2020 bush-fires and COVID-19: what does it mean for our respiratory system?

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2019 - 2020 A double jeopardy
Bush fires in SE Australia November 2019 – March 2020

- Air quality dropped to hazardous levels in all southern and eastern states
- Air quality index from mid Dec 2019 in ACT was at hazardous levels (>200) on 27 days out of a possible 46
- 2 January 2020, NASA estimated that 306 million tonnes (337 million short tons) of CO2 had been emitted
- By 7 January 2020, the smoke had moved 11,000 kms across the South Pacific Ocean to Chile and Argentina
- Fires
  - burnt an estimated 18.6 million hectares (186,000 square kms)
  - destroyed over 5,900 buildings including 2,779 homes
  - killed at least 34 people
  - killed nearly three billion terrestrial vertebrates alone – the vast majority reptiles
  - killed and deprived millions of birds and animals of their habitats
Pollutants in bushfire smoke

- complex mix of multiple air pollutants and air toxics
- hazardous particulate matter ≤10 μm in diameter (PM$_{10}$), and fine particulate matter ≤2.5 μm in diameter (PM$_{2.5}$)
- PM$_{10}$ and PM$_{2.5}$ increase the risk of hospitalization and ED visits in people with asthma and COPD
- Size and specific chemical composition of PM will differ according to the source (e.g. bushfire, plant, synthetic or traffic related)

Temperature

- Heat and humidity stimulates airway C-fibres → asthma symptoms and increasing airway resistance >> rapidly than cold air
- Each 1°C increase in summertime temperatures is associated with a 5–7% increase in mortality from COPD and other chronic diseases
- High temperatures and sunlight also catalyse the formation of ground level ozone → airway irritation and inflammation
Health impacts of bushfire smoke exposure in Australia

Walter et al, Respirology 2020; 25, 495–501

- Narrative review of background airborne particulate matter vs smoke exposure arising from fires. Bushfire smoke shows
  - higher acute respiratory symptom risk associations than background AP
  - strong associations of smoke event days and asthma hospital & ED presentations
  - impact of bushfire smoke increases with age, with the lowest risk estimates for children, followed by adults and then elderly; higher risks for adult females > males
  - Cardiac arrest impacts appear to occur in the first 48 h of exposure with greater effects seen in males
  - Ischaemic heart disease (IHD) impacts were observed at lagged exposure intervals of 2–3 days and were stronger in females and Indigenous Australians
  - Trends to higher cardiac mortality days 2-5 post acute exposure
Chronic or recurrent bushfire smoke exposure

- Effects very poorly understood
- Some international evidence has revealed associations with low birth weight
- Recent Australian study examining fire fighters’ exposures during prescribed burns found high mercury concentrations - cumulative impacts remain largely unknown
- Animal models of exposure suggest bushfire smoke suppresses phagocytic activity
- Exposure to biomass smoke is associated with an increased risk of respiratory viral RTI
- Occurs through a number of mechanisms: epithelial barrier dysfunction, inflammation and decreased anti-viral defences (in mouse studies)
- Different thresholds may exist in males and females with regard to the stimulus level required to trigger inflammatory mediators after wood smoke exposure
Illustration created at the US-CDC showing the ultrastructural morphology exhibited by coronaviruses. The spikes that adorn the outer surface of the virus impart the look of a corona surrounding the virion, when viewed by EM.
Coronaviruses

- Enveloped, non-segmented, positive sense RNA viruses, belonging to the family Coronaviridae
- Broadly distributed in humans and other mammals
- Most human coronavirus infections are mild (also true of SARS-CoV-2)
- Two severe epidemics have been the two beta-coronaviruses
  - Severe acute respiratory syndrome coronavirus (SARS-CoV), mortality rate 10%
  - Middle East Respiratory Syndrome coronavirus (MERS-CoV), mortality rate 37%
  - Have caused more than 10,000 cumulative cases in the last 20 yrs
- Some coronaviruses are causes of the common cold
- The SARS-CoV-2 is a large sized virus (approximately 120 nm/0.1μm in diameter)
- Primarily spread person to person by respiratory droplets (>5-10 μm diam) within 1.5m range
- Some experts and evidence suggest aerosol spread may also be important
- Some emerging data that previous coronavirus infection may enhance resistance
100 μm
❖ Sea turtles have lungs very like human lungs
❖ They can hold their breath for up to 10 hours when sleeping
❖ Their lungs are much bigger than their brains
❖ They can “breathe” through their rear end
Spanish Flu

- Began in N. hemisphere Spring-Summer 1918
- First wave was a relatively mild disease, few deaths
- Late August 1918, a more virulent strain emerged
- Main wave of global pandemic spread Sept-Nov 1918
- In some US cities > 10,000 people/week died
- Almost 1/3 of US population became ill
- Mortality rate 2-3%
- Most deaths occurred in young adults
- 99% excess deaths occurred in < 60 yr olds
- Reduced mean life expectancy in US by 10 years
- Majority who died succumbed to secondary bacterial pneumonia
Have we been here before?

H1N1-09 Influenza Cases in New York April – May 09
COVID - 19

- Began N hemisphere winter 2019
- First wave highly contagious $R_0 > 2.0$
- So far no mutation to more lethal form
- In some US cities > 10,000/month died
- Outbreaks in all countries
- Mostly < 10% population becomes ill
- Mortality rates highly variable → 15%
- Mortality age related, increases > 60
- Affects 20 – 40 year olds >> older adults
- Children not a reservoir nor source of transmission
- Most deaths due to respiratory failure
Global comparisons: mortality

1st case of COVID-19 in UK was reported 184 days ago on 30/1/2020. Since, the UK has reported 306,309 cases, and 46,286 deaths.

The first case of COVID-19 in India was reported 185 days ago on 31/1/2020. Since, India has reported 1,803,695 cases, and 38,135 deaths.

The first case of COVID-19 in US was reported 193 days ago on 22/1/2020. Since then, USA has reported 4,667,955 cases, and 154,860 deaths.
## COVID stats 4th August 2020

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>Deaths</th>
<th>Case fatality rate</th>
<th>Deaths/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>306,309</td>
<td>46,286</td>
<td>15.1%</td>
<td>69.61</td>
</tr>
<tr>
<td>Spain</td>
<td>288,522</td>
<td>28,445</td>
<td>9.9%</td>
<td>60.88</td>
</tr>
<tr>
<td>Italy</td>
<td>248,070</td>
<td>35,154</td>
<td>14.2%</td>
<td>58.17</td>
</tr>
<tr>
<td>Sweden</td>
<td>80,422</td>
<td>5,743</td>
<td>7.1%</td>
<td>56.40</td>
</tr>
<tr>
<td>France</td>
<td>225,198</td>
<td>30,268</td>
<td>13.4%</td>
<td>45.18</td>
</tr>
<tr>
<td>Germany</td>
<td>212,828</td>
<td>9,163</td>
<td>4.3%</td>
<td>11.05</td>
</tr>
<tr>
<td>US</td>
<td>4,771,080</td>
<td>156,806</td>
<td>3.3%</td>
<td>47.33</td>
</tr>
<tr>
<td><strong>New Zealand</strong></td>
<td><strong>1,567</strong></td>
<td><strong>22</strong></td>
<td><strong>1.4%</strong></td>
<td><strong>0.45</strong></td>
</tr>
<tr>
<td><strong>Australia</strong></td>
<td><strong>17,938</strong></td>
<td><strong>208</strong></td>
<td><strong>1.2%</strong></td>
<td><strong>0.83</strong></td>
</tr>
<tr>
<td>China</td>
<td>87,985</td>
<td>4,669</td>
<td>5.3%</td>
<td>0.34</td>
</tr>
<tr>
<td>South Korea</td>
<td>14,456</td>
<td>302</td>
<td>2.1%</td>
<td>0.58</td>
</tr>
</tbody>
</table>
COVID-19: A respiratory virus like no other

- Major predisposing risk factors
  - Age > 60, >>70, >>>80
  - Obesity (BMI > 30)
  - Diabetes
  - Hypertension (Rx?)
  - CAD/IHD
  - Male (F = RR 0.8)

- Non-survivors
  - Older ≥80 (70% do not survive ICU)
  - Mostly die from ARDS (81% vs 45%), >90% require mechanical ventilation
  - Most have multi-organ damage: ARDS, acute kidney injury, CVA, PTE, cardiac injury, liver dysfunction
  - Only around 30% of people in resp failure have a cytokine storm
  - Secondary bacterial infection is NOT the usual cause of death from lung disease

- Surprises
  - Less predisposed to acquire?
  - Less predisposed to have severe disease?
    - Smokers
    - Asthma
    - COPD
Cases by notification date, age group and gender

4th August 2020

Cumulative number of cases of COVID-19 by notification date

Number of new cases of COVID-19 by notification date
total COVID-19 cases in Victoria is 13,035
725 new cases since yesterday, 561 under investigation
There are 2,281 cases that may indicate community transmission
increase of 122 since yesterday
538 people are in hospital
42 patients in intensive care
4th August 2020


Cases by Age Group and Gender

Lives lost by Age Group and Gender

Note: The definition of a confirmed case is a person who tests positive to a validated specific SARS-CoV-2 nucleic acid test or has the virus identified by electron microscopy or viral culture, at a reference laboratory. Data reported at 8pm daily. Case counts reported for a particular notification date may vary over time due to ongoing investigations and case review.
Viral load, lessons for transmission

DOI: 10.1056/NEJMc2001737

Zhou et al. NEJM correspondence

A Nasal Swabs

B Throat Swabs

RED = severe
Black = moderate
Blue = 2° contact
Aimed to characterise viral load dynamics, duration of viral RNA, and viable virus shedding of SARS-CoV-2 in various body fluids: 79 studies on SARS-CoV-2, included.

Mean SARS-CoV-2 RNA shedding in URT, LRT stool and serum were 17.0, 14.6, 17.2 and 16.6 days, respectively; max in URT was 83 days.

Pooled mean duration of SARS-CoV-2 RNA shedding was positively associated with:

- Age (p=0.002), but not gender (p = 0.277)
- **No study to date has detected live virus beyond day 9 of illness despite persistently high viral loads**
- SARS-CoV-2 viral load in the URT appears to peak in the first week of illness

Shedding can be prolonged but duration of viable virus is relatively short-lived.

High SARS-CoV-2 titres in week 1 of illness + an early peak at symptom onset to day 5 of illness.

Underscores the **importance of early case finding** and isolation but containment may be challenging even with effective track and isolate.
Clinical course and PCR viral positivity

- 80% of PCR +ve detected cases are mild
- This will rise and case fatality will go down as testing protocols expand
- When entire populations are tested, about 50% of patients who test positive are asymptomatic at testing
- In North America
  - about 10% of cases are hospitalized
  - 25% of admitted patients require intensive care support
  - 25 – 50% ICU-admitted patients die
  - 1-20% die from the original PCR +ve symptomatic cases
- For those requiring admission
  - mean time from symptom onset to hospitalization 4 - 7 days
  - to ICU admission 5 - 12 days
  - Mean hospital stay (survival or death) about 2 weeks
7736 patients with Covid-19, hospitalized at 552 sites in Hubei as of January 29, 2020, obtained data regarding clinical symptoms and outcomes for 1099 patients (14.2%)

- Median age of the patients 47 years; 41.9% female
- 5.0% admitted to the ICU, 2.3% underwent invasive ventilation, and 1.4% died

- Most common symptoms were fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). Diarrhea was uncommon (3.8%)
- Median incubation period was 4 days (IQR 2 to 7)
- On admission, ground-glass opacity was the most common radiologic finding on CT (56.4%)
- No CT abnormality 17.9% with non-severe disease and in 2.9% with severe disease
- Lymphopenia was present in 83.2% of the patients on admission
Multicenter cohort study, 2215 adults with laboratory-confirmed COVID-19 who were admitted to ICUs at 65 hospitals in US from March 4 to April 4, 2020

2215 patients, mean age, 60.5; 64.8% male; 78.5% > 1 chronic comorbidity

At 28 days after ICU admission, 35.4% had died, 37.2% were discharged, 27.4% remained

Factors independently associated with death included

- Older age (>80 vs <40 years) OR 11.15
- Male sex OR 1.50; higher BMI (>40 vs <25) OR, 1.51
- Coronary artery disease (OR, 1.47), active cancer (OR, 2.15)
- Hypoxemia (PaO2: FIO2<100 vs >300mmHg: OR, 2.94), liver dysfunction OR 2.61, kidney dysfunction OR, 2.43
- Patients admitted to hospitals with fewer ICU beds had a higher risk of death (<50 vs >100 ICU beds: OR, 3.28; 95%CI, 2.16-4.99)
- Hospitals varied considerably in the risk-adjusted proportion of patients who died (range, 6.6%-80.8%)
Radiologic and CT imaging changes

(A) Day 8, (B) Day 11 after onset of illness
NEJM 2020;382:727

51M day 8 and day15
Guan et al  NEJM DOI: 10.1056/NEJMoa2002032

60F day 1 and day 4

64M, no h/o COV-19 exposure Cheng et al
10.2214/AJR.20.22959
Our predictive score for COVID-19 lethality included age ≥ 65 years, diabetes, early-onset diabetes, obesity, age < 40 yrs, CKD, hypertension, and immunosuppression and significantly discriminates lethal from non-lethal COVID-19 cases (C-statistic = 0.823).

- 177,133 subjects (May 18, 2020), 51,633 with SARS-CoV-2 and 5,332 deaths
Treatment: RECOVERY trial

- A large RCT (175 hospitals in UK) of possible treatments for patients admitted with COVID-19
- Over 11,500 patients randomised to the treatment arms, or no additional Rx
  - Lopinavir-Ritonavir 400/100 BD x 10 days
  - Low-dose Dexamethasone 6mgs daily orally or by IVI for 10 days
  - Hydroxychloroquine (now ceased due to lack of efficacy) 200mgs x 4, then daily for 10 days
  - Azithromycin 500mgs daily for 10 days
  - Tocilizumab (2nd randomisation)
  - Convalescent plasma against SARS-CoV-2 (2nd randomisation)
- DXM reduced the 28-day mortality rate by 17% (0.83 [0.74 to 0.92]; P=0.0007)
- Greatest benefit among patients requiring ventilation (test for trend p<0.001)
  - Found no evidence of benefit for patients who did not require oxygen
  - Did not study patients outside the hospital setting
- Follow-up complete for over 94% of participants
28-day mortality in the usual care group was
- highest in those patients receiving IMV (40.7%)
- intermediate in those receiving oxygen only (25.0%)
- lowest among those who were not receiving respiratory support at randomization (13.2%)

The greatest absolute reductions in 28-day mortality were seen in the sickest patients
Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis

Investigated by systematic review
- the optimum distance for avoiding person-to-person virus transmission
- to assess the use of face masks and eye protection to prevent transmission of viruses

Obtained data for SARS-CoV-2 and β-coronaviruses that cause SARS and MERS from 21 standard WHO-specific and COVID-19-specific sources

Transmission of viruses was lower with physical distancing of 1 m or more, compared with a distance of less than 1 m, pooled adjusted \( OR \ 0.18 \), 95% CI 0.09 to 0.38

Protection was increased as distance was lengthened

Face mask use could result in a large reduction in risk of infection \( OR \ 0.15 \), 95% CI 0.07 -0.34

Stronger associations with N95 or similar respirators compared with disposable surgical masks or similar

Eye protection also was associated with less infection \( OR \ 0.22 \), 95% CI 0.12 to 0.39,
**Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis**


<table>
<thead>
<tr>
<th>Studies and participants</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effect (95% CI), eg, chance of viral infection or transmission</th>
<th>Difference (95% CI)</th>
<th>Certainty*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical distance ≥1 m vs &lt;1 m</strong></td>
<td>Nine adjusted studies (n=7782); 29 unadjusted studies (n=10736)</td>
<td>aOR 0.18 (0.09 to 0.38); unadjusted RR 0.30 (95% CI 0.20 to 0.44)</td>
<td>Shorter distance, 12.8%</td>
<td>Further distance, 2.6% (1.3 to 5.3)</td>
</tr>
<tr>
<td><strong>Face mask vs no face mask</strong></td>
<td>Ten adjusted studies (n=2647); 29 unadjusted studies (n=10170)</td>
<td>aOR 0.15 (0.07 to 0.34); unadjusted RR 0.34 (95% CI 0.26 to 0.45)</td>
<td>No face mask, 17.4%</td>
<td>Face mask, 3.1% (1.5 to 6.7)</td>
</tr>
<tr>
<td><strong>Eye protection (faceshield, goggles) vs no eye protection</strong></td>
<td>13 unadjusted studies (n=3713)</td>
<td>Unadjusted RR 0.34 (0.22 to 0.52)</td>
<td>No eye protection, 16.0%</td>
<td>Eye protection, 5.5% (3.6 to 8.5)</td>
</tr>
</tbody>
</table>
Physical distancing, face masks, and eye protection to prevent person to person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis


❖ Risk of virus transmission is reduced by 82% with a physical distance of 1 m in both health-care and community settings (OR 0.18)

❖ Every additional 1 m of separation more than doubles the relative protection

Absolute risk of transmission from an individual infected with SARS-CoV-2, SARS-CoV, or MERS-CoV with varying baseline risk and increasing distance
To Do or not to Do : Masks

- Masks and respirators reduced the risk of infection by 85%, with greater effectiveness in healthcare settings (RR 0·30) than in the community (0·56)
- N95 respirators are 96% effective (OR 0·04) vs other masks ~ 67% effective (OR 0·33)
- Eye protection resulted in a 78% reduction in infection (OR 0·22)
- For the community and households cloth masks are effective
  - should be made of water-resistant fabric
  - multiple layers (minimum 3)
  - good facial fit
- Cloth masks can be washed daily
- When lockdown is eased, masks and physical distancing are key measures to control virus spread
- Growing evidence for pre-symptomatic and asymptomatic transmission of S-CoV-2 further supports universal face mask use
Protection – masks?

- Considerations when using a surgical mask (HCW’s)
  - In the majority of situations where standard respiratory protection is needed, a single use surgical mask is appropriate (minimum Level 1 barrier).
  - Masks should be changed between patients and when they become soiled or wet
  - Masks should never be reapplied after they have been removed
  - Masks should not be left dangling around the neck
  - Touching the front of the mask while wearing it should be avoided
  - Hand hygiene should be performed upon touching or discarding a used mask

- High particulate respirators (P2/N95) masks
  - For COVID-19 the use of P2/N95 masks should be reserved for AGPs or where the risk assessment places the patient in airborne precautions.
  - When there is a high probability of aerosol transmission due to the infectious agent or procedure e.g. bronchoscopy, nebuliser use, chest physiotherapy
Encouraging results from phase 1/2 COVID-19 vaccine trials

Immunogenicity and safety of a recombinant adenovirus type-5 vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial

ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques

Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques

Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates
Conclusions

❖ This is the fight of our lives
❖ There are positive outcomes despite the tragedies
❖ Many future possible disasters are preventable
❖ Science, scientists, clinicians and public health expertise will make the difference that maximises survival of humans over the virus
❖ Resetting our political, economic and moral compass
  ❖ Environment
  ❖ Innovation and flexibility
  ❖ Connectedness and Gratitude
  ❖ Role of government vs politics
  ❖ Civic society vs individualism
  ❖ Articulate a different future
  ❖ Value of scientific endeavour for societal good