COVID-19 vaccines

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Johns Hopkins Global Map 15/08/2021

- Total COVID cases: 206,766,151
- Total deaths: 4,354,636 (2.1%)
- Total vaccine doses administered: 4,655,333,711

A LOT of vaccines have been given.

We collectively have good data on benefit / risk, pros / cons.

Common Side effects are well defined

Definition of very rare side effects continues

Understanding of “breakthrough infections” and implications evolving

How did vaccine trials start? DBPC trials

- Phase trials run together and overlapping for speed (1/2; 2/3; 3)

Eg: Pfizer Trial 43,000 subjects: placebo cases/placebo+vax cases X100 =%
162 placebo infected, 8 Vax cases: 162/170 x 100 = 95% (NEJM 12/20)

Eg: AZ trial Pooled 4 trials in UK, Brazil, South Africa (placebo vs vax)

11,636 in analysis with Overall efficacy 70% (90% in ½ dose, 62% full dose)

- These trials have overlapping confidence intervals (Result not sig. diff)
- Trialled in different countries, with subtypes, and protocol variations

- These numbers would NOT detect clot issues, or rare immune issues

Scotland results: AZ and Pfizer (Lancet, May 2021)

- Constructed an open, real-time prospective observational cohort with national level coverage in Scotland with dataset linking vaccination, primary care, laboratory testing, hospitalisation, and mortality data
- Assessed hosp. admit data in 5.4 million cohort (8/12/20 till 13/2/21)
- Vax group 1,137,775 (35%) of populatN.
- Pfizer Vaccine effect 85% (CI: 76 to 91) reduction for COVID-19 related hospitalisation at 28-34 days post-vaccination.
- AZ Vaccine effect 94% (95% CI 73 to 99) using same criteria.
- Vax effect comparable when restricted to age ≥80 years
  (81%; 95% CI: 65 to 90 at 28-34 days post-vaccination)

- Effectiveness of first dose of COVID-19 vaccines against hospital admissions in Scotland: national prospective cohort study of 5.4 million people Dr Eleftheria Vasileiou PhD, Usher Institute, The University of Edinburgh, Edinburgh, EH8 9AG, UK, eleftheria.vasileiou@ed.ac.uk,

COVID vaccine breakthrough infections: USA

MMWR/May28, 2021

- Small % fully vaccinated develop symptomatic/asymptomatic infection
- 10,262 reported in USA among 101 million vax'd to April 30, 2021.
  - 27% asymptomatic (2,725), 73% low level symptoms
  - 10% hospitalised (995)
  - 2% died (160); mean age 82; 28 died non-COVID cause
- Currently 99.5% mortality is in unvax'd, but as % vax'd goes up and fewer die of covid, the % dying will be smaller and a higher % vax'd
- Concern breakthrough rate higher in immuno-compromise

What about Allergic side effects

Common side effects of Vaccination (ANY Vax)

- Fevers, chills, myalgia, tiredness, headache, nausea, arthralgia
- Local pain, redness and swelling
- Local adenopathy a few days later.
- Itching at the injection site a few days later
- Side effects may be more or less intense after second shot
- The intensity of the reaction varies in the population.
- These features are those of an active immune response

- Can be managed with simple analgesia or antihistamine
- May occur after 1 – 7 days; should NOT preclude 2nd dose of same vax

Anaphylaxis

- Rare: current estimates 4.5 per million based on 10 million doses
- Rates similar AZ and Pfizer, and similar to the other vaccines we use
- Anaphylaxis occurs in 80% in 15 mins and 90% in 30 mins.

- There is a lot of concern about anaphylaxis, but is rare
- DO tryptase levels 1, 4 and 24 hours (helps to really know if re-vax)

- Patient report of “allergic” symptoms / anaphylaxis at higher rates

Study at Massachusetts General Bringham

- Studied staff vaccination via self report of symptoms (txt, survey etc)
- 61,057 vaccinated (37% Pfizer, 63% Moderna) and 50,167 did survey
- Self report of “allergy symptoms in 1,261 (2.5%)
- 99% had second dose after review/reassurance, 0.7% did not (576)
- 860 reported after second dose with 146 having minor symptoms.

Second study in Boston by Krantz et al, 2021

Studied 189: allergic symptoms ≥1, onset <4 hours, review by team

All received an mRNA vax:

28% flushing/erythema
26% dizziness, light headed
22% throat tightness
21% wheezing/SOB
21% Hives/urticaria

159 patients agreed to second dose and safely completed it.

32 (20%) reported repeat symptoms managed with antihistamine alone

Included 19 believed to have anaphylaxis (?? Likely overcalled)

Diagnostic criteria for anaphylaxis

Anaphylaxis is highly likely when any ONE of the following three criteria is fulfilled:
1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
AND AT LEAST ONE OF THE FOLLOWING:
A. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
B. Reduced BP* or associated symptoms of end-organ dysfunction (eg, hypotonia, collapse, syncope, incontinence)
2. TWO OR MORE OF THE FOLLOWING that occur rapidly *after exposure to a LIKELY allergen for that patient* (minutes to several hours):
A. Involvement of the skin mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
B. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
C. Reduced BP* or associated symptoms (eg, hypotonia, collapse, syncope, incontinence)
D. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
3. Reduced BP* *after exposure to a KNOWN allergen for that patient* (minutes to several hours):
A. Infants and children - Low systolic BP (age-specific)* or greater than 30% decrease in systolic BP
B. Adults - Systolic BP of less than 90 mmHg or greater than 30% decrease from that person's baseline

BP: blood pressure.

* Low systolic blood pressure for children is defined as:
  - Less than 70 mmHg from 1 month to 1 year
  - Less than (70 mmHg + [2 x age]) from 1 to 10 years
  - Less than 90 mmHg from 11 to 17 years

Vasovagal reactions —

- Characterized by hypotension, pallor, diaphoresis, weakness, nausea, vomiting, bradycardia.
- If severe, loss of consciousness, collapse.
- Cutaneous signs of pallor, sweating +/- flushing but not itching, NOT urticaria/angioedema.

VCD

Stridor, hard to talk (loss of voice), breathless, throat fullness.

O2 Saturation Normal, typically hypertensive, not hypo. VERY distressed, hyperventilating, can be jerking and confused if severe with elevated lactate on B/GAS.

What about other “Allergic” reactions?

- Delayed urticaria >2 hours after 1st dose NOT a contraindication to repeat dose. Use antihistamines NOT steroids. Often one off
- Delayed local reactions looking like cellulitis, Mx: topical steroid. Can give second dose other arm, AHs if needed, but usually not recurrent.

- H/O fluvax NOT a contraindication to vaccine (anaphylaxis overstated)
- Egg allergy relevant in Yellow fever Vax only; Not flu or COVID vax.
- H/O anaphylaxis NOT a reason for PF vs AZ. (PEG / polysorbate 80)
- Skin testing to vaccine rarely needed: false positives, delays an issue.

- For VCD and anxiety, Verbal reassurance / distraction during injection and observation VERY effective. Sipping water also helps.

Delayed reactions

Serum sickness to vaccines can occur, but rare

- Features fever, arthralgia, rash (maculopapular)
- Dx is Clinical; No good test to assess, tryptase normal, FBC may show neutropenia, eosinophil elevation, complement changes.
- Skin tests no use

Severe dermal reactions (case reports, short case series)

- Toxic epidermal necrolysis, Stevens Johnson syndrome very rare.
- Hard to tell whether associated or random event
- Treat as per the condition; consider switch vaccine platform
- Skin tests no use. Do Bx of the rash to help define.