1. **Is anticoagulation therapeutic needed as prevention AKI and other organ failure? thoughts**

There are trials underway (elsewhere) examining the role of anticoagulation given reported associated with micro and macrothrombosis, but no proven benefit currently

2. **I get the impression that we are using a cocktail of antimicrobial (antiviral,antibiotics etc) in Covid pneumonia. Am I correct in thinking its just a trial?**

We are trying to be rationale with antimicrobial use. All therapies targeting COVID19 are experimental. In severe disease some are using anti biotics because of concern of superimposed bacterial infection, but will depend on the clinical circumstance. Generally should be limited.

3. **Is there any utility for antivirals?**

All treatments for COVID19 are currently experimental; none are proven yet to be effective

4. **What is the role of immunosuppressive drug et tocilizumab?**

Being investigated in RCTs. Has been used extensively in Europe but no trial results yet reported. Currently not recommended outside of a clinical trial by Infectious Diseases Society of America or Association of Medical Microbiology and Infectious Diseases Canada

5. **Is myocarditis being seen with covid 19 frequently?**

Myocarditis is a serious 1omplication of Covid19. It may be a cause of cardiac death. I don't the exact incidence. -mdh

6. **Why has it taken so long to get clinical trials going in Alberta?**

This has been remarkably quick in the scheme of things. Need Health Canada approval and university REB approval, plus logistics.

On average it takes about 1 year to plan and start a major RCT. This one has taken 3 weeks. We are doing well -mdh

7. **Has anyone seen the presentation mimicking Chilblains of the toes in young adults and children with covid ?**

Yes, I tweeted about this today and many clinicians on Twitter seem to have seen it also. Seems primarily younger adults or adolescents and associated with mild disease. Not clear if related to microangiopathy/thrombosis or just inflammation as seen in lupus

8. **Would you update us on ongoing research re: face mask reuse / sterilization? And are there any trials planned comparing types of cloth face masks?**

There is a study of N95 vs surgical masks in HCW but I am not aware of any studies of resterilization/reuse in Alberta. This is being studied in Manitoba and in Nebraska (among other places). Not aware of any studies regarding cloth masks

9. **Why testing Hydroxychloroquine so much (as opposed to other drugs)? Is that just because of the French bad buzz or do we have serious reasons for real hopes in that molecule in particular?**

Many current studies including the 2 we will discuss tonight were conceptualized and the processes started prior to POTUS remarks. It has in vitro antiviral activity and is off patent. The last part is probably the most important because it is readily available (or at least it was until POTUS's pronouncements) for trialists. The fact it is being used so widely increases the urgency of establishing whether it works or not.

10. **What is the current knowledge around immunity and serum/plasma for treatment?**

Currently we THINK that natural infection generates immunity and reinfection is unlikely but this hasn't been proven in humans yet. Convalescent plasma looks very promising and a Canada wide trial is being organized

Great question. There is a large national study planned using convaelescent plasma -mdh

11. **Is ACE or ARB use going to part of exclusion criteria as a result of the possibility of interaction with viral adherence as well as interference with the downregulation of the inflammatory response?**

Patients who are high risk are the ones we want in this study, including patients with hypertension or CHF. So patients on ACEi or ARB are included -mdh

12. **What about use of steroids/immunomodulators in phase 2 of illness (not too early, not too late) ?**

Still experimental and under investigation. Steroids seem to be associated with worse outcomes and are not recommended. IL-6 inhibitors like tocilizumab are under investigation but are not recommend outside of a clinical trial.

13. **Should patients with toes microangiopathic changes be tested or included in testing ?**

Great question. most patients probably have some other URTI symptoms that would qualify for testing. So far we don't have enough data to know how common isolated cutaneous findings are. In the absence of testing, they should be presumed to be infected and should self isolate at minimum 10 days from symptom onset.

14. **How is HO chloroquine used in virus when it is anti plasmodium?**

HCQ seems to interfere with viral replication in the cell, reducing viral release. -mdh

Has broad antiviral properties and activity against SARS-COV-1, SARS-COV-2, dengue, chikungunya. Has not been proven to be helpful in humans though for any viral infection.

15. **Will courier send drugs to all zones ie. North Zone remote areas?**

All zones. Anywhere in AB -mdh

16. **Should we do a EKG on patient prior to starting HCQ ,to monitor the Qtc?**

There is a risk of long QTc and ventricular arrhythmias IF they are on concurrent meds that also prolong QTc. HCQ on its own is not significantly risky. We will exclude patients on other QT prolonging drugs. -mdh

The exclusion criteria limit the trials to patients who are not taking concomitant QT prolonging drugs. Any patient with history of ventricular arrhythmia or known long QT would be excluded. The risk of arrhythmia with a 5 day course is low. Given that we are considering patients who are infected (or in the PEP study, exposed and therefore possibly infected), the risk of spread is probable greater than the benefit from doing an EKG

17. **CNN reporting today that a French Trial (only 84 patients) did not show any statistically significant difference with hydroxycholorquine - comments?**

Yes sure but 84 patients is not enough. If there is an effect, we all expect it will be modest. On a population basis, a modest effect is useful -mdh

Yes, there was a propensity score analysis of 181 patients with COVID19 in 4 French hospitals. There was no difference found in rates of ICU admission or death whether or not patients were receiving hydroxychloroquine

18. **What if the patient is admitted later to the hospital, how would we know if the patient was on the drug? would the patient started on hydroxychloroquine if needed regardless?**

In all trials, there is a mechanism to unblind if necessary. In general, though, we expect with a 5d course only, this is not likely to occur -mdh

19. **The cardiotoxicity of chlorquinnine will be exacerbated if Covid is associated with myocarditis, or cardiomyopathy. This can obviously be progressive during the infection; how can you distinguish between symptoms related to cardiac disease progression versus pulmonary especially if people are outpatients?**

Great question. It may not be possible. If someone gets that sick, they will need admitting to hospital for detailed investigation -mdh

20. **Have you consider changing the inclusion criteria to include atypical presentation such as anosmia, dysgeusia (no fever)?**

We will include these patients with these symptoms -mdh

21. **What about incarcerated population? is it too difficult to consent etc.?**

Good question. It is illegal in the US to enrol prisoners in trials. In Canada, we legally can, IF and only IF it is ethical and we can get follow-up. If it occurs, we will try to help. It may be circumstantially determined -mdh

22. **Who is the PI? Question re: pregnancy**

All 4 of us are coPIs. Luanne Metz is the nominated PI for Health Canada etc. Patients who are pregnant are excluded -mdh

23. **For Hopecovid study: How are hopecovid.ca patients to be managed as inpatients if they do get admitted (obviously unplanned)? To bring meds to hospital and complete?**

If they are hospitalized they will have reached the trial endpoint. The decision to continue will need to be made by the MRP but it would be considered outside of the trial.

24. **Are there any trials for patients currently intubated in ICU?**

There are. Dr. Richer will talk to some of these -mdh

25. **Patient with coronary stent in past excluded?**

No, specifically included since CAD is considered a high risk factor -mdh

26. **Is there any truth about having had BCG vaccine giving some immunity reg Covid? Any studies But people in Africa getting sick….**

T - no solid evidence that I am aware of. -mdh

27. **Any direction for healthcare providers for when patients in the HOPE trial are admitted to hospital?**

Let us know: hopecovid.ca We have an email on the site.
Treat the patient as you would normally - in or outside of a trial -mdh

28. **Possible use of invermectin? no in vivo studies though**

Would not recommend ivermectin.

29. **Is hydroxychloroquine not considered a zine ionophore - is this not it's mechanism of action?**

A - possibly yes, I do not know for sure. Let's ask Ilan. Meanwhile, a clear mechanism of actioon is at the cytosolic phase of viral replication where changes in pH and binding to virus proteins reduces viral assembly and replication. -mdh

30. **Have similar studies been done in other countries?**

No high quality RCTs. Above all we need real data, not anecdote and case series -mdh

31. **There's a theory that people with alpha thalassemia trait is protected, and people who've had BCG vaccines are protected. Is there strong evidence for this and science behind this?**

I have not see anything to support these theories either. -mdh

32. **Is there any truth in Covid having a direct effect of RBC ? Some talk out there about destruction of RB cells causing increased ferritin or is this increased ferritin just a marker of the inflammation?**

I have not seen any data on hemolytic anemia from Covid19. Have you seen anything in the JAMA papers from Wuhan or Italy? -mdh

33. **Are residents of continuing care facilities (eg: nursing homes) eligible for inclusion, if another resident is tested +ve?**

Yes, pending their risk factors. We will screen them -mdh

They will be eligible if they are assisted living but not SL4

34. **What if patients are taking Zinc supplements? Is this information you ask? Apparently this was thought to be important in the french study.**

This is not a contraindication to enrolment. Zn has some minimal effect on the common cold. There is simply no evidence (currently) for efficacy for Covid19 -mdh

35. **For post exposure prophylaxis- if there are eligible patients with limitations in internet access- are there are resources available to support them to answer questions by phone only instead of online or would they be exempt from study?**

Unfortunately, internet access is a requirement to enter the study. This will limit the generalizability - which is addressed by the trial design of the HOPE study. Ideally interested participants could have someone help them with the enrollment.

36. **Rationale for different loading doses in these 2 studies?**

Peter - probably not substantively different biochemically because of the long half-life of HCQ -mdh

37. **Do we know the main mechanism of this virus attacking our system? A scientist in the States said it's mainly the hemoglobin that's attacked, not the lungs, hence people get SOB. Is there evidence for this?**

No. That is not supported by the evidence. SARS-COV-2 enters respiratory epithelium

Binding to Angiotensiin-II receptors in the lung and pharynx. Binds with very high affinity which is why the virus may be so contagious - only a very small number of viral particles needed to induce infection -mdh

38. **What are your thoughts about convalescence plasma?**

See notes above. There is a national study planned in Canada. -mdh

39. **Should we keep HCQ in ER because there are high chances of exposure to the virus while loking aftre +ve patients**

No evidence to support this. The drug is NOT proven. Be careful about off-label treatments as you would in any other disease. -mdh

If there are exposures in the ER, please send HCW to PEP website covid-19research.ca and study medication can be sent by the next day

40. **Any information on people that had BCG re possible immunity to the virus?**

Currently the evidence for a protective effect of BCG is ecological and considered to be very weak. I suspect this will be debunked as more testing is performed in places where BCG is widespread.

41. **Will the data collected be able to used on population basis to identify risk factors for severe disease, or is it too limited?**

We hope so yes -mdh

We also plan to develop a population based outcomes study based on admin data to be more inclusive.

42. **Are incarcerated people / prison inmates eligible for inclusion in the PEP trial if other inmates are tested +ve?**

By current definitions these would not be considered household contacts and would not be eligible. We are encountering a similar challenge with LTC facilities, and may need to address this with the REBs. But currently they would not be eligible.

43. **If a pharmacy has a patient that has filled rx and then is later + for Covid, could all pharmacy staff be eligible or only ones with more "direct" contact?**

Would need to be direct patient contact >10 minutes

44. **Would you be able to put the N95 vs Procedure masks study PI or Research Coordinator in touch with researchers at Ualberta also looking at face masking? If so, please contact me.**

The N95 mask study PI is Stephanie Smith at UofA

45. **Are the PPE and HOPE available to participants who speak languages other than English?**

PEP is available to French speakers.

46. **Does Covid cause a viral and a bacterial pneumonia (hence the use of antibiotics in treatment as well as antiviral medications)?**

S - viral pneumonia. It is always possible to get a secondary bacterial infection. -mdh

Secondary bacterial and fungal infection a concern. not clear how often this is occurring. bronchoscopy rarely done because of concerns about aerosolization.

47. **I am a TARRANT sentinel, is there overlap to identify participants or is it up to sentinel to suggest that there may be trials that a + COVID case may participate?**

If you are screening for ILI and you do a swab, test and get a positive result, we will screen your patient for enrolment - mdh

48. **Did we learn anything from research done in the virological lab in Wuhan?**

Lots. Much published in JAMA. -mdh

49. How close are we to getting serologic testing? weeks? months?

I think that's hard to guess, but the serological studies are underway. My guess is weeks to months.

50. Are there any ongoing / planned studies in Pediatric population?

Very few children getting seriously ill. Seems to be mild illness in kids. Some plans at HSC in Toronto -mdh

51. Are SLE patients aready on hydroxychloroquine getting COVID-19?

We don't have the answer yet, but will be monitoring the data in the patient population as well as others (e.g. on NSAIDs or ACEi)

Yes, they do get COVID-19. We are doing a registry study in Alberta, but there is also global registry data that suggests that patients with SLE or RA on HCQ do get COVID-19. Doses lower than what we will be using (usually 200 mg daily)

52. Which hospitals in Alberta will be able to enroll their hospitalized COVID+ patients in clinical trials?

In the adult population I expect that Foothills, Royal Alexandra, and University of Alberta Hospital will be recruiting. Maybe the other panelists could comment as well.

53. For the plasma study, your note says men <67 -what about women?

Sandra. As we discussed live, it relates to transfusion reaction risk.

54. Is there variation in age wise with cytochrome storm syndrome?

Unknown. This can be seen in young and old but I cannot quote numbers to you. WIth H1N1 it was the young that got this and died; with this Covid19, we are seeing the reverse with older patients having the severest infections. -mdh

55. Are there any Canadian studies looking at Covid antibodies in breastmilk?

I bet there are. I am not aware of details -mdh

56. In the 1918 flu pandemic the U.S was initially hit with a mild flu-like illness which is what this seems to be but they thought it passed into the pigs in the states and gained a potency that massacred the entire population. Is there any cause for concern that this zoonotic illness can pass to our livestock and are the animals at large facilities being swabbed for COVID-19 as well?

Cats, ferrets and primates. -mdh

57. Would you be sending the slides to the participants?

Yes. they will be posted online and you will receive an email with links by the end of this week.

58. **Regarding the HOPE trial: If a patient is enrolled, are the patient's care providers prevented from ordering Azithromycin? I am not sure if it was in the list of medications that could not be co-administered (recognizing it can cause QTc prolongation).**

We are recommending that it not be ordered while on the study medication.

59. **Do any of the panelists have comments on ACE2 expression and ACE2 levels in serum and prognosis. These are higher in males and go up with age. Fits with the portal of entry and the clinical data**

Gavin Oudit at U Alberta has a very strong interest in pursuing these questions. A observation study is underway. A biomarker study is also in development. I'm less sure about Calgary.

60. **Are there any Canadian studies looking into environmental changes might be cause of this Pandemic?**

I think yes. The markets and the animal - human interaction appears to have been key. The virus is thought to have started in bats.

61. **Would you need any pharmacy services in Calgary as a part of the trial?**

We are using the central research pharmacy in Calgary.

62. **How about any point of care testing even for asymptomatic patients? Perhaps with better sensitivity**

SpartanBio rapid testing just approved by Health Canada. 250 units purchased by gov of Alberta and 10,000 test kits apparently. Hopefully this will allow rapid testing in settings without acceptable lab turnaround. Also will be used on admission for select patients

63. **Is there a plan to collect serial samples to look at cytokines, viral load, dna polymorphisms and the effect of these trials?**

The HOPE trial was designed very pragmatically to make it feasible. Substudies however are being proposed, but not yet underway.

There will be samples collected for the inpatient studies, but not these outpatient ones

64. **How long after contracting covid 19 can you detect antibodies?**

We don't know yet. Studies pending. Earliest is 6 days. How long they last is uncertain.-mdh

65. **What dose of Hydroxychloroquine is being used in the post exposure prophylaxis?**

1400 mg initially (separated by 6-8 hours) and then 600 mg a day x 4 days

66. **If you are already on Hydroxychloroquinine is there a study looking at outcomes or antibody titres or anything?**

Yes, a registry study for rheumatology patients through UofA division of Rheum (can't recall the acronym for the study but its an existing registry)

67. **How do we clear patients? I had patients cleared by public health with no repeat swab - is there a standard protocol?**

After 14 days post infection, patients are clear. Most have Antibodies day 8 and no lonoger shed live virus. Follow public health guidance on this. -mdh

68. **The AHS antimicrobial management document recommends against systemic steroid use due to poor patient outcomes, etc. However, the SCCM suggests to use systemic corticosteroids in MV patients with COVID 19 and ARDS. Could you comment on this please?**

All the data that I have seen has suggested systemic steroids are a bad idea in COVID-19 - associated ARDS.