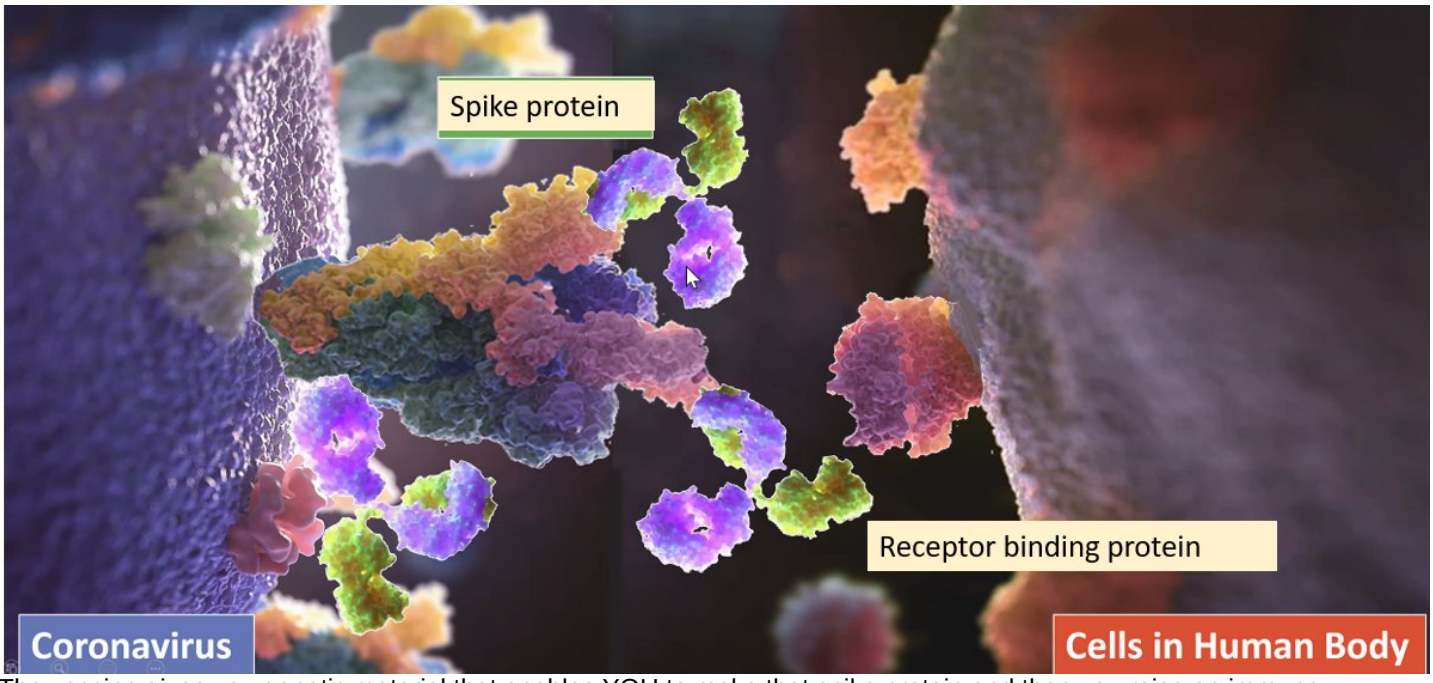
Twitter Thread by Monica Gandhi MD, MPH



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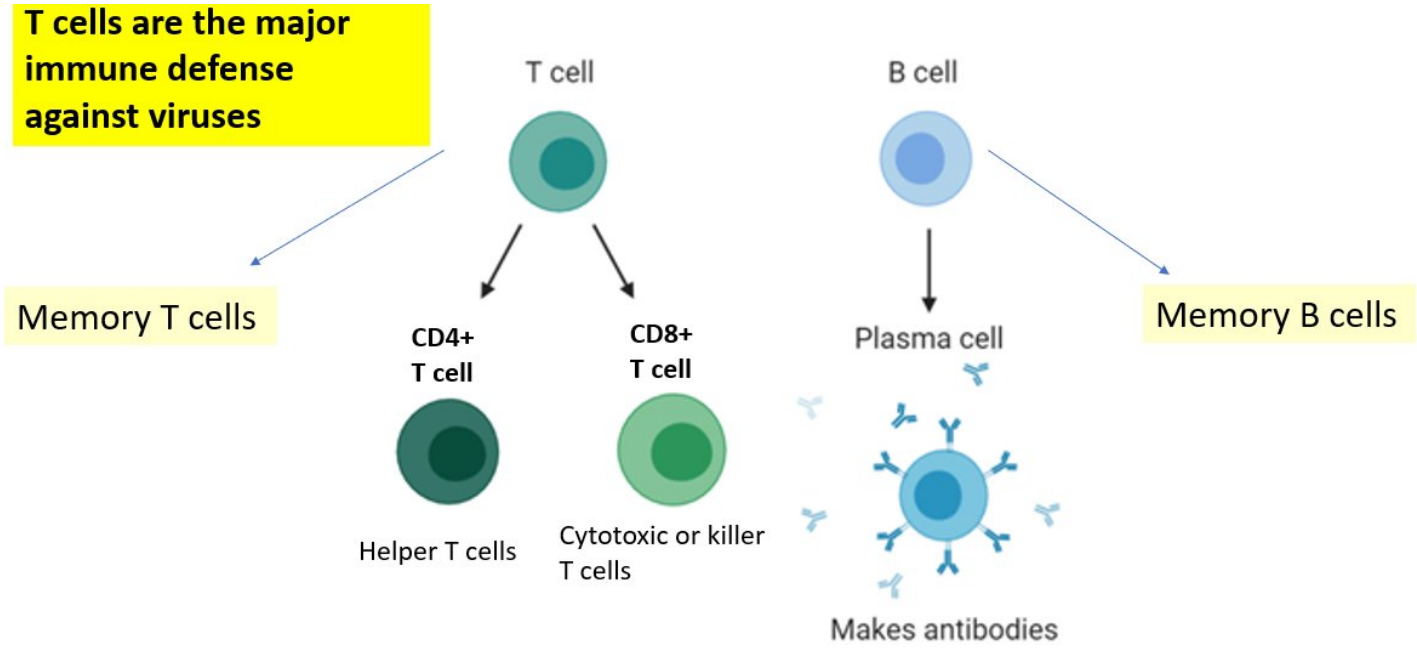
DELTA variant. To discuss this, let's actually start with discussing the spike protein of the virus. Remember, the spike protein of the virus is how the virus binds to our host cell. The spike protein is the protein that is encoded by the mRNA & adenovirus-DNA vaccines (J&J)



The vaccine gives you genetic material that enables YOU to make that spike protein and then you raise an immune response against it (of course natural infection makes you raise an immune response against virus). Genetic material goes away & you have immune response. J&J just one

step "upstream" from mRNA vaccines so gives you DNA which you MAKE into mRNA and then you make spike protein. mRNA vax allows you to make protein directly. Not that different though J&J vax takes longer to give full immunity (phase II trial, up to 60 days)
https://t.co/RHLOe6leWZ

Okay, now consider this fact: you make at LEAST 87 T cells that line up across the spike protein to combat the virus from a vaccine (will explain 87 in bit). And likely many more. T cell measurement takes fancy machines, show you the breadth of the T cell response.



So, this paper is by our CA colleagues @settelab shows you make T cells against 1400 little bits of the virus and postulates 100 or more across the spike protein (enriched for spike protein T cells). And the paper from the AztraZeneca trial in S. Africa
https://t.co/vUG15U8VnT

shows us that 87 T cells line up across the spike protein to fight the virus when you give the vaccine. So, even with the beta variant (used to be called B.1.351), 75 of those T cells still fight that spike protein (the mutations only knock out 13).
https://t.co/GpFJSyDMvQ

So, it will be very difficult to ever knock out your T cell response with mutations along the spike protein. Okay what about the DELTA variant? 12-13 mutations across spike protein so the T cell response you get from vaccines will still cover it. Ok, so
https://t.co/XQ1fGBEAXQ

what do our antibodies do versus T cells? T cells help protect us against severe disease as shown in this article so this is why our T cells from vaccines & natural infection will protect us against hospitalization/death from COVID. In fact, this is why
https://t.co/LlhJntURL8

data from Public Health England yesterday June 14 showed us 2 doses of the vaccine protects you against hospitalization from the delta virus - both the mRNA vaccines and the AztraZeneca vaccine (which is like J&J vax), but 2 doses better for this variant
https://t.co/mZZhi5LtiA

Okay what about antibodies? Since antiboies cluster in the nose (both IgA and IgG antibodies), you want your antibodies high in your nose to not even get mild infection in your nose (like loss of smell, runny nose). The mRNA vaccines do produce Abs
https://t.co/xKeiwTcjxY

to neutralize that delta variant but you really want TWO doses to produce adequate levels. Moreover, after natural infection with COVID, you have those "in breadth" T cell responses that cross the spike protein but you may need an antibody "boost"

in your nose to not get mild

infection from the delta variant, which is why giving 1 dose of the mRNA vaccines after natural infection may be indicated (indeed, so many studies now show us that antibody response after 1 dose of mRNA vax boosts antibodies after natural infection more than 2 doses when didn't

have #covid19 before. If variant transmits more readily like delta variant, will go around and infect those unvax'd or cause mild nasal symptoms in those who have had natural infection if nasal antibodies go down. But rare to cause severe disease in those vax'd /natural infection

Children less likely to get infection even in nose after exposure (3-fold less than adults), less likely to get severe disease from any variant or original. Virologists don't think strain more virulent (e.g. cause more severe disease). NOT vax resistant
https://t.co/uZP0BOHy4I

And, yes, J&J vaccine gives great antibody and T cell responses across spike protein so will protect you against this variant as well (look at that T cell response)
https://t.co/VxdLQzE9dt

The reason we want the 2 doses of Pfizer to protect against delta variant is here (don't have data on J&J in "real world" but above tweet shows the T cell immunity)- 1 dose not as effective for delta (33-50%) so need 2 doses
https://t.co/2dRIgYq3Le

Great delta variant-relieving study even in face of high circulating virus with this variant in India. Study in 31,621 health care workers in India Jan-March. Even after 1 dose (some had 1 dose, some fully vax with 2 doses) >95% protected! 4.28% infected
https://t.co/dno3fTziqx

post-vax & most non-serious (no deaths). Most got AztraZeneca & this is important: after 1 dose, 5.14% re-infected, after 2 dose 4.09% re-infected (again most mild) so that is helpful to know how protective 1 dose is in the face of MOST of virus being delta variant & circulating

at high levels & this is healthcare workers who had a lot of exposure! Remember, the risk of us extrapolating from one study (UK) without looking at other studies (India) can lead to a lot of concern. Delta ore transmissible; likely not more virulent; not vaccine resistant

**Heard back from colleagues in UK. 33% efficacy after dose 1 for delta averaged over two weeks following 1st dose while immune response increasing (continue precautions 1st 2 weeks. Immunity to dose 1 against delta was 80% after 1st 2 weeks. Consistent with India data above.

This tweet thread from @EricTopol may be helpful to add to my delta variant thread. I am intent on & will continue to explain the immunology behind these findings about the variants- maybe more transmissible but not more virulent nor immunity resistant.
https://t.co/LH81ioFZFB

> There are many statements asserting that the Delta variant is more deadly than Alpha. There are no data to back that up https://t.co/xBWAB0B6Mo
> "The crude case fatality rate remains lower for Delta than other variants at present" @PHE_uk /1
>
> — Eric Topol (@EricTopol) June 20, 2021

Try to explain delta variant verbally here - reason important to not "parrot discuss" delta is 1) UK gave 1st dose 1st strategy; should be careful 2 weeks after 1st dose with 33% but after that, 80% effectiveness against delta, consistent with India https://t.co/juK9X8puHf

data which is largest dataset on this; 2) delta being used as reason to keep parents scared by some papers (@DLeonhardt at @NYT notable exception) which may not allow parents to think about myocarditis risk of 2 doses in young males & await @ACIP recs; 3) delta pushed by some to

keep schools restricted instead of following metrics-based approach where restrictions for kids cease when @CDC metrics of low hospitalizations (<5/100K in population reached); 4) doom based messaging so common but can paradoxically decrease vax uptake
https://t.co/xiDMjy61Lc

Helpful article by @DLeonhardt at @NYT on delta variant in children. Agree with @JenniferNuzzo that we haven't seen data that this variant more dangerous for children.
https://t.co/bds5xsQDcl

See scientists trying to "motivate vaccines" by discussing delta variant. Like alpha, not shown to be more virulent; more transmissible or will become dominant strain, nor vax resistant. natural immunity/high vax rate in vulnerable great- please read this:
https://t.co/APXkEUNO1P

Dr. Fauci at White House today said "eliminate" COVID but had indicated previously goal in US is "control" which is achievable goal (like measles) which allows life to stop disruption. By the way, he said elimination in this article for word "eradication"
https://t.co/iD3zBnD0GG

Good definitions!
Control: Reduce # of people infected & those who become sick/die from disease in LOCAL settings
Elimination: Stopping transmission of disease in specific area or country, not worldwide
Eradication: Eliminating world (only smallpox)
https://t.co/MTJZ8eBKFy

In summary, seeing some of the ? below- no evidence that delta variant more virulent (that would result in an increased hospitalization/case ratio and that ratio is actually going down because younger unvax'd getting it); no evidence delta evades vax; no need for mRNA after J&J

One way to explain: If higher virulence, then will see more hospitalizations per case - so say 1 out of every xx cases get hospitalized, do we now see 2 or 3 of every xx cases get hospitalized with new variant? Hospitalization/case ratio (H/C)

increased?
https://t.co/2UijxHkaVr

> Okay 2) Increased virulence: The cleanest way to look at this in US is to look at states with highest prevalence of B117 and see if "hospitalization per case" rate has gone up. Meaning, if virus is more virulent, more cases will end up being hospitalized. Will call this ratio H/c
>
> — Monica Gandhi MD, MPH (@MonicaGandhi9) April 7, 2021

We went through this with alpha- lot of conflicting data since as cases go up, admissions go up but doesn't mean it causes more severity. Think cleanest way to look at this is H/c ratio; we did that analysis with B117 & didn't see (see thread above & here)
https://t.co/HfZl8IAVXq

At this point, it is important to get vaccinated, I encourage it. Delta or not, vaccines are here & young (who are less at risk & busy) should get. Tomorrow, we will hear ACIP recs on younger males for side effect. Think fear variant will evade vax disputed by T cell immunity

Remember when looking at H/c ratio, depends on if you are capturing all cases (decreased testing with vax going up, cases or denominator will be lower). So much confounding in epi. Best to go back to principles of Virology on variants, author of TEXTBOOK
https://t.co/XR0wypOU5Q

BREAKING NEWS ON DELTA VARIANT (except not really, preprint was posted PHE on June 14): Vaccine effectiveness against hospitalization with delta was similar to that seen with alpha - 94% after 1st dose, 96% after 2nd dose Pfizer. 71% after 1st dose with AZ; 92% after 2 doses

> doses of any vaccine. This compared to 0.44 (0.28-0.70) and 0.64 (0.24-1.72) with Alpha. VE against hospitalisation with Delta was similar to that seen with Alpha: 94% (46-99) after 1 dose and 96% (86-99) after 2 doses of BNT162b2; 71% (51-83) after 1 dose and 92% (75-97) after 2 doses of ChAdOx1 (Table)

Preprint here. Just like in India data. So, let's do this. Decide on young males 2nd dose with safety in mind as effectiveness of even 1 dose of Pfizer very high. Stay calm with variants. T cell immunity can't evade. Message confidence in vax to increase uptake

Preprint here from Public Health England: https://t.co/qUwl2cMObV