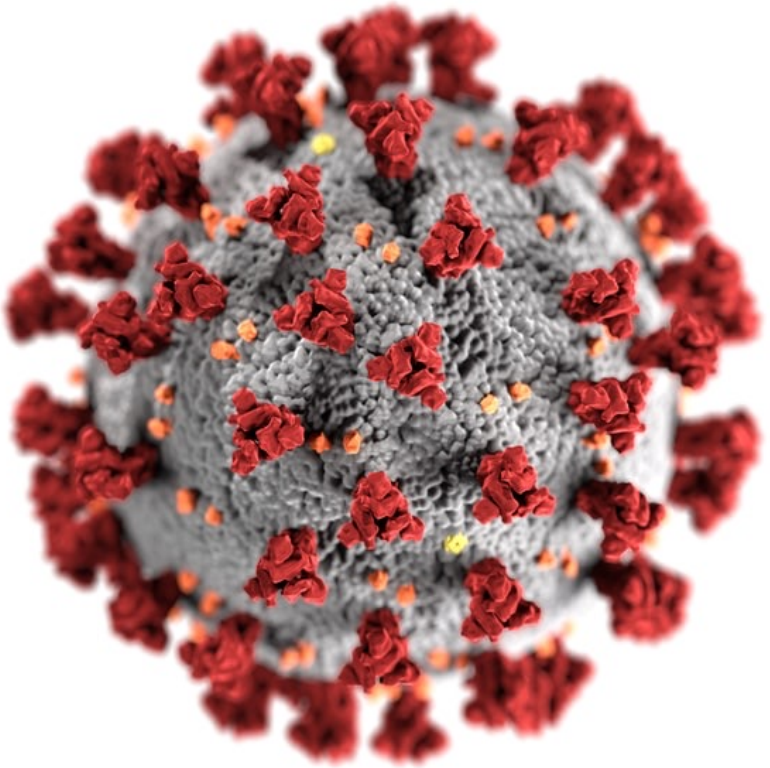


# COVID-19. EXPLAINED.

## AN E-BOOK BY
## RAVISHANKAR IYER

Image credit: CDC from Unsplash

## Introduction: Why I'm writing this e-book

The deadly Second Wave of Covid-19 impacted all of us.

At various stages I felt afraid, angry, uncertain... but most of all helpless.

Then I realized: perhaps I should use this emotion and create something out of it. I'm a big fan of good science-storytelling and thought "*hey, maybe I should take a crack at understanding the biology of this*".

And that's how this e-book was born.

I had published Chapter 1: **'Getting to know the virus (and your lungs)'** on 15-May-21.

Today (12-Jun-21) I'm publishing Chapter 2: **'The Human Immune System: Our Defense Forces'**.

The book is still not complete. Hopefully over the next few weeks, the third (and final?) chapter would be ready.

Meanwhile, I hope you find this fun, educational and easy to understand.

*(For those who are wondering, who the heck am I, my LinkedIn profile is a good place to start)*

## Slightly lengthy (but necessary) disclaimer

*This story-series aims to provide a layperson understanding of the Covid-19 disease, including:*

- *What is this virus?*
- *How do your lungs normally function?*
- *What harm does the virus do to our body?*
- *How does the disease progress across stages*
- *How our immune system fights back*
- *The treatment*
- *The vaccines*

*Needless to say, this is NOT medical advice. Please check with your physician for any case-specific advice.*

*I have written this from an edutainment perspective. I have taken massive liberties in giving personalities to various bio-organisms.*

*I've also gone nuts on analogies (to paraphrase someone wise, 'All analogies are wrong; some are useful').*

*If, after reading this e-book, any reader is motivated to learn more about the science of the human body, I would consider my mission accomplished!*

## Heartfelt acknowledgement

Many thanks to Prof. Satyajit Rath for his invaluable inputs.

This gargantuan video was a great resource for me to understand the disease.

In addition, he displayed utmost kindness in spending two hours with me explaining the functioning of the Immune system in great detail!

Thanks also to Dr. Karishma Kaushik and other medicos who kindly read through this and gave useful inputs.

Any mistakes in the document are all mine, of course!

## Final note (promise!)

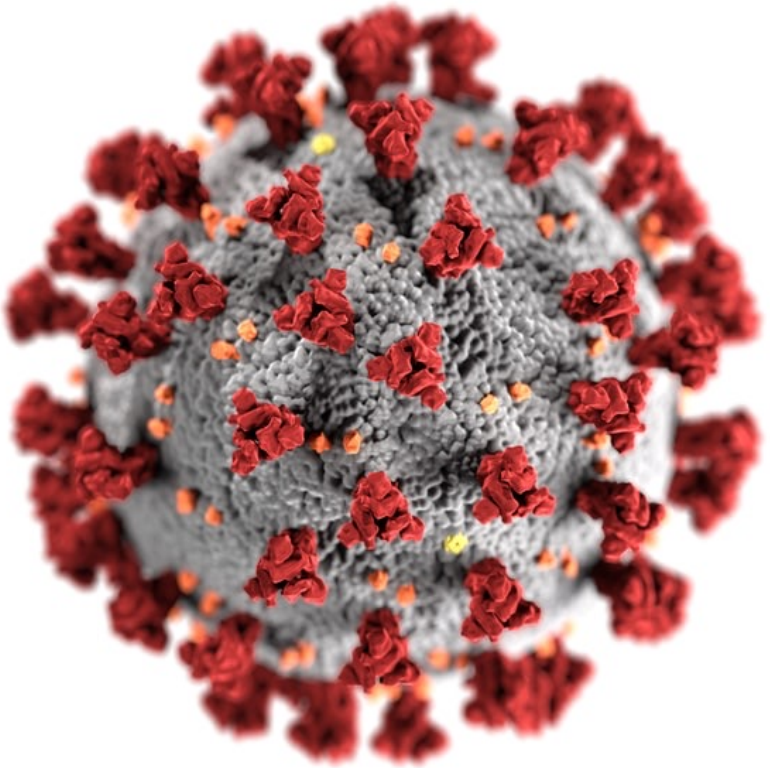
Some of you may have already read Chapter 1.

I would still suggest you re-read the same.

For one, I've made some additions and modifications to the material.

And two, it would refresh your memory of the concepts so that Chapter 2 is easier to understand.

Happy reading!



## CHAPTER 1

# GETTING TO KNOW THE VIRUS (AND YOUR LUNGS)

Image credit: CDC from Unsplash

# A. The Virus

Hi there.

I'm a virus.

Aka, "a piece of bad news wrapped up in a protein"*

I have a confession. I can't do much on my own. As in, I can't even ... reproduce.

But all you need to do is take me in. Through the nose, mouth or other opening. Then, once I enter a human cell, I come alive, and begin to do my thing.

Making copies.

I live for one objective only: to make as many copies of myself as I can.

Which will make further copies. Which will make more.

You get the picture.

* Defined evocatively by biologists Jean and Peter Medawar , 1977.

But in order to do that, I need one of your cells. Because, you see, your cells have an inbuilt copying machine which I can hijack....

...only once I enter the cell.

Entering your cell is tricky – they are pretty well defended. Except there are some entry points...

So cells in some parts of your body have a “receptor protein” called ACE2

Receptor proteins do a bunch of stuff, but some are like gates for a cell. Think a USB inlet in a laptop.

Oh, but you would need a USB stick to access that inlet right?

Guess what those spikes of mine are for?

Through a process of evolution (or... human design? Shhhh), my spikes fit your ACE-2 receptors like a key to a lock.

And voila, I can enter your cell... and begin doing my replication thing.

I know what you're thinking ...

"Ok, but viruses have been around for quite some time... what makes this guy so bad?"

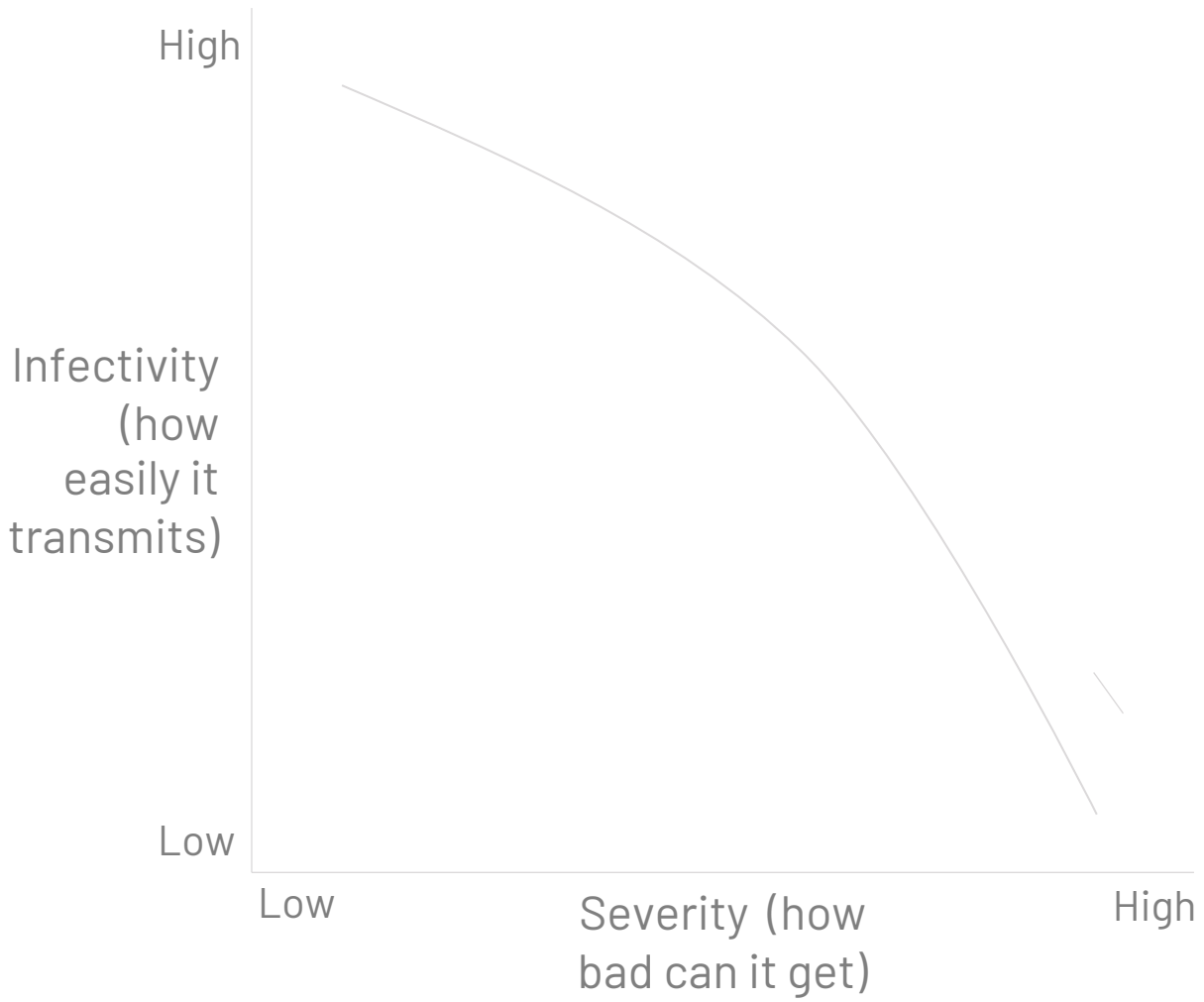
I'm glad you asked.

I call it "the Goldilocks" effect

Let me explain.

You see, I come from a family of coronaviruses.
And it takes a bit of artistry to create something like me

I'm going to use this 2x2 chart
(Oooh, so Mckinsey of me)




Scale and values indicative and for representation purposes only

You see, I come from a family of coronaviruses.
And it takes a bit of artistry to create something like me

## 1. Meet Cousin Common Cold

He gets high marks for effort. Works his pants off. But doesn't inspire any fear. Wimp!




Scale and values indicative and for representation purposes only

You see, I come from a family of coronaviruses.
And it takes a bit of artistry to create something like me

**1. Meet Cousin Common Cold**
He gets high marks for effort. Works his pants off. But doesn't inspire any fear. Wimp!

High

Infectivity (how easily it transmits)

**2. And then there's Cousin MERS (Middle East Respiratory Syndrome)**
He's the family showoff. I keep telling him during reunions – If you kill your hosts so soon, how will you reach others?

Low

Low

Severity (how bad can it get)

High

Scale and values indicative and for representation purposes only

You see, I come from a family of coronaviruses.
And it takes a bit of artistry to create something like me

**1. Meet Cousin Common Cold**
He gets high marks for effort. Works his pants off. But doesn't inspire any fear. Wimp!

**3. Sars-CoV-2**
Finally, that's me.
Just the right balance.

**2. And then there's Cousin MERS (Middle East Respiratory Syndrome)**
He's the family showoff. I keep telling him during reunions – If you kill your hosts so soon, how will you reach others?

High

Infectivity (how easily it transmits)

Low

Low

Severity (how bad can it get)

High

Scale and values indicative and for representation purposes only

Why am I so deadly?

One, stealth. My genius was to not be an over-achiever like MERS.

“Tao guang yang hui” (Keep a low profile) – Deng Xiaoping, China

Most people who get me remain blissfully unaware as I multiply in them. And spread to others.

But the other reason that makes me deadly (unlike Common Cold) is that I strike you where it really hurts. A lot.

Your lungs.

---

**On that note, let’s change track and understand one of our most important organs.**

**One that has a critical weakness.**

# B. The Lungs

Hey folks.

We're your lungs. Our celebrity quotient may be low (esp. compared to Heart), but we're a pretty big deal.

So, your body expends energy all the time. It gets this energy from food. But the sugar – and other elements – trapped in food need to be released for you to get the energy.

This release operation needs a fuel. That fuel is oxygen.

Think of your body as a large industrial complex with different factories engaged in different tasks, all requiring energy. All these tasks are fueled by oxygen.

We, the lungs, are the central power-plant suppling this oxygen to the entire body. And we work 24x7x365...

* Lungs Image credit: Carl Holderness from the Noun Project

Visually, think of us as an upside down tree. Your trachea is the main stem.

The main branches are called bronchi. These keep splitting into tiny branches called bronchioles. Each lung has about 30,000 bronchioles. Yup, it is dense.

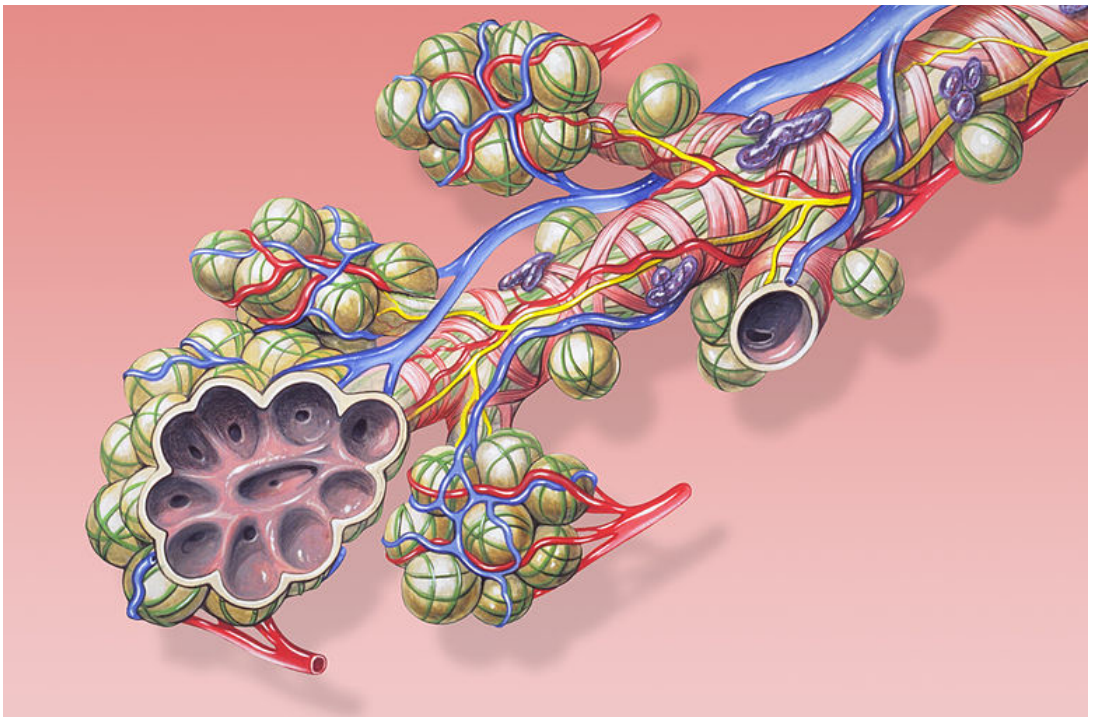
But that's not where the action happens.

The real action happens at the ends of bronchioles. Meet the alveoli.

Think of alveoli as the leaves on your lung-tree.

Alveoli are tiny sacs (that are clumped together look like bunches of grapes).

Hang on, this will need a diagram...



Don’t get grossed out – that’s just you!

So the grape like clumps are alveoli (singular ‘alveolus’).

Notice the blue and red lines? They are your capillaries carrying impure blood (blue) from the heart and oxygenated blood (red) to the heart.

The system of transfer – from alveoli to bloodstream - is quite amazing...

Imagine a goods train passing slowly by a platform. It cannot stop, but it still needs to load and unload some cargo.

The alveoli is the platform. The capillary is the train. The Red Blood Cell is the wagon.

And the items getting transferred are oxygen and carbon dioxide

So, as the dense network of capillaries passes by the alveoli, it unloads the $CO^2$ (to be exhaled out) and loads each RBC with some life-giving $O^2$.

This exchange happens *every* living moment of your life.

Your body has 300M such alveoli-platforms.

Two things about them which are critical to know...

One, they have reeeeaaaaallly thin walls. You would too, if you needed to pass material 24x7 between them.

If an alveolus is blown up to the size of an apple, the wall would be about as thick as the apple's skin.

Remember this, we'll revisit it later.

Two, the alveoli's surface consists of two types of cells, imaginatively named Type 1 and (you guessed it) Type 2.

Type 1 cells cover 95% of the surface area. The smaller Type 2 cells produce a key ingredient which holds the shape of the alveolus.

Oh, and the Type-2 guys are also abundant in... ACE-2 receptors[1] (yup, those same USB inlets).

That's good news for you-know-who.

1. They are not the only cells with ACE-2 receptors. These are found throughout your respiratory system (apart from other regions) - for instance in your nose and mouth too – which is why you lose your sense of smell and taste when you get the disease. But we focus on the alveoli since they are vulnerable sites

# C. Virus, meet Lungs

They say size does matter.

I think that's rubbish.

Take me. I'm between 50-140 nanometres in diameter.

Oh really, my alveoli are about 0.2 millimetres (or 200 microns across)

WHOA.

That's Huuuuuge.

(Btw, the guys reading this have no clue)

Yup, time to use a Bill-Bryson-esque 'blow-up' analogy...

Imagine standing in front of FIVE Burj Khalifas stacked on top of each other

That's a 2-m tall human inside this circle

Facing a stack of 5 Burj Khalifas

That's how I'll look in front of an alveolus.

That's me inside this circle

And this is the alveolus – about 200 microns or twice your hair's breadth

Needless to add, this is not to scale.

Burj Khalifa by Lazar Nikolic from the Noun Project

Ok, we get it. You're tiny.

But how exactly do you affect us?

I mean we do have a mean defense system, you know right?

Haha, right, your defense system.

Hey why don't you tell the readers about that and I'll share my strategy to breach it...

PS: Gross alert, guys

Haha, very funny.

You don't realise the difficulty of my job.

Have you felt the air quality in our cities?

Sigh, let me explain how I (try to) keep myself safe...

Hehe, start with the mucus na. Pretty please!

Alright, alright.

Nasal-hair, mucus, cilia, White Blood Cells. These are my lines of defense. Happy now?

So the nasal hair is not something useless you pull out when bored. It filters out largish foreign particles when you breathe. (Gross out all you want, it's a life-saver)

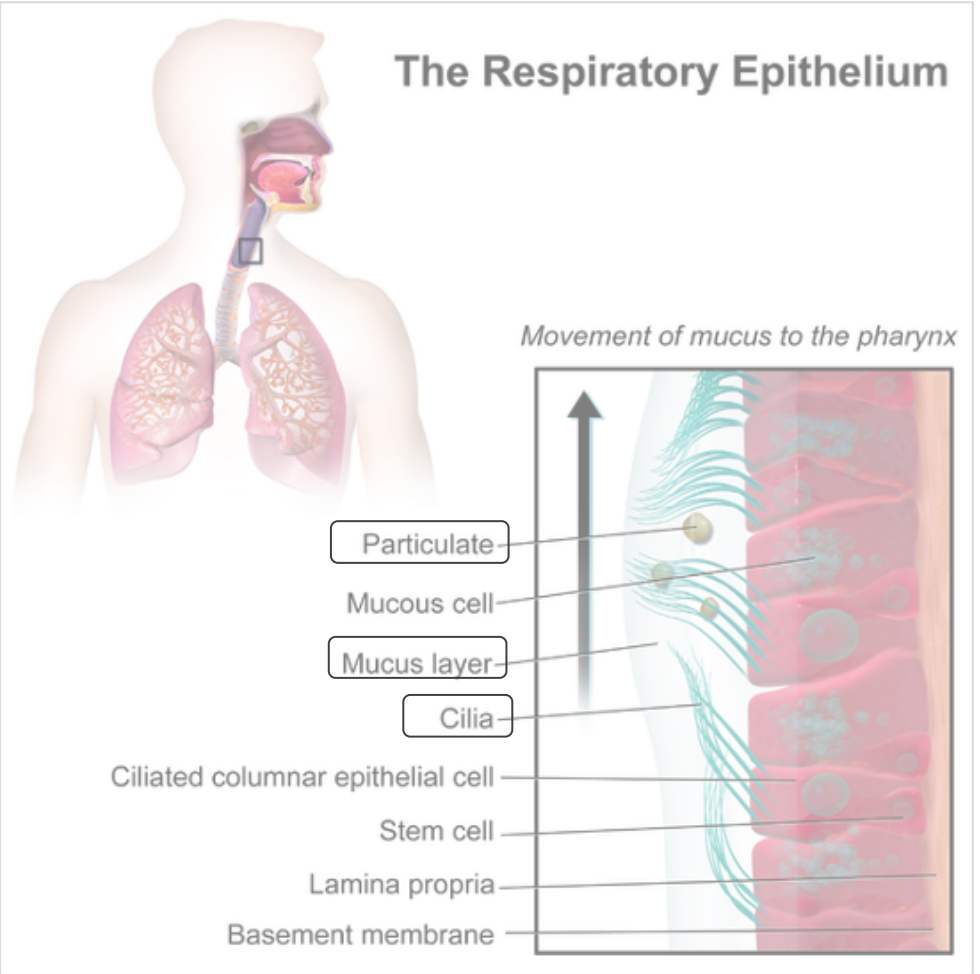
Any foreign particles that pass the nose will mostly get stuck in the sticky mucus that lines the airway to the lungs.

The airways are also lined with millions of hair-like particles called cilia... Who am I kidding... this will need an image... (brace yourself)

Right, here's the deal.

- Particulate: Bad guys
- Mucus layer: Sticky layer which traps said bad guys
- Cilia: hair like paddles which 'beat' the bad guys up, where they're expelled usually by coughing

But we still haven't seen the really tough cops....



If some naughty microbes, bacteria etc. do escape the initial lines of defense, they have a tough fate awaiting them.

The alveolar macrophages.

Remember the alveoli? Where the Oxygen exchange happens?

Well, we realized that it is a vulnerable spot, given its mission-critical Ops and thin walls.

So we built in a powerful security system.

Think of the alveolar macrophages as an elite Z-Category security detail for your alveoli.

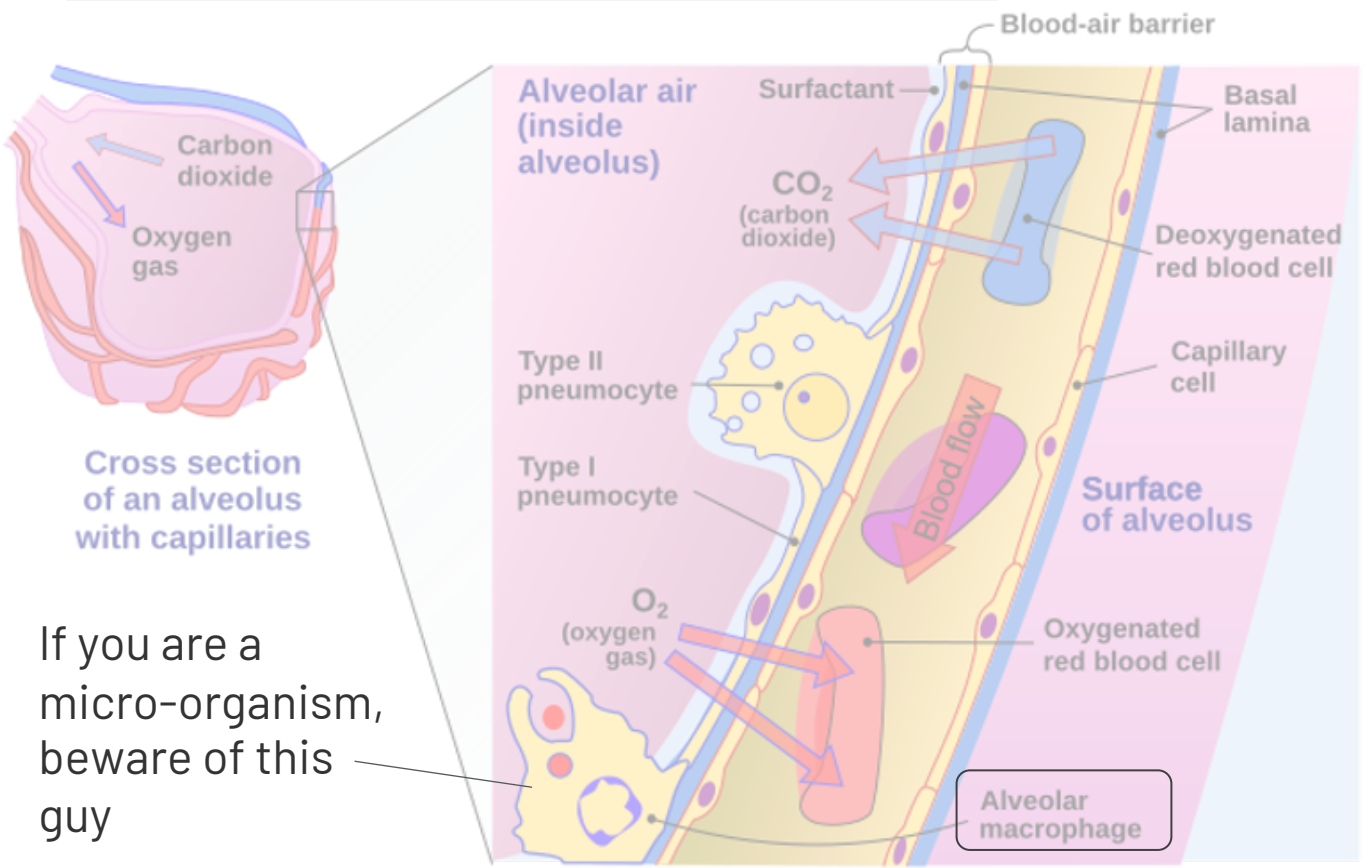
They stand guard on the platform as the exchange takes place

I like how they deal with offending micro-organisms...

They. Just. Gobble. Them. Up.

No niceties, arrest, trial, judge business.

Direct – “aaaaa-gobak”




If you are a micro-organism, beware of this guy

(Clap, clap) Impressive stuff!

Now, I’m sure you guys want to know what exactly happens when I invade right?

Yes, but before that , I think we need to introduce my Defense Forces.

The Human Immune System.

It’s time to get in some new characters in the story...

# CHAPTER 2

# THE HUMAN IMMUNE SYSTEM

## OUR DEFENSE FORCES

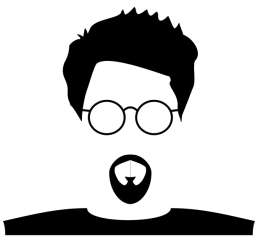
Image Credit: Pic by Specna Arms on Unsplash

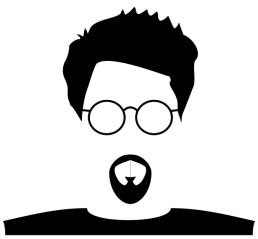
Hi folks, this is your writer, Ravi[1].

As I was crafting this e-Book, I had a realisation about Covid-19.

To really study Covid-19, you need to study several sub-specialties within medical science.

There's of course, Virology.



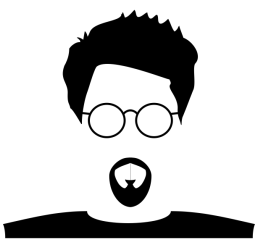


Then, there's Pulmonology – which studies your lungs, the most likely organ impacted by the virus.

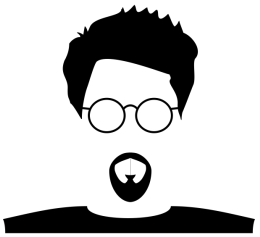
But the most important sub-specialty is another one: Immunology.

Your Immune system is THE most important actor in this ailment.

It protects you, it cures you, and sometimes, unfortunately, it can also kill you.



1. Can you believe that I got this image on the Noun Project? Free!
Image: man face by Nick Novell from the Noun Project



And so, as I was lost neck-deep in the science of the Immune System, I came across a joke in a fascinating article[2] on the topic.

A guy kidnaps two doctors: A cardiologist and an immunologist.

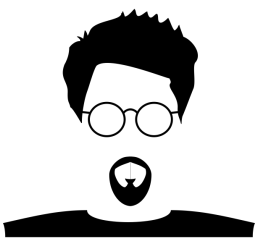
He threatens to shoot both; but offers to spare whoever has made the greater contribution to humanity.

The cardiologist says, "Well, I've identified drugs that have saved the lives of millions of people."

Impressed, the kidnapper asks the immunologist. "What have you done?"

The immunologist says, "You see, the immune system is very complicated ..."

The cardiologist sighs: "Just shoot me now."



2. The joke is attributed to Prof. Jessica Metcalf of Princeton

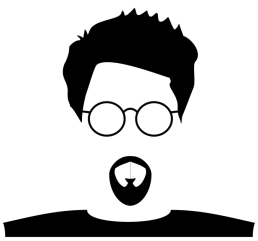
Somehow, reading that joke made me feel better and lighter.

Over the last several weeks, I've tried to get a crash course in Immunology.

It hasn't gone well.

*Fascinating* as the immune system is, it's also incredibly complicated and messy.

Just when you think you've got a hang for how it functions, it'll confuse you with six new elements and sub-processes.



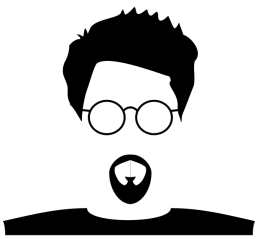
And so, this is an extra  good ol' disclaimer from the CA in me.

In trying to write about the Immune response, I have over-simplified at several places.

(Perhaps mis-represented some facts too).

So, two things.

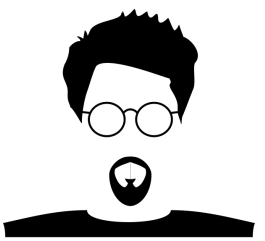
One, please DO NOT quote from this e-book for your next exam on Immunology (I know you're taking one).

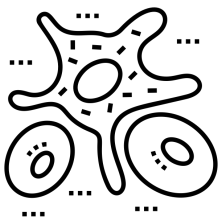


Two, everything here is for edu-tainment purposes only. Please do not take any medical decision based on what you read in this e-book.

With that out of the way, let's dive in.

Let's get to know our Defense System.





WBC

Hi there! I'm a White Blood cell (WBC) and represent your Immune defense system.

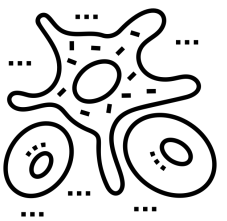
We're a network of diverse WBCs which form a multi-layered defense setup to offer you 24-7 protection against pesky micro-organisms.

You're welcome.

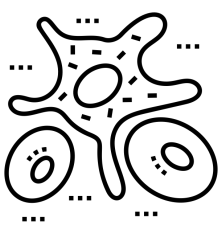
Think of the layers like an escalation matrix.

Depending on the issue severity, I bring in the bigger guns.

At a very broad level, there are two levels of security...



WBC



WBC

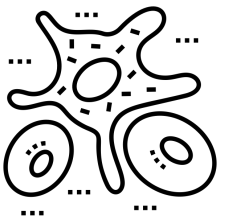
Level 1 is called '**Innate Immune system**'. Think of this as pre-loaded anti-virus software in your body.

Even babies have this – they get it from their mom.

White blood cells by ProSymbols from the Noun Project

Level 2 is the '**Adaptive Immune system**'. Think of this as specific code created by your body's OS in response to a specific threat.

We keep building adaptive immunity as we grow.



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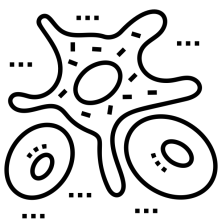


WBC

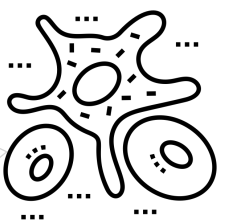
Have you seen a kid pick a biscuit off the floor and gobble it up before her parents can swoop in?

Said parents usually rationalize by saying, "Koi nahi, immunity badhega" (It's ok, she'll build immunity).

They mean 'Adaptive Immunity'.

Interestingly, this simple distinction might be the reason for why kids have been able to evade Covid-19 (so far, touchwood) but senior citizens have been adversely affected.

Since kids are building their Adaptive Immunity, their Innate Immune System's 'dial' is turned up to 'Very High'.



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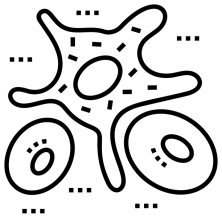


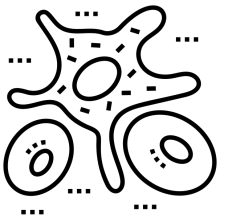
WBC

That means they are on high-alert for any foreign looking pathogen – anything new could be a threat.

Bear in mind- the SARS-Cov2 is a 'novel' or new virus. But for the kids' 'Innate Immune System', it's probably like any other 'new' virus threat – and so is able to deal with it.

With senior adults on the other hand, their Adaptive Immune System has slowed down... It can react to old/ known pathogens quickly. But anything new, and it struggles to cope.

Reminder - the SARS-Cov2 is a 'novel' or new virus! This is the key reason why seniors' Immune systems find it difficult to identify and neutralize the virus[1]



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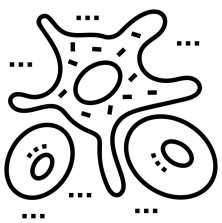


WBC

Ok, I think it might be time to introduce the main actors of the Immune system.

Things are about to get messy. Brace yourself.

1. In addition many adults have compromised immune systems because of co-morbidities or pre-existing immune-system ailments

# The Human Immune System

(A very, *very* crude representation)

STORY rules

**Innate Immune system**

Skin – our first line of defense

Nasal hair, cilia – the second line

Sensors within the human cells – the third line

**The Specialists: Different types of White Blood Cells (WBCs, aka Leukocytes)**

Macrophage

Dendritic cell

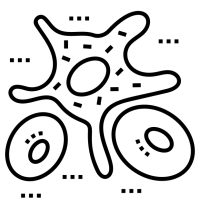
Natural Killer cells*

* Seriously, that is what they are called. Immunologists can get quite graphic with their names.

**Adaptive Immune system**


B-Cell (many types)


T-Cell (many types)

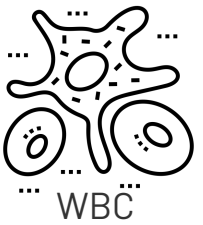


Confused yet? Good, you should be.

ICYMI, the Immune System is complex.

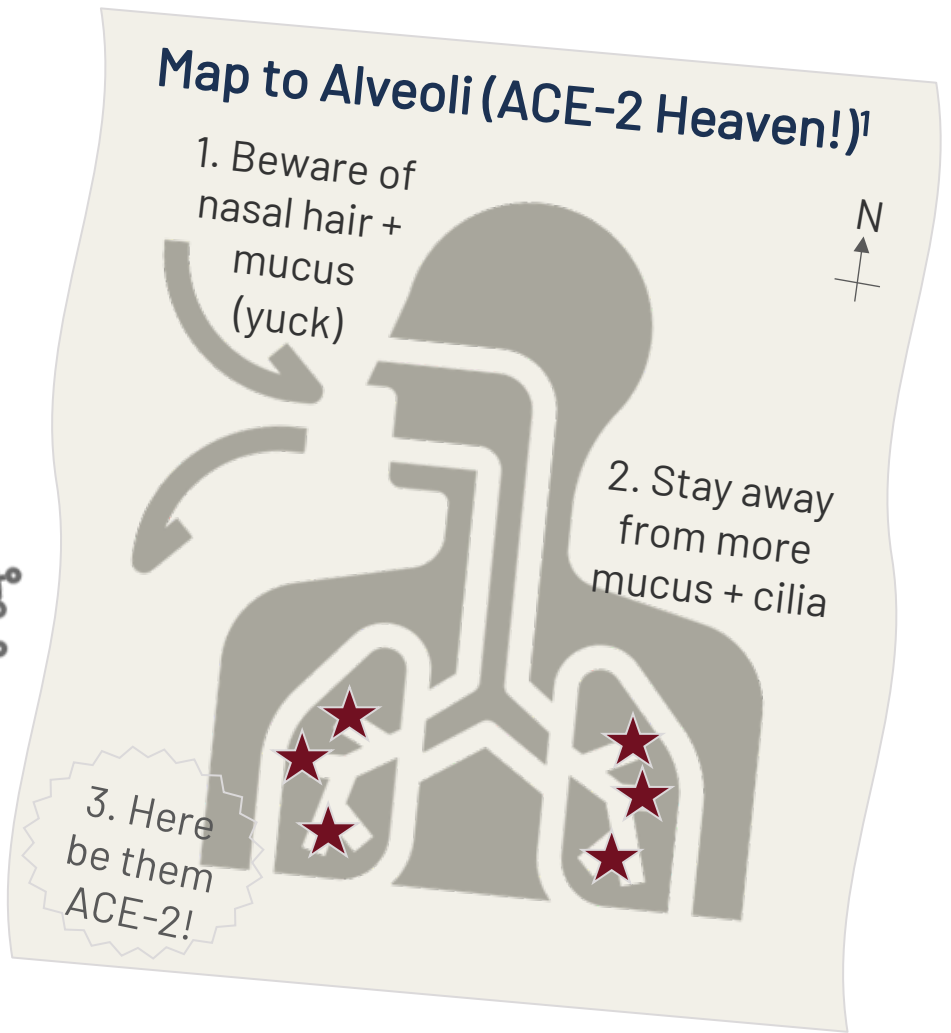
Instead of theory on how these work, let's do a case study.

It's time for the story's villain to make a re-entry...




Remember me?

Here's my perilous journey




1. Alveoli: the tiny air sacs in lungs where air exchange happens; ACE2: the receptors jutting out of a certain type of cell on the alveoli

Actually the ACE-2 receptors are just my entry points into the human cell. The real target is a crucial element inside the cell itself.

On that note, I think you should meet...

Human Cell

Hola there, I'm a human cell –the basic building block of your body. You have a gazillion (ok around 40 trillion) of us.

Each cell does a bunch of functions. But one crucial function is making proteins.

Protein making is fascinating. Think of a protein as a Lego structure made using different blocks.

The instructions or *blueprint* for building the Lego structure comes from your DNA (which is in the cell's nucleus)

Human Cell

Human Cell

The *material* for creating the Legos come from your cell's cytoplasm (inner fluid).
But the actual production unit is something called the **ribosome**.

Ribosomes are extremely tiny - each cell can have as many as 10M ribosomes.

Think of a Ribosome as a 3-D printer. Reads instructions, assembles material and prints the proteins.

Human Cell

Human Cell

The thing is though, it doesn't directly read DNA. For reasons beyond the scope of this e-book, ribosomes read instructions in a different format. (You know, like a printer which needs the document to be in a specific printable format).

That format is called RNA.

So the cell's nucleus translates the DNA (master instructions) into the printable format: called messenger RNA (or mRNA).

mRNA is single stranded (unlike DNA which is double stranded).

Remember this – it is a crucial detail.

Human Cell

Human Cell

So the ribosome's job is simple. See RNA. Read RNA. Print Protein.

It's a simple 3-D printing factory. It doesn't discriminate. Which me..

...ans good news for me!

Hello! I'm all RNA inside[1]!

You're telling me, that all I have to do is insert my RNA into these magical 3-D printers, and it can print copies of me?!

Let the production begin!

Human Cell

Unfortunately, that is true.

Once the virus enters the cell, it commandeers ribosomes to do its bidding. Which means that regular cell functions start getting impacted. And the virus takes over the cell.

But I do have a trick up my sleeve...

1. The SARS Cov-2 virus is an 'RNA virus'. Which means that the instructions to make copies are in the RNA format

You see, as a cool design element, cells have internal bio-sensors to check for anomalies in the production process.

Ideally the ribosome should only be getting *single*-stranded RNA

Human Cell

Human Cell

It turns out, the virus has *double*-stranded RNA.

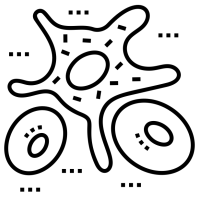
A-ha. Gotcha.

Think of these bio-sensors as internal security guards of the cell. They don't have guns. Oh, but they have whistles.

If the sensors inform me on time, I send out a distress signal called Type-1 Interferon, which tells surrounding cells: "INTRUDER ALERT!" (Interferon is a type of chemical known as a cytokine. We will revisit that soon.)

The release of interferon informs the passing neighbourhood police: the WBCs. It's retaliation time.

Human Cell



WBC

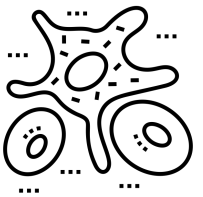
Hi there, WBC here again.

Once we hear a distress signal, we follow a similar strategy to what humans do: Containment and Clearance.

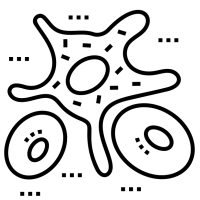
Let's discuss the Containment pathway first.

Just like you guys do lockdowns and containment zones, we cordon off an area around the infected cell/s.

When this happens, it is called an inflammation.



WBC



WBC

At the inflammation sites, one key objective is to stop the further replication and spread of the virus.

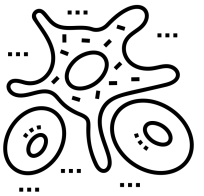
This is partly done by the afore-mentioned 'Interferon' chemical which ... *interferes* with virus replication[1].

In order to help this pathway, we sometimes use a key ally. Heat.

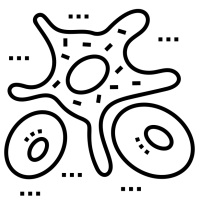
1 That is how it got it's name - I'd told you about Immunologists and their penchant for cool names

It is known that high temperatures reduce virus replication. So we do a neat maneuver.

Remember we mentioned that the body is like a massive factory complex? Well that complex has a thermostat – a small unit which controls temperature. It's called the 'hypothalamus' and it sits deep inside the brain.



WBC



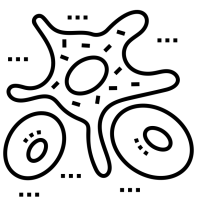
WBC

Now the hypothalamus doesn't understand germs, or inflammation.

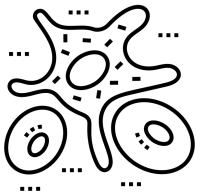
It only understands temperature. If the outside temperature is cold, it increases the body temperature. If it's warm, it reduces.

So we resort to a bit of trickery.

We send chemical signals known as pyrogens, which goes and switches on another chemical called Prostaglandin E2 (PGE2)... A lot of fancy names, but essentially acting as a simple messenger...



WBC



WBC

A messenger which tells the hypothalamus: ‘Bro, it’s cold outside. Can you please turn up the thermostat?’

The hypothalamus dutifully does that. And you get a fever[1].

Alright, so that’s about containing virus replication. Now let’s come to our core strategy for solving this issue.

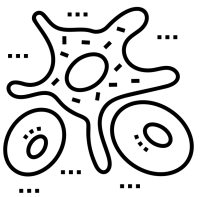
Virus clearance.

Let’s get back to the site of inflammation.

While one pathway is focused on containment, another set of cells have a different task on hand.

To hunt down and neutralize the virus and the infected cells.

Let’s recall our A-Team.



WBC

1. Two things. One, despite its ubiquity, fevers are still not clearly understood by scientists. I’ve clearly over-simplified a complex and layered phenomenon
Two, while fevers do help in reducing virus replication, a prolonged fever can be damaging for normal body cells. Which is why your use of paracetamol or aspirin (which basically inhibit PGE2 release) is needed. Of course, you need to consult your physician before taking any medication!

# The Human Immune System

(A very, *very* crude representation)

STORY rules

**Innate Immune system**

Skin – our first line of defense

Nasal hair, cilia – the second line



Sensors within the human cells – the third line

**The Specialists: Different types of White Blood Cells (WBCs, aka Leukocytes)**

**Macrophage**

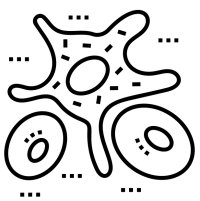
**Dendritic cell**

**Natural Killer cells**

**Adaptive Immune system**


B-Cell (many types)


T-Cell (many types)



Just sharing this visual again as a reminder!

We saw what the cell sensors do. Now let's look at what the WBCs from the Innate Immune system can do.

Macrophage

Dendritic cell

Natural Killer cells

Hi, we are back

Natural Killer cells

I'll go first. Lets talk about the cool name first.

So, some WBCs take out pathogens. I, on the other hand, take out the infected human body cells.

Why the 'natural' in the name? Now, some other WBCs need to be 'primed' to kill infected cells. I don't need any priming or 'activation'.

007. Terminator. Call me what you want.

You see, I'm born with a license to kill.

The name's Killer. Natural Killer.

Let me show how I go about my business.

Natural Killer cells

Natural Killer cells

I roam around the body (and especially in inflamed areas) looking for infected cells.

These give out some tell-tale signs on their cell membrane. I'm trained to spot these signs.

When I do, I attach myself to the cell's surface and (this is the gory part) quietly release some chemicals.

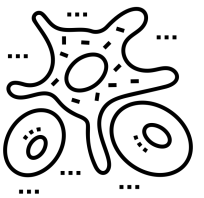
The cell – it sleeps with the fishes[1]. RIP.

The Natural Killer Cell sounds suave.

But it's basically doing a cleanup job.

The virus still needs to be neutralized. Which is where we need the other two Innate Immune system heroes.

The Macrophage, and the Dendritic cell.



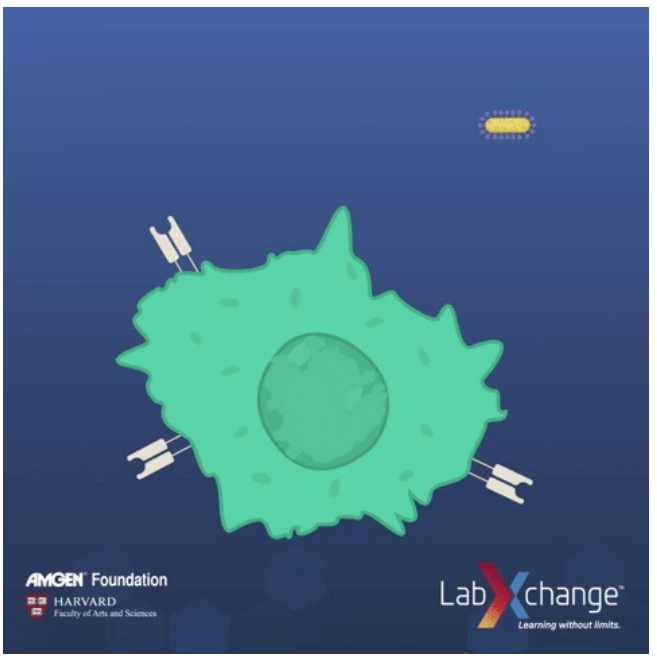
WBC

1. Look out for another 'The Godfather' reference soon!

Me Macrophage. Me like bugs. Me eat bugs.

And Me. Always. Hungry.

Macrophage




*Incredibly cool graphic of a WBC gobbling up a micro-organism*

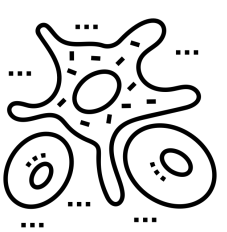
Dendritic cell

Hi there. I'm a Dendritic cell. For the longest time, scientists confused me with the Macrophage.

Perhaps it's because, I also enjoy wolfing down micro-organisms

Don't go by the simple demeanor though.

What these two do next is spine-chilling. The Mafia could learn a trick or two...

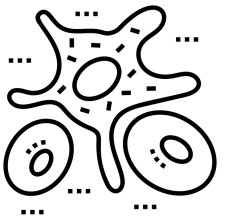


WBC

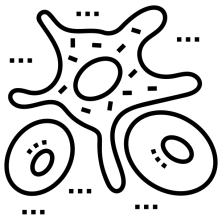
Source: Giphy by Amgen Foundation, Harvard Faculty of Arts and Sciences

These cells *retain* a part of the pathogen. In case of the SARS-Cov2 virus, their most tell-tale sign: the Spike Protein.

(That same appendage that enables them to attach to our cells).



WBC



WBC

This tell-tale part of any pathogen is called: The **Antigen**.

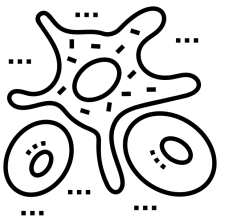
And the next act of the Dendritic cells (and macrophages) is called 'Antigen Presentation'.

Why do they do this? Where? And who do they 'present' it to?

So, they don't do it to leave a threatening note to other viruses...

(Although, that'd be badass, right?)

They do it to warn the real police – the Adaptive Immune guys: **BAD GUY FOUND!** Btw, here are his fingerprints.

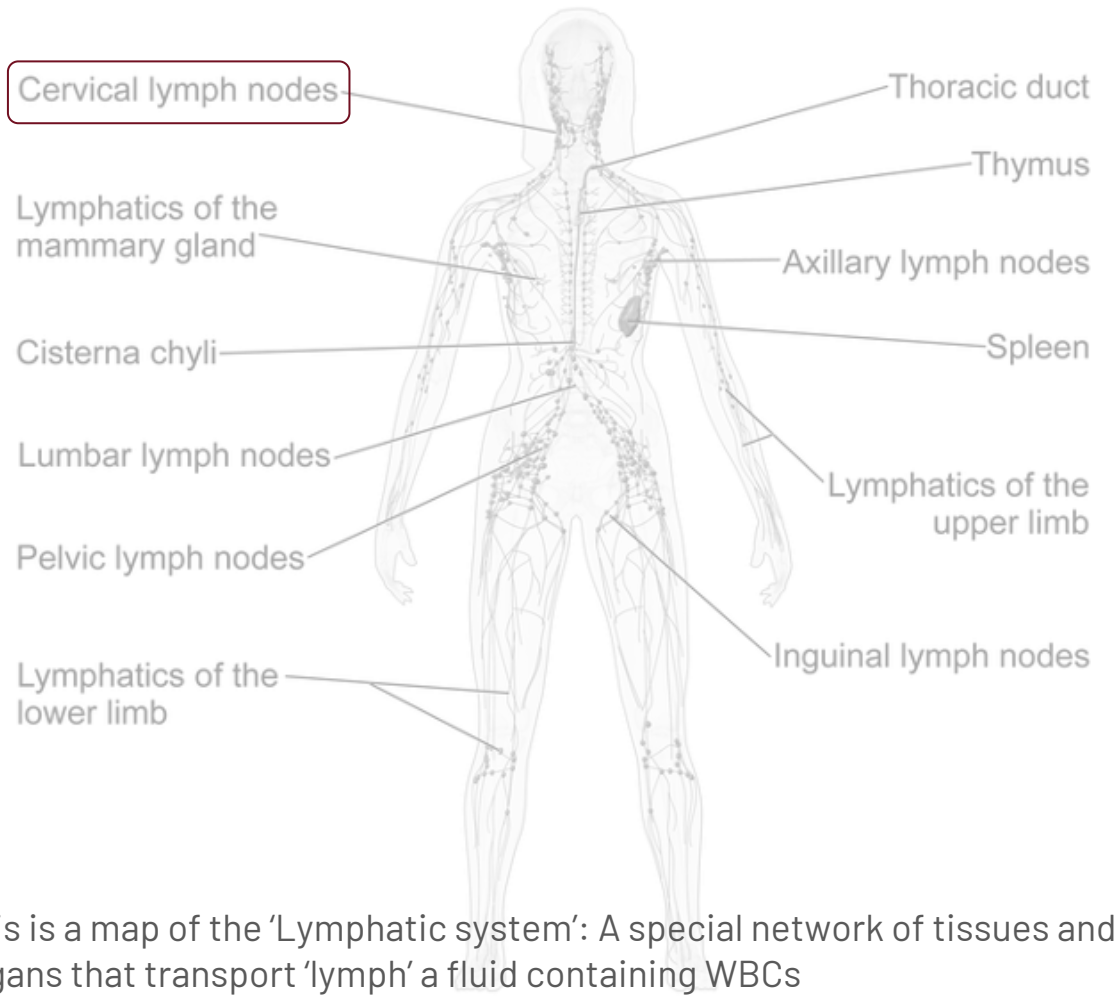


WBC

Dendritic cell

Ya, so we take the antigen to a lymph node: a cool hangout place where we can meet a ton of other WBCs.

Most importantly, we meet our friends from the Adaptive Immune system: The B-Cells and T-Cells




This is a map of the 'Lymphatic system': A special network of tissues and organs that transport 'lymph' a fluid containing WBCs

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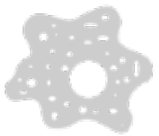
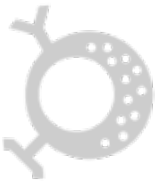


Macrophage

Dendritic cell

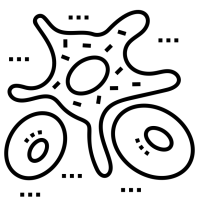


Natural Killer cells

**Adaptive Immune system**


B-Cell (many types)

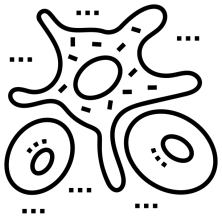

T-Cell (many types)



WBC

Just sharing this visual *again* as a reminder!

We saw what the Innate Immune system does. Now let's look at how Adaptive guys work.



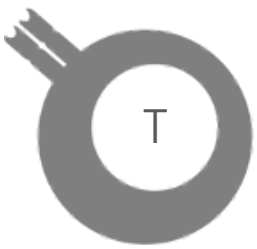
WBC

I think it's time to introduce my next two guests in the program: the main actors of the Adaptive Immune System.

The B-Cells and T-Cells

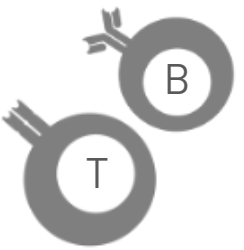
Hi, I'm a B-Cell. Why 'B'? So, I originate in the **b**one marrow (found in the centre of several bones in your body).

The bone marrow is the biggest factory for producing all sorts of blood cells, including all WBCs

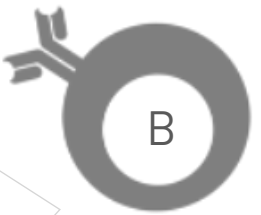

And I'm a T-Cell... Actually, I too originate from the bone marrow, but I 'mature' in an organ called the 'Thymus' (located in your chest, above the heart). Which is why 'T-Cell'.

We have our own differing ways of dealing with the microorganisms.




I'll go first. So when the Dendritic cell/macrophage reaches the lymph node carrying the antigen, something magical happens.

We'll come to that in a bit. But first – what is my attack plan for the virus?




My approach: Subtlety and efficacy.

No gobbling up of pathogens for me. I believe in the Hindi saying "Na rahega baans, na bajegi bansuri" (No bamboo, no flute).

So the virus' spike protein (a.k.a. the antigen) is its main entry vehicle, right?

How about we simply neutralize that entry point?


Do you remember how the spike protein attaches to the ACE-2 receptor in our cells? Like a key to a lock right?

Well two can play that game...

What if we create a 'key' – a specific component which can plug the spikes that stick out of the virus.

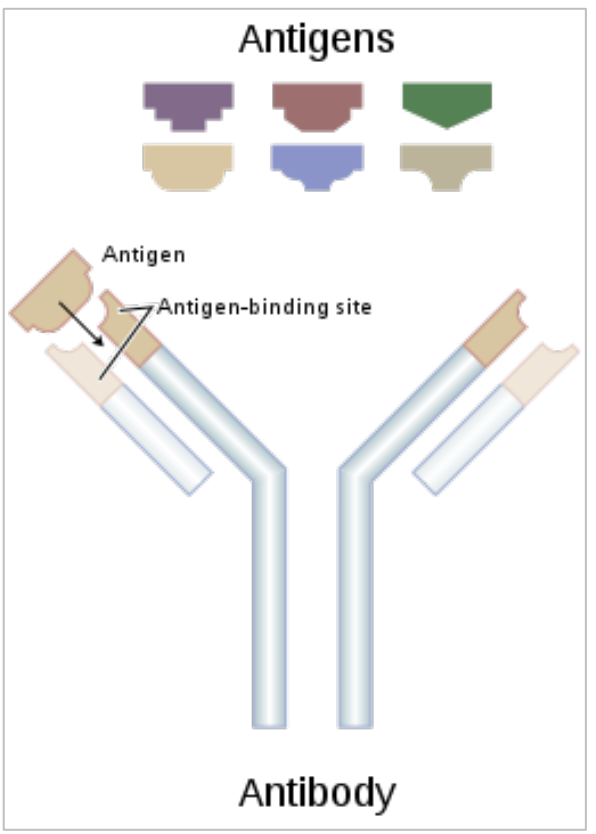

If this key binds to all 'entry-points' of the virus, it would have rendered it ineffective.

This Y-shaped key – your MOST important weapon in the fight against Covid-19 - is called: **The Antibody.**


The image to the right illustrates how an antibody has to be made *specific* to an antigen.

Just like a key is made specific to a lock.

Now that's not easy




Antibody image by Fvasconcellos, Public domain, via Wikimedia Commons

Remember I mentioned – when the antigen presenting cell reaches the lymph node, something magical happens? Let's talk about that.


Now, each B-Cell comes pre-built with a specific type of antibody. In other words, it carries a specific key.

All the Dendritic cell/macrophage has to do is to find the right B-Cell.

Here's the issue. The Lymph node is packed with B-Cells.

Dendritic cell

Oh boy, tell me about it. There are millions of them in there.

It's like entering the city of Mumbai and hoping to find someone wearing a specific shade of maroon-coloured shirt.

How do I find the right one?

It's analogy time.

So, imagine a customer who's bought a nice sari for a wedding[1]. And now has to find the right blouse piece.

She enters a blouse-piece store to find a matching colour. Trouble is, the blouse shop has rows and rows of blouse pieces.

How does the shopkeeper do a quick check?

He takes the sari and does a rapid sweep of the shelves from top to bottom, till the customer says: "That one"

Dendritic cell

Dendritic cell

The Dendritic cell is the shopkeeper. The Antigen is the sari. The B-Cell's antibody is the blouse piece.

And quietly overseeing this process, in the background, is a crucial actor.

The Helper T-Cell

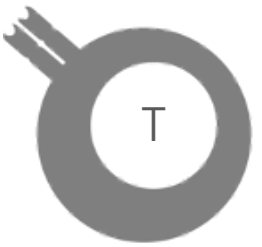
1. This vivid, colourful and evocative analogy is courtesy the brilliant Prof. Satyajit Rath

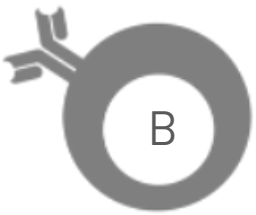
That's me. I'm trained to find a quick-and-dirty antibody match from the millions of B-Cells.

Then comes the fun part. We get the chosen B-Cell to quickly reproduce itself and create minor variants.

Say, one shade lighter maroon. One shade darker. A wee-bit more etc.

We are essentially refining the key, to ensure as perfect a match as possible.




Once the target antibody-carrying B-cell is locked, then it's time to hit the 'mass manufacture' button.

Each B-Cell can make copies of itself. But that process will not be fast enough for the millions of antibodies needed.

So the chosen B-Cell is sent (through the lymphatic system) to the mother factory.

It's time for a visit to the bone marrow.


And so, the body creates and releases millions of antibodies into the bloodstream.

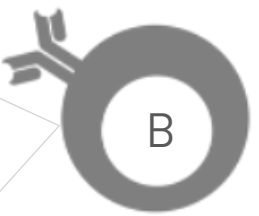
These antibodies are ready to (literally) lock on to their target: the virus

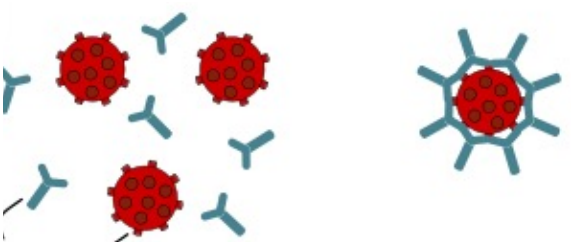
There are two major ways in which the antibody defeats the virus.

One, neutralization.

A horde of antibodies descend on the viruses and lock onto their spike protein receptors.

With no way to attach to a cell, the virus is essentially neutralized.

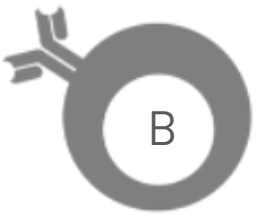



The second way involves help from an old friend...

Me Macrophage. Me back.

Me still hungry.



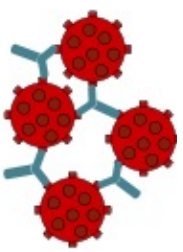

So, the antibodies do a neat maneuver called ‘agglutination’.

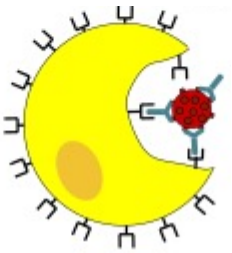
Fancy name for “let’s-catch-a-bunch-of-ruffian-viruses-by-the-neck-and-show-them-to-the-hungry-macrophage”

Me see food. Lots of it.

Me go ‘Aaaa-gobak’

Buurrrp.






Did I mention, subtlety?

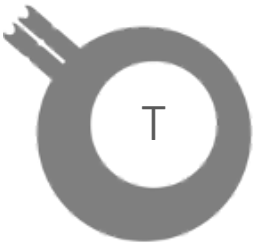
Oops, my bad!

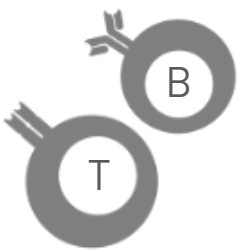
While this virus clearance is happening, another process is underway. Cleaning out any remaining infected body cells.

(A similar process to what the Natural Killer Cells were doing earlier).

This infected-cell cleanup is done by a special category of T-cells called – wait for it – Killer T-Cells[1].

I just love our names.



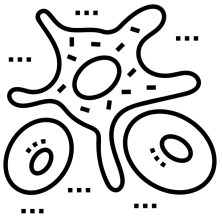




That's not all. We are also supported by a category of cells called Memory B-Cells and Memory T-Cells

These smarties retain the information of the 'Antigen' (the fingerprints) so that if that pesky virus decides to return... you know the drill.

How long do these antibodies last? The number varies, but one study found presence of antibodies, and Memory B-Cells even 6 months after the original infection

1. It also goes by the boring pseudonyms of CD8 T Cell and Cytotoxic T Cell.



WBC

Right then. This entire process – virus entering body to its clearance – can take around 2 weeks.

And this is the process in most asymptomatic or mild cases of Covid-19.

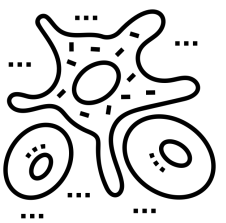
Basically your immune system (combined with paracetamol for fever regulation) is good enough to defeat Covid-19. Most of the time...

But what really happens in severe cases? Why do our lungs bear the brunt?

Why does the Immune system get overwhelmed? What treatments help?

And where does the vaccine fit in all this?

All coming up in Chapter 3!



WBC


COMING SOON

# CHAPTER 3

# SEVERE DISEASES

## CAUSED BY THE SARS-CoV-2 VIRUS AND ITS TREATMENT

Image credit: By Mika Baumeister from Unsplash

# Story sources

While I've tried to be comprehensive in my list of sources, I may have missed some out – apologies for the same!

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How Novelty means severity: https://www.theinsight.org/p/novelty-means-severity-the-key-to

# Stay safe. Get vaccinated.

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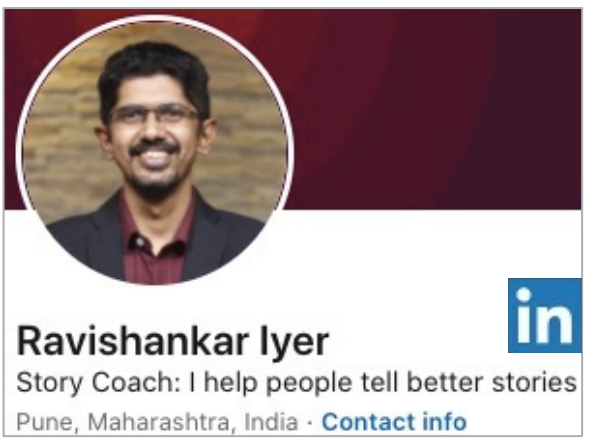


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