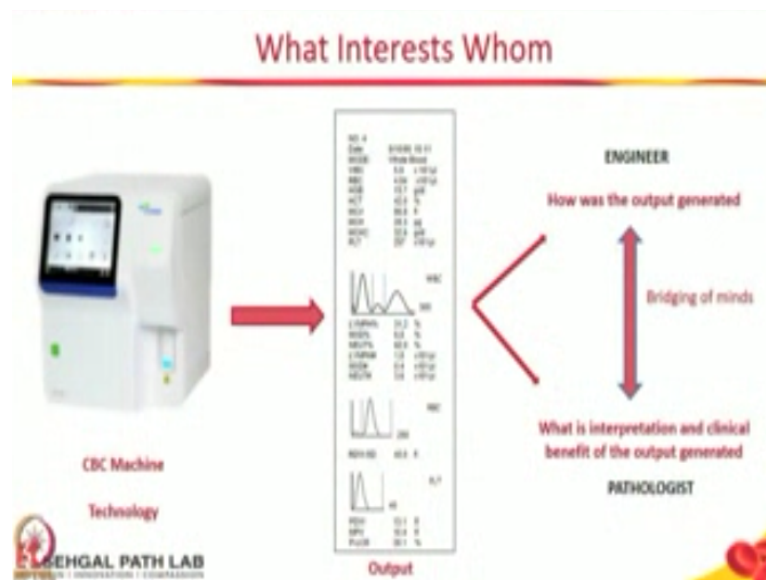
Bridging the Gap- Pathology meets Engineering

Dr Kunal Sehgal, M.D
Director, Sehgal Path Lab
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(()) (02:46) It is a pleasure to come here. This is my first time talking to engineering students like you. I like to thank Dr. Sanjeeva for having me here today. I intend to talk pathology meets engineering on bridging the gap and the idea or where it all began was when an engineer is working say in a lab or in a research setup trying to build something, the ultimate aim is you wanted to be used. You wanted product.

You want the technology output to be used massively by clients and in the medical field by doctors and by patients and when a doctor is looking at a technology product, he is more interested at what is the output of a technology product.

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And he says how can I use this product for my patients. So the interface, which typically an engineer looks at is the interface between the machine and the output to how the output was generated and a doctors typically looking at the interface from the output to the result. Can I just show you an example of how this works? For example, if you see this is a CBC machine. This is the technology and this is the output, which is a strip coming out from the CBC machine.

Which tells your hemoglobin, WBC, and platelet count and the engineer wants to know how is the output generated, how can I better it, what was used to generate this output and I as a doctor typically want to know what is the interpretation of this output, how can I use it for the patient.

Majority of us laboratorians do not care or do not understand and that is why we do not care to how the instrument works or what the output is, what went wrong.

And we call the service engineer, please do the needful. I want my reports today before the lab, the patient has to collect the report. So this is the typical attitude, which majority laboratorians always have and it is not out of lack of interest or lack of time and lack of understanding and the idea is can we bridge this gap between the engineers and doctors and why am I talking about bridging because this is how I am here today possibly.

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Interaction between Hinduja Hospital and IIT Bombay

Hinduja Hospital – Joined Health Consortium at
IIT- Bombay in August 2013

Consortium Membership

- | | | |
|--------------------|------------------------|-------|
| ➤ IIT Bombay | ➤ Strand Life Sciences | ➤ KEM |
| ➤ TMC | ➤ InnAccel | ➤ SRL |
| ➤ NIBRH | ➤ Hinduja Hospital | |
| ➤ Span Diagnostics | ➤ Drishti | |

I was at my previous place of work, which is Hinduja Hospital and I was there for five years and while I was at Hinduja Hospital, we interacted casually with a few IIT faculties and then we came to know that is health consortium in IIT Bombay, and Hinduja Hospital joined the consortium.

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Objectives for partnering with IIT

- Bridging the Gap between medicos and engineers
- Indigenisation of products for better and cheaper availability
- Innovation in context of local needs

The objective of me and Dr. Deshpande who were heading the hospital team at that time can be partnered with the engineers and bridge the gap between the medicos and the engineers, can we look at indigenization of products for better and cheaper availability and can we look at innovation in context to local needs. Because you know there is innovation, but you need to use it for the Indian needs and the Indian patient's purpose.

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Dr C Balkrishnan
Consultant Rheumatologist

Sjogren's syndrome

- Dry eyes, dry mouth (immune-inflammation of the tear & salivary glands)
 - A proportion get other organs involved.
 - Dry eyes – good ways to assess dryness
 - Mouth – whole salivary flow over a certain time etc
- Can the deficiency of saliva be quantified**
? Chemical analysis / ? Can humidity in the mouth be analysed.

So this is where we have to multiple on meetings we interacted, IT faculty presented certain papers, then at one of the meetings, what we did is, we circulated to all the doctors in the hospital. There were 100 of them and we said, just give us a wish list where you would want

somebody from IIT Bombay to work on, which would help you improve your patient diagnosis and Dr. Sanjeeva asked me to share a few examples from that presentation.

So I am sharing that today just to give an idea what, you know how different can be a need of a doctor and if you know the need of a doctor, you would love to work in that area potentially and that is why I am here today. So Dr. Balkrishnan was a rheumatologist, a joint who looks at joint problems, autoimmune problems, he sees these patients very often Sjogren's syndrome. Basically, a disease where you have dryness of mouth and dryness of eyes.

If I ask you do you have dryness of eyes, maybe 5 of will tell me, but how do I compare the dryness of eyes of patient A to patient B to patient C. There is no objective way of measuring it. Dryness of the mouth, can you study the deficiency of saliva, can the humidity analysis be done, can the chemical analysis be done. There is no test available today. Then I remembered somebody asked in the meeting, one of the IT faculty raised.

Can we use a bubble gum or a chewing gum and give it some colour reaction, intensity of colour change and there was an idea right there. So you know it is just talking just producing an idea. So the idea was just to share our wish list, put this wish list on your common forum, there might be somebody from one amongst you who would say this is an area, which I would like to work. Another example from, if somebody has seen an MRI machine or gone under that, it is extremely claustrophobic, extremely alone.

You are lying down with eyes closed in a dome, you cannot see anything, you are in loud sounds, can there be a silencer for the MRI machine, so why are we not building towards that and how does it helps.

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Dr.J.S.Bapat
Consultant Anaesthesiologist

1.To evolve silencer mechanism for MRI machine.

2. To develop wireless ECG monitors to use during surgeries with specific frequency filters to avoid artifacts generated by surgical cautery machines.

Can there be a wireless ECG monitors? In movies, you would have seen or you would have seen ECG monitors, multiple wires through your chest, hands and legs. Why cannot in today's (()) (07:44), we have wireless monitors. This becomes very important because in surgeries, doctors use cautery. The frequency of a cautery mixes with the frequency of the leads causes artifacts, so that is one of his wishes.

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Dr Jacqueline D'Mello
Consultant Anaesthesiologist

- **Transport ventilator:** A ventilator that can be used for ventilating patients while they are being transported from one place to the other.
- **Peripheral vein locator for intravenous access:** A device that helps to locate veins in patients whose veins are difficult to find and in whom intravenous access is required.
- **Patient controlled analgesia pump:** A pump that delivers an analgesic solution to the patient who is in pain and the patient is able to take boluses of the drug with the help of a hand held device.



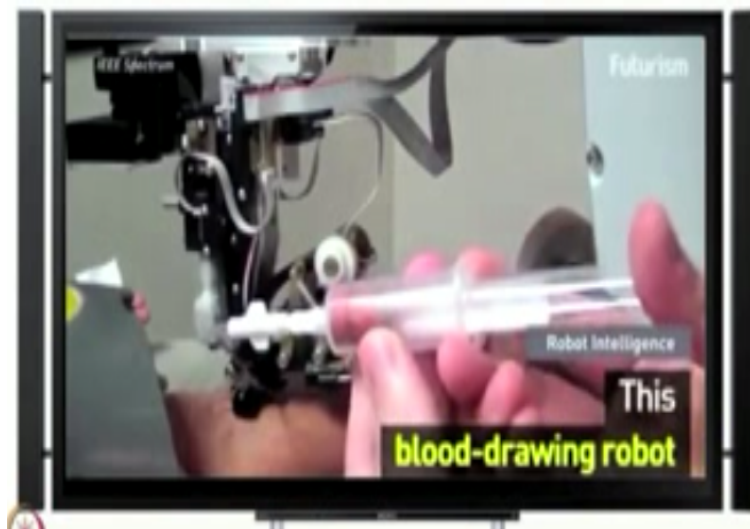
Another anesthetist, Dr. D'Mello said many a times, the patient is admitted to a local nursing home ICU is on a ventilator. He wants to move to a higher institute, can we have transport ventilators. There might be some available, they are corporate, they are expensive, can we have

indigenous simpler ones. She said as the anesthetist, when the patient comes to the OT, other doctors for various needs had fired all the veins.

You cannot even get intravenous access to blood or to give them blood. It is so difficult; so can we have an automated intravenous vein locator. This has been very difficult, very difficult on children, cancer patients or on chemotherapy and her third question was can we have a patient controlled analgesia pump. If I am having chronic pain because of cancer sitting at home, can I have a pump, which can modulate the dose of my drugs and I can pump myself in a regulated manner.

So these are certain questions just to highlight. They are very simple, but currently we doctors do not have solutions for that and we need you guys to help us, work towards these kinds of things. While I was going through this wish list and preparing it last week, I got this video on WhatsApp, which I would like to share. This is something called as Veebot venous blood collector, this is an US based company, which has produced this. I do not know if the video is playing.

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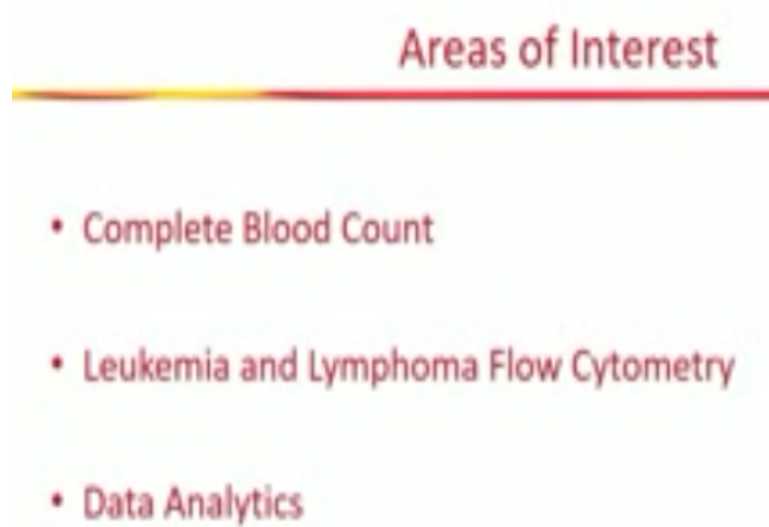


There it goes. So basically what it does and it will go into the site. I will not go into the whole thing detail. It uses technology very simple. There is a robotic arm. Like you see, it will go and the patient put his arm, it will do image analysis, highlight your veins, it will also do ultrasound,

it will see if the vein is big enough, it will put in the needle, the person is just collecting the blood sample at that vein.

If you have a pediatric patient, if you have difficult veins, and this case is very often. This the most common thing done in every hospital laboratory. Just think about automating it and mass production of this technology every lab is going to do. Typically, this is an US based technology, by the time it comes to India, it would be 5 years, 10 years down the line, it will be very expensive. Can we look at indigenization or simpler things? This is just one example that I would like to share with you.

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What various doctors in every field is thinking. Today, I am here as a laboratorian, but every doctor would have his/her wish list. So I'm here to present my list in a way or share with you the areas I work in and 2 areas I touch upon is, 1 is CBC, which is like a routine test, which we do day in and day out, many of you would have given blood sample and checked your hemoglobin. That is a CBC test. The other area is blood cancer, that is the main area I work on.

Third area I just touch upon a little bit on data analysis from a laboratorian perspective.

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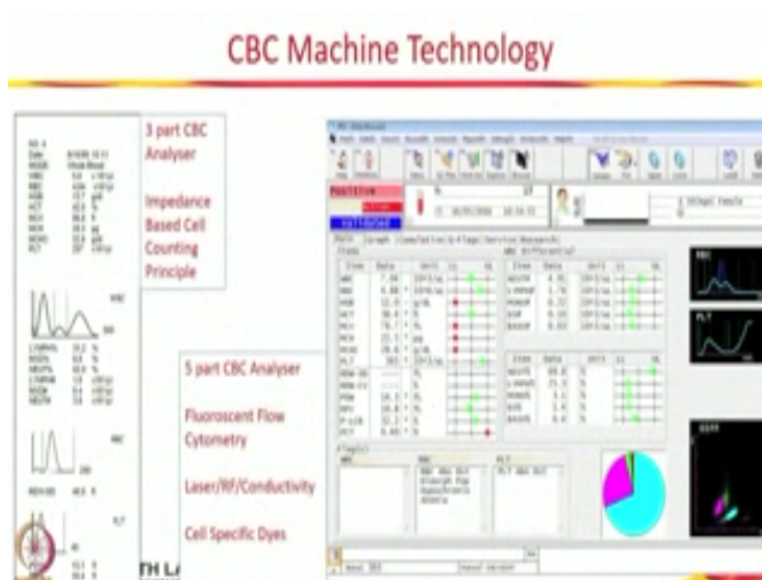
Complete Blood Count

- The most basic screening test required by all physicians
- Includes Hb, WBC Count and Platelet Count
- CBC machine has been at the forefront of technology changes in a laboratory
- We have moved from manual Hb measurements in 1980's to Automated 6 part cell flow cytometer with more than 100 reportable parameters

As I said the most common test that is the CBC. This CBC machine has been a forefront of technology change as far as laboratories are concerned. From manual methods from hemoglobin measurement if you have to do manually in 1980s and I have done it with my father in my dad's lab. I have done the manual method when I was maybe 8 or 10 years old and then you had those floor based machines, then came the bench tops, now we have almost desktop size machines.

My dream would be having a portable machine maybe in your cellphone and that is the way we are progressing. This has been forefront of technology and that is why said, let us start with this machine.

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Typically, this is a 3-part machine, what will able a simplest machine. This is very popular in India. This is like a 5-part machine. Typically, from an engineering aspect it will do the simple electrical impedance in typical cell count. Now the newer machines in addition to electrical impedance, fluorescent flow cytometry is used. They use flow cytometry light scatter, they use combination of laser light scatter or radiofrequency, conductivity.


Look at cell population and differentiate from each other to give us a WBC count. They also look at specific dyes. So you have certain dyes binding with certain cells, it will say, this is this cell and this is some other cell based on a protein or a diet, which it binds to. It is continuously evolving. So if you see, this 1 gave us numbers and some graphs; this gives the same numbers and graphs.

In addition, what it does is automatic analysis of these graphs and give us some plats and said, okay the RBC are at normal distribution. There are dimorphic population, 2 sizes of red blood cells. I can see there are 2 populations over here, two peaks. An experienced person or a technician who is never trained for doing graphs cannot see it. So the company had automated the interpretation over here and giving you this is dimorphic property. So there is more the software is doing, a better result, a better data for better use.

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CBC ADVANCE

- CBC and Peripheral Smear
- Automated Beta Thalassemia Screening
- Automated Malaria Detection
- Automated Reticulocyte Count
- Reticulocyte Production Index
- Advanced CBC parameters - Ret He, IPF & others



Syntex XN-6 350

How can I put these parameters into clinical use and take them forward? So this is the test which has started and what all does it do?

CBC ADVANCE			CBC ADVANCE		
HEMATOLOGY			HEMATOLOGY		
COMPLETE BLOOD COUNT (Hemogram)			DIFFERENTIAL COUNT		
TEST	DESIRED VALUE	REFERENCE RANGE	TEST	DESIRED VALUE	REFERENCE RANGE
Hemoglobin	13	12 - 16 g/dL	Neutrophils	62	40 - 75 %
H&C Count	1.06	4.3 - 6.1 million/mm ³	Lymphocytes	22	20 - 45 %
PCV	35.4	40 - 54 %	Eosinophils	08	1 - 6 %
MCV	84.1	78 - 101 fL	Monocytes	11	2 - 12 %
MCH	26.20	27 - 32 pg	Basophils	01	0 - 1 %
MCHC	31.7	30 - 36 %			
RDW	14.3	11.5 - 15 %			
Total WBC Count	340	4000 - 11000 /mm ³			
DIFFERENTIAL COUNT			PERIPHERAL BLOOD SMEAR		
Hematocrit	35.4	40 - 54 %	RBC Morphology	Normalcy Normochromic with few normochromic lymphocytes	
MCV	84.1	78 - 101 fL	WBC Morphology	WBC Normalcy	
MCH	26.20	27 - 32 pg	Platelet Count	60000	150000 - 400000 /mm ³
MCHC	31.7	30 - 36 %			
RDW	14.3	11.5 - 15 %			
Total WBC Count	340	4000 - 11000 /mm ³			

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Thalassemia Screening - Sehgal Index for BTT

$$\text{Sehgal index} = \frac{\text{MCV} \times \text{MCV}}{\text{RBC}}$$

Sehgal Index < 972 – Suspect Beta Thalassemia Trait

Sehgal Index and Mentzers Index <14 had best combination of sensitivity and specificity for identifying BTT patients in a tertiary care hospital

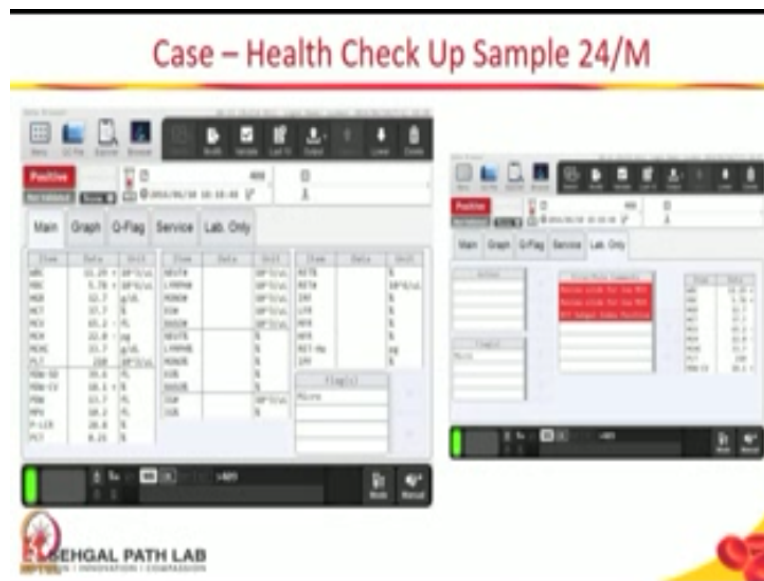
Some of you have not heard about thalassemia or genetic disease where if a father and mother are thalassemia carriers and a carrier is almost 5% of our population in Mumbai, which is huge. There is 50% chance that a baby will be born, will have thalassemia disease. This baby beyond 6 months of life is dependent on blood transfusion and does not lead a complete life. So very common disease in our country is still extremely, easily preventable.

We think it is very common in Gujaratis, Muslims, Boras, Sidhis, Punjabis, Eastern parts of India, and in India, we still have caste based system and caste based barriers. If somebody asks me before marriage, (()) (14:17)), I said no thalassemia ka screening karo. Okay, because that is far more important for you and your family then have a (()) (14:23) but you get distressed down and you will see people say I wanted to do HIV and hepatitis B.

Okay, I want to see hepatitis C for my partner or spouse. Whereas first set of thing you should do is get thalassemia screening done. So idea is why get it done, can we predict that this patient requires a testing, this is what you have done. Based on thalassemic carriers having small RBC size and higher volume, then numerous formula is available in literature and around 4 years ago, I published this Sehgal index and you will find it extremely sensitive and specific to our needs.

So what we have done is, we have taken use of the technology in this machine, where I can put in my own formula into the software of the machine, it does the calculation.

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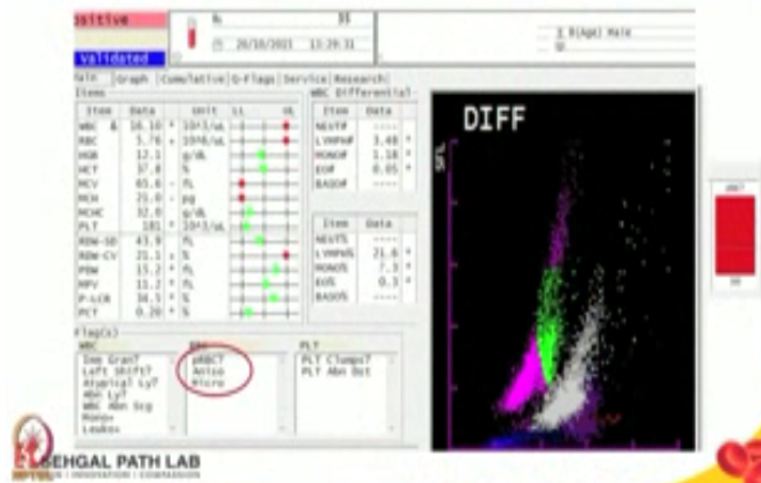
The patient walks in while technician runs the sample. Everything is normal. There are no flags, clear. There is something positive sign coming here for my technician, says read what it is. Goes to the next screen, it says BTD Sehgal index positive. The technician knows without any calculation; this is a thalassemia suspect patient. When that flags come to me, I write in the report, it goes off, the patient gets evaluated for thalassemia and 85% of them based on the sensitivity of this, actually turns out to be thalassemia carrier.

So we are helping in screening disease. What did I use? I use the MIS or the information system technology available in the machine, the software, put the 2 together and I am helping the patient off. This is one example that is currently available and we are doing it. There is another example malaria, extremely common, somebody in your family or somebody you know has to have had malaria, especially in the monsoon epidemic, almost everyone in Mumbai has it.

How do you detect? doctors, if you go to a doctor, he will say, okay, do a CBC and malaria parasite test, we will screen this line. This particular machine model screens for malaria automatically.

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Automated Malaria Detection



So you see there is a flag, which comes here which is called as a PRBC flag and you have there some purple dots, which are parasitized RBC. This machine has a fluorescent dye. It can bind to the parasites. It is based on the light scatter property. It comes in a particular region, then it is there for certain number, the machine flags it. Currently we do it only for only 1 type of parasite that is vivax, which is more common. As you speak, I am currently working with the company on a project for falciparum.

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Sensitivity of pRBC Malaria Flagging

		pRBC Flag		
		Positive	Negative	
Microscopy / Rapid Malarial Ag	Positive	57	11	68
	Negative	02	596	598
				Total - 666 cases

Sensitivity - 84%, Specificity -99%



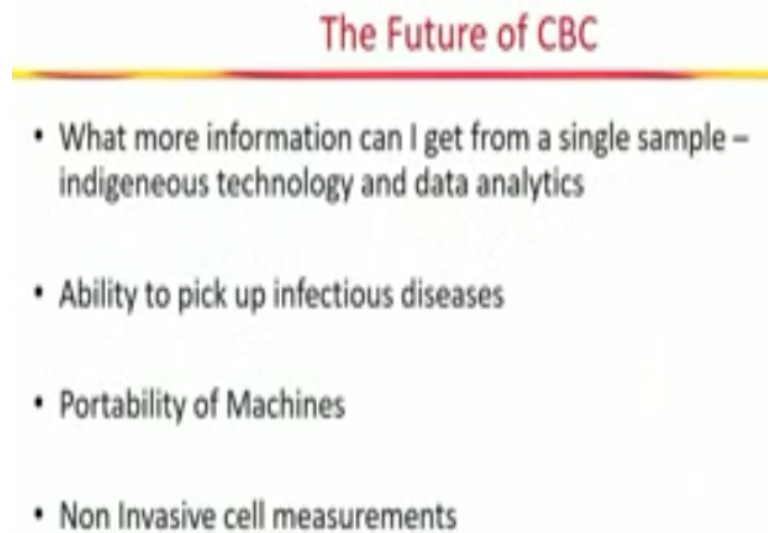
So 3 years back, we evaluated this flag and we found it to be sensitive 84%, specificity 99%. In practice, what happens in the monsoon season, when the patient walks into me; they might have walked into me with a letter from a doctor saying CBC and urine test. When I ran the CBC, it

showed me the flag, I call up the doctor, after having seen the slide and confirming it is malaria, the doctor and the patient are both very happy.

Because he did not even ask for malaria and in the monsoon season, 1 out of every 100 patients, who walks in with fever unsuspected, the machine fix it up for us. Now rather me picking it up, my staff comes running to me, I have screened it in the machine, confirmed it with the slide, I just need to look at it for 10 seconds and normally I would have wasted around 5-10 minutes, not wasted but spend that amount of time.

So again, automation, use of technology something to our local needs nowhere in the world, and this company states it has maximum machines in Japan, Japanese based company Sysmex and the other end is in US, none of them have malaria. They do not use it over there. The technology is there. This is in local needs. So we have been working with them because now it is big business for them, but we need to initiate that technology and take the need of doing these kind of things.

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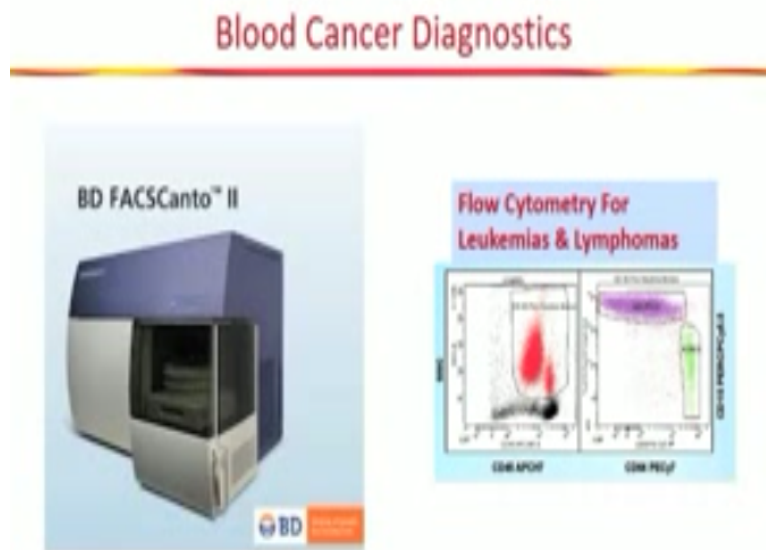


Future of CBC and this is where you guys come in that what more information can I get from a single sample. That is always my dream. I run 1 sample it should tell me the infection I have, it should tell me whether I am thalassemic, confirm it for me, okay. Do everything, can it be

portable, can I pick up other disease like malaria, can I pick up dengue, can I pick up typhoid from the same machine and we already have non-invasive hemoglobin measurements now.

Can we have non-invasive cell measurements? Those are the kind of dreams, which a patient would love to have, walk in, scan in, get your CBC report. So here are some questions which I just raised the potential looking at we can do.

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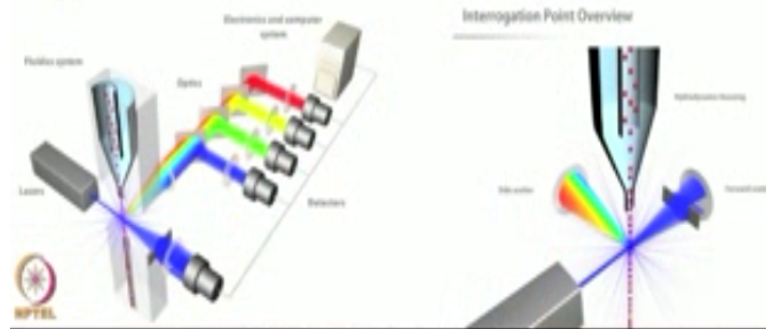
So next topic I go to is blood cancer diagnostics. How many of you know of flow cytometer or heard of flow cytometric technology? You guys are in the engineering field. So I am sure you would have, most of you are aware of flow cytometry technology, the basic principles. Not all of you.

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Flow Cytometry Tutorials

Thermo Fisher Website – Introduction to Flowcytometry

<http://www.thermofisher.com/in/en/home/support/tutorials.html>



So I recommend if you are interested, there is a Thermo Fisher Company, very popular company. This is the website; the link is there. This talk will be available for all of you at anytime, go to this link basics of flow cytometry are given beautifully, there is use tutorial, introduction to flow, what it does, what are lasers, what are fluorescents, fluorochromes, what are optics, much easier for you guys to understand and us biologist to understand and that is this.

What do we do with flow in a lab? Looking here, which is blood cancer, we try to diagnose leukemia, we try to subtype it, we try to look at certain markers, which would help us say, this is a good leukemia, intermediate, or bad leukemia, which will help us in treatment. We look at minimal risk disease, which is looking at 1 in million abnormal cells after a cancer patient has been treated. We pick that cell up and say this patient is going to relapse. The relapse will happen after 3-6 months. Can you take some action today?

Because we have picked 1 in million cells and do, give some extra therapy or change the modality of treatment to prevent the relapse of cancer. So these are the kind of chains the machine does.

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CD Markers

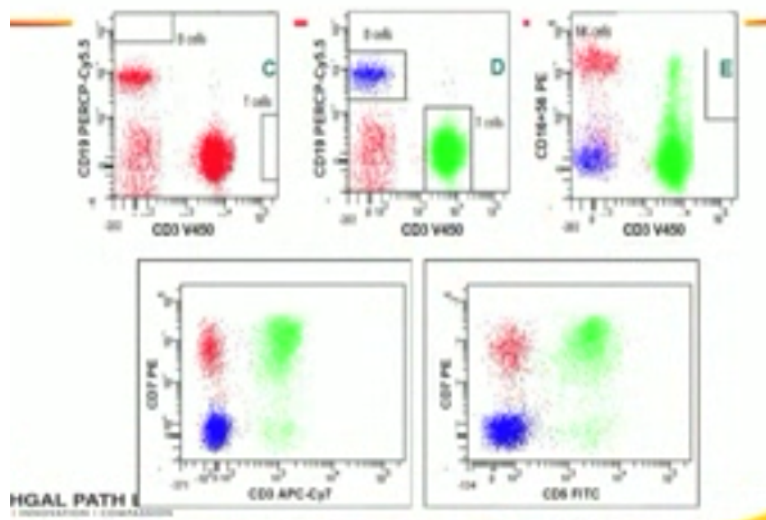
T Lineage	B Lineage	Myeloid Lineage	Immaturity markers
CD1,CD2, CD3,CD4, CD5,CD7, CD8	CD19,CD20, CD22	CD13,CD33, CD117	CD34,HLADR, CD117
Lineage specific CD3	Lineage specific Cyto CD79a, Cyto CD22	Lineage specific Anti MPO	

CD45- Leukocyte Common Antigen

And typically we use what we call CD markers or proteins of different cell lines. So you know WBCs are white blood cells typically basic biology, T cells, T lymphocytes, B lymphocytes. There is a neutrophils or myeloid CD cells and every cell has your own markers. We combine these markers into 1 panel, so there is 1 tube which would have T cell markers, 1 tube which will have B cell markers, the third tube will have myeloid cell markers.

Run it through a flow machine, then you do some data analysis, okay, these cells, the green ones are CD3 positive.

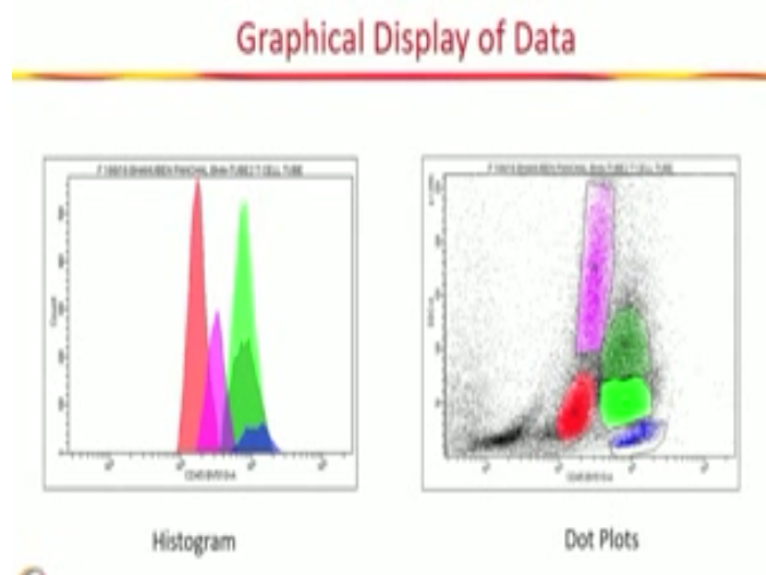
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These are T cells, these are (()) (20:37) positive so I know these are B cells. This is simply looking at lymphocytes, subsets, then you look at few more cells, and we say okay, these tumor cells are of B type. These tumor cells are of T type and these are all myeloid type. Because every type has a different treatment or different prognosis. So this is in just what we do. See instead of going into flow cytometry, I thought for you guys, let us look at the from the data analysis perspective because that would interest you more.

Typically, when you are looking at flow cytometry data or any data if you look at, you can see a histogram.

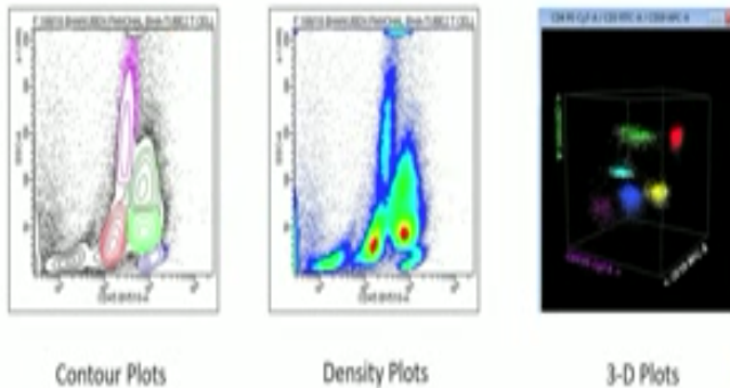
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Very simple, single parameter, so we are evaluating the intensity of CD45 in the blue space, which is more than that in pink and orange or you can look at a 2 parameter plot. We take 1 protein CD45 and you will get side scatter, which is nothing but the clarity in the cell and you are comparing two parameters within separate populations. When we had 1 colour, 2 colour, 3 colour machine, the life was simple and I remember in 2008, we were using 3 colour machine.

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Graphical Display of Data

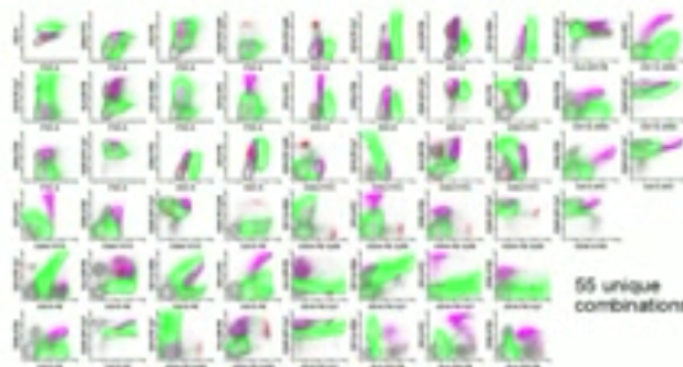


There was this advent of this 3D plot, okay and I said wow, in which you are looking 2 antibodies, like I look at all 3 together and this is just 2008, when I just thought it doing flow cytometry. In the period of time, the flow cytometry have gone from 3 colour to what you clinically use now 8 and 10 colour and research lab you have 15 and 17 colour. The problem is for a simple 9 colour flow cytometer, if you look at different combination of antibodies, you will have minimum of 55 unique combinations.

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Data Visualisation

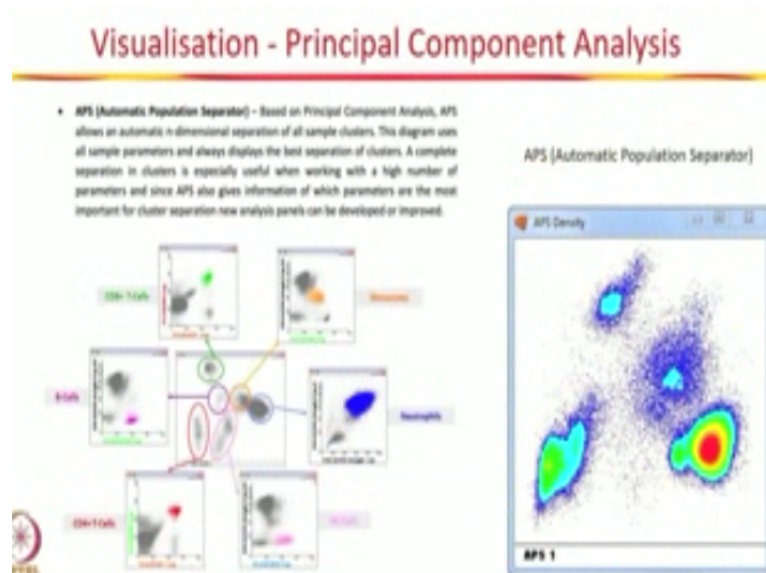
9 Color Flow Cytometry



This is for one 9 colour tube and on average we run 3 9 colour tubes. So I have to go back to 165 plots, you can imagine the amount of human error I can make in interpreting these plots. Then look at normals and abnormal and then I am talking about detecting 1 in million cells. Because

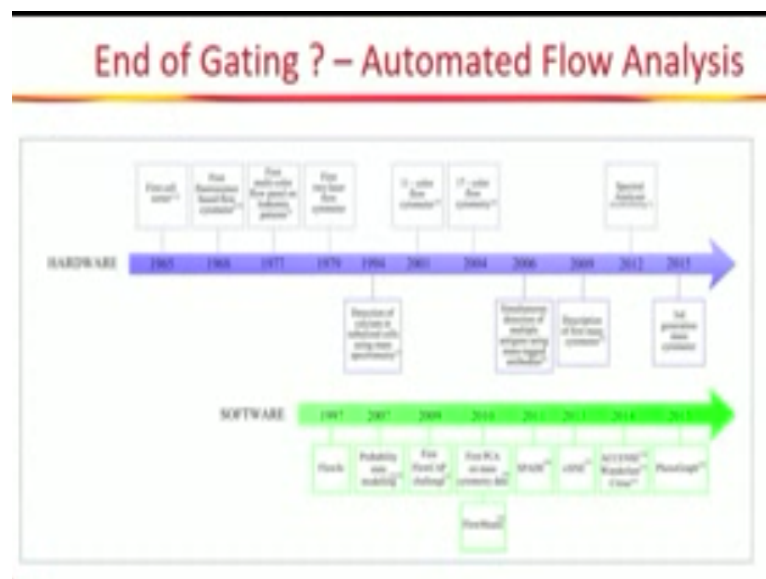
there are million dots, I have to look for a needle in a haystack, okay. This is not going to work. So the field of software analysis is hugely expanding in all fields of science, flow, sequencing, proteomix.

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One of the software they will, for example, is using principle component analysis. I will not go into details.

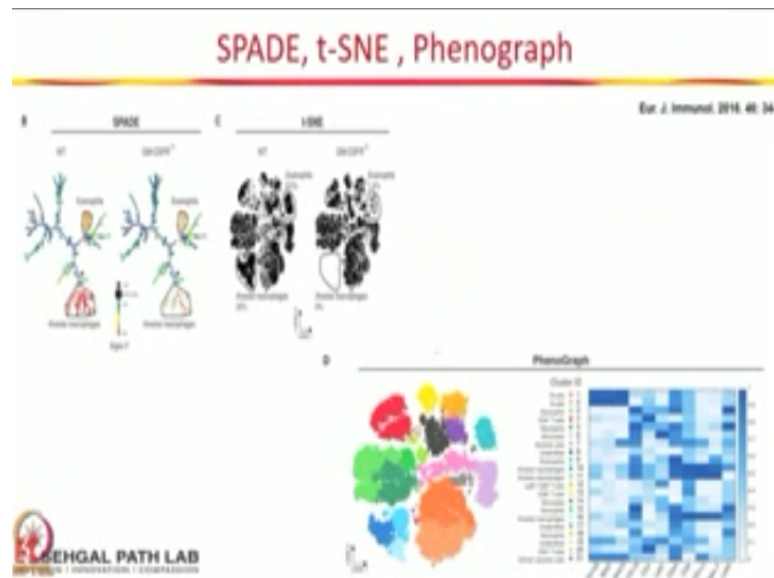
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And this is a very beautiful related to flow which states end of gating and if you say upper line shows you 1965 onwards the hardware progress. Beyond 2000, path breaking process has been

less, software progress is all 2000 onwards. In every 2 years, you have something new path breaking coming up.

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These are some softwares, which are used in different modalities. Instead of looking dot plots, there is something called as spade, the names are confusing. It is called as stochastic neighbor embedding. The names are too complex for doctors like us, I have to really mug this up to even, you know, share it with you. So there are heat maps, there are phonographs, there are different kinds of software available, which are doing it.

We doctors do not understand anything about it. We need help from data scientist to come and guide us to how to use it to make indigenous softwares to our needs again and that is where people like you guys can come in as data scientist for helping us. Future of cytometry and I think my personal interest or interacting with the (()) (23:50) lab for so long, I get to learn a lot. I get to learn about fields, which I have never been exposed to.

In the few projects, which I have shared, I had learnt a little bit about mass spectrometry and Maldi-Tof. I never knew a word about it. By the time in the last 5 years, I see the field of flow expanding, what is it doing? The latest instrument coming to the market or in the future will be combination of mass spectrometry and flow cytometry.

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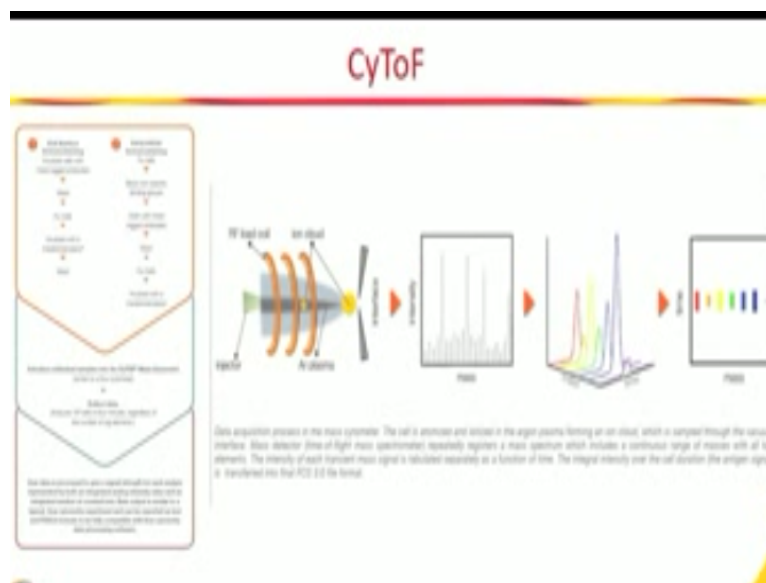
Future

- **Mass cytometry**, or CyTOF (**Fluidigm**), is a variation of flow cytometry in which antibodies are labeled with heavy metal ion tags rather than fluorochromes.
- Readout is by time-of-flight mass spectrometry. This allows for the combination of many more antibody specificities in a single samples, without significant spillover between channels.

It is called as mass cytometry because the limitation of flow cytometry is this. every fluorochrome I use has an excitation wavelength. It overlaps with the next fluorochrome. For separating or the resolution has not yet done. I can use a maximum of 5, 6, 8 or 10. Now instead of labeling my cell proteins with fluorochromes, I am going to label it with heavy metal ions. So I can use 100 or 200 in separate demo, very simply put.

And I do not know too much about it. If you have any questions Dr. Sanjeeva is the right guy to ask it about mass effect.

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The idea is once this comes into practice for our clinical, I stay in the cell surface or I stay in the cell cytoplasm, put it through mass effect. I will give me the data. What interests me even more the data, the data generated, I said I am more interested in the data, the output is exactly similar, the same file called FCS 3.05, which is called as the flow cytometry standard file, I can analyse it the same way I have been analyzing flow cytometry data, okay.


So I have already used to analyzing the data, this is for my clinical needs, the technology used is different where I get far more data. The software used will be different, so that is what excites me. So one example, which I had showed you in that T versus B plot, there were around 6 bodies in that tube, okay. This is the simplest of CyTof data, it has 27 antibodies, simply doing only lymphocytes of 6, only cell surface antigens has in it for me at least.

Because it is the way the technology is moving. So this is just to highlight it how fast things are moving and bioinformaticians, data scientist is going to be the key one and hence I wanted to put in laboratory data analytics.

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Laboratory Data Analytics

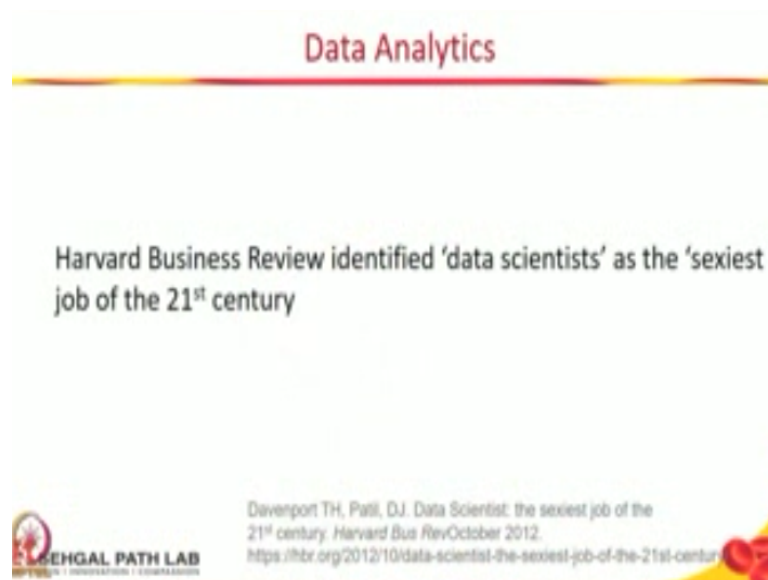
- Historically Laboratorians have been a transactional enterprise
- Whether in a hospital or reference laboratory, we receive an order, collect the specimen, perform the test, report the results, and that's the end of our involvement
- We now also need to go beyond that traditional role and analyze the data in the context of other information about the patient or about the population

 **NEHGAL PATH LAB** Big Data Analytics in Healthcare – How Laboratories Can Play a Leading Role
Kaufman, Harvey Medical Director, Quest Diagnostics

It is a nice article by Dr. Harvey, who is from Quest diagnostics USA and he says historically we laboratory people have been, you know, just transcription enterprise or translation enterprise. Somebody gives a sample, we collect it, we run the test, we report, full stop. We need to look beyond this traditional approach. We need to go and say, let us go back to my data and analyse

what more can I get out of it. And actually if you read a very good article from Harvard Business Review.

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It says, data scientist as a sexiest job of the 21st century and I completely agree to him. Because given the opportunity, I would go back and start looking at data from my own lab. We generate billions of test results in our country, every single day. You can, if you guys know every new start up is behind collecting data, okay and I have been approached by 6 or 7 startups who are coming to me, can you share your patient data.

Currently there are huge medico ethical problems because in India, we do not work with consent, with paper work. We do not work. So we do not know how somebody is going to use. So it is a problem, okay. But most of the medical startups, see I am saying in the pathology sector are all after data and I tell you the reason why.

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Big Data

- Next Generation Sequencing.....Bioinformatics.....Big Data.....Data Scientists.....????
- What about the vast amount of Data sitting in our laboratory information system
- Mine of information – Waiting to explode

Eg – Datasets of people who come for health check ups - Demographic trends, disease trends, Community patterns, Reference Ranges.....

So when I first heard the term big data, it was in connection to next gen sequencing and simply for me, as I said with most laboratorians, big data means big in size. That is all I knew about it. I still do not know much about. Am I worried about data? I am not even worried about what next gen sequencing will do, I am not doing it in practice, but it is coming in a big way. What I am worried is what about the vast or the really big amount of data sitting in my own laboratory information system and it is a mine.

You know, it is about somebody sitting there and mining it and I know 1 doctor, Dr. Sujay Prasad, they have Anand Pathology Lab in Bangalore. It is a 5-storeyed lab. They actually currently have hired. It is a clinical pathology lab. They have hired 2 data scientist both full time only looking at data for the last 2 years from their own laboratory and it is fantastic and the example that he showed and one of the example that I will show to you.

This is from what he shared with us. This is where I feel or he feels we should be having seamless data recording. Forget about the technology part which I showed you, okay.

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Seamless Data Connection

- 60 year old gentlemen Visits a Hospital for a health check up
- Hematology Laboratory - CBC –Low Hb and Small Red cell Size - Iron Deficiency Anemia
- Clinical Pathology Laboratory- Stool - occult Blood Positive
- Radiology Department - USG – Abdominal mass
- **HIS- Data Interpretation** – Advised Colonoscopy and Biopsy to rule out colonic cancer as the cause of Occult bleeding leading to Iron Deficiency Anemia

Imagine this 60-year-old gentleman who walks into a hospital. He gives 1 CBC sample, which goes to the hematology lab and they say he has iron deficiency anemia, the report is gone from their lab. My job is over. He now goes, gives a sample, the sample goes to, the stool sample, it goes to a clinical pathology lab, the lab is separate. Technician is separate, doctor sign the report is separate. He says small amount of blood in stool.

He gives out the report. It goes to the radiology department. He says I suspect small abdominal mass, close to the intestines. He gives out the report. The patient collects the report in a good hospital, the report goes to the doctor. If you are a very good expert, he will go through all the 3 reports, correlate the data, assemble in his mind and say, are the 3 related, but if my laboratory information system data gives me 1000s of patients who are exactly the same.

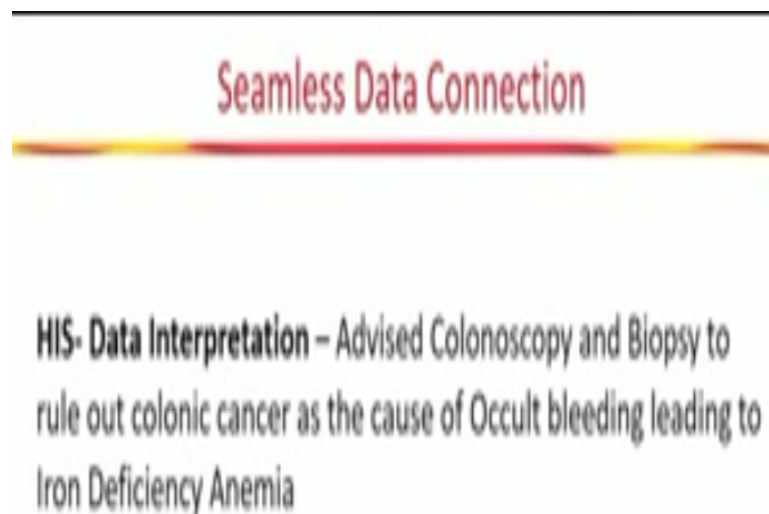
In majority of them, there was actually a mass in the intestine, which is actually a cancer, which is the cause through all the 3 reports, correlate the data, assemble in his mind and say are the 3 related, but if my laboratory information system data gives me 1000s of patients who are exactly the same. In majority of them, there was actually a mass in the intestine, which is actually a cancer, which is the cause of all 3.

The probability of the algorithm working is far higher. In my dream or we know what Dr. Anand presented was basic and is extremely common that in practice if you tell me at 65-year-old

gentleman has iron deficiency anemia, the first thing I will say if he is well off or not having nutritional issues, from a well to do family, let us get you screen for stool occult blood and an ultrasound.

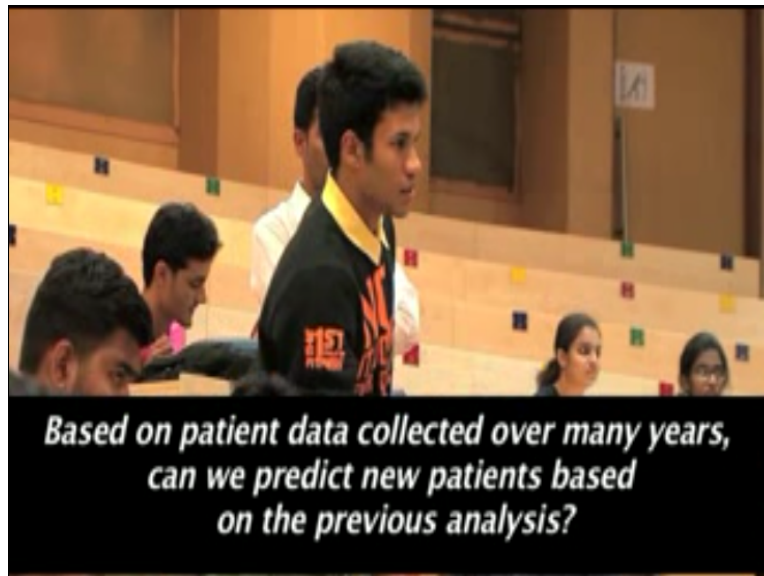
Because colonic cancers are known to cause this, okay. This data is there in the system. It is only for somebody to build the algorithm and give it to the laboratory. Something similar to what I showed you about thalassemia screening. Data is all there, we put an algorithm, the staff picks it up. We put the algorithm in the HIS.

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The hospital system, it would flash. If it flashes, doctor will not even miss it even if he is not an expert. So that is what this sort of seamless data analytics or data scientist can do. So this is the 3 things I wanted to share with you and I think, it is end of time. Thank you for patient hearing. We will love to have questions from you, from your perspective. Thank you so much.

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His question is if you collected a data of every patient over the last say 10 years, can you pick up the new patient a little earlier based on the data analysis. This is what an expert physician does, okay. So, but the problem is when I have fever, the first person I will approach is my parents or a family physician or local doctor, he will give some medications. If it does not resolve, he will say, okay go to an MD physician.

And he will do a couple of tests, okay, if it does not resolve, he will say, go to another expert and okay he will see 2, 3 more tests and he will send to another expert. So by the time that you reach the expert and you have gone through 10 or 12 tests. Now why does the hematologist pick up that these are signs of blood cancer because fever can be due to anything, because he has not looked only at fever.

He has looked at fever, he had looked at my CBC report, where I have low platelets, where I had query abnormal cells, I have certain enzymes in my body, which are high, okay, I have a slightly enlarged liver and ultrasound and doctor know, $A+B+C+D$ is potentially a sign of blood cancer. See if this patient had directly gone to the hematologist right upfront, he could have picked it up, but that also means every person who has fever should go directly to the hematologist?

That is not possible. In our country, it is never going to happen. That is where exactly what he said, for example we ran around 400 cases of leukemia or blood cancer last in our lab, related,

not all blood cancer, lymphomas, leukemias, other types of samples. Currently what I would sit and manually do is cipher through the data and I understand which marker came in which diseases, which was the rare disease, which is the common problem.

Is this disease rare, is this disease common. In a small powered laboratory, it becomes very difficult. Even in an institute like Tata Memorial Hospital, they go through 30 cases a day. It is almost like doing 1000 cases a month and they do almost 5000 cases of new cancer patient of blood cancer every year. Imagine if there is a software, which automatically collects from the reports every data and out data scientist is there.

He may not know the biological interpretation, but he will say, okay this looks something different to me. This look something different to me, does it make clinical sense. So we need to talk. So that is what exactly a clinician does, but that is where a data algorithms can really help. Some patients come with my red colour urine. You have blood in urine. You go back and ask them, did you start on vitamin B12 or iron tablets?

That causes red colour urine, okay, very common. You have red colour urine, there are 1000s of causes, what we read on Google is cancer first. We read TB first, so that is there, that is dangerous, but not going to self analysis, I am looking at data analytics from a point of view of the report, the system, not looking at a technology, but community data, you know disease trends. Monsoon season and malaria everyone knows.

But I do not know about a cancer patient coming into Tata Hospital from a certain region of Bengal, is there something else environmentally happening there, okay. Can we look at into it more preventive manner? So that is what data can do, okay. Thank you very much.

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TAKE HOME MESSAGE

- Important to know the need of a doctor
- There are very simple problems for which there are no solutions.
- Can you help in predicting that a particular patient requires a particular test?
- Data science is the most important these days