In the News:

1. **WHO Breastfeeding and COVID-19**: Mothers with suspected or confirmed COVID-19 should be encouraged to initiate or continue to breast. Mothers should be counselled that the benefits of breastfeeding substantially outweighs the potential risks for transmission. [https://www.who.int/news-room/commentaries/detail/breastfeeding-and-covid-19](https://www.who.int/news-room/commentaries/detail/breastfeeding-and-covid-19)

2. **CDC Updates**: Duration of Isolation and Precaution. July 17th, 2020  
   - Ending isolation and precautions for persons with COVID-19 should be based on a symptom-based strategy (10 days after symptom onset, resolution of fever for at least 24 hours and with improvement of other symptoms)  
   - Severe illness may produce replication-competent virus beyond 10 days and may warrant extending duration of isolation for up to 20 days after symptom onset.  
   - Asymptomatic isolation and precautions can be discontinued 10 days after the date of their first positive RT-PCR test  
   - ***Data is not known for children or immunocompromised persons

Articles:

1. **Wang et al.** Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study  
   *Diabetologia* July 10th, 2020. [https://doi.org/10.1007/s00125-020-05209-1](https://doi.org/10.1007/s00125-020-05209-1)

Background:
• Hyperglycemia is associated with an elevated risk of mortality in community-acquired pneumonia, stroke, acute myocardial infarction, trauma and surgery, among other conditions.
• The authors examined the relationship between fasting blood glucose (FBG) and 28-day mortality in COVID-19 patients not previously diagnosed as having diabetes.

Methods:
• Retrospective study involving all consecutive COVID-19 patients with a definitive 28-day outcome and fasting blood glucose (FBG) measurement at admission from 24 January 2020 to 10 February 2020 in two hospitals based in Wuhan, China.
• All patients were categorized into three groups according to WHO guidelines in terms of admission FBG (<6.1, 6.1–6.9, and ≥7.0 mmol/l).
• Two outcome measures were examined: the independent risk factors for 28-day mortality and percentage differences in in-hospital complications between different FBG groups.

Results:
• A total of 605 patients without a previous diagnosis of diabetes (448 from Wuhan Union West Hospital and 157 from Wuhan Red Cross Hospital) were included in the analysis.
• The patients were categorized in terms of their glucose levels into three groups: patients with FBG <6.1 mmol/l (n = 329, 54.4%), patients with FBG 6.1–6.9 mmol/l (n = 100, 16.5%) and patients with FBG ≥7.0 mmol/l (n = 176, 29.1%).
• 114 patients (18.8%) died within 28 days during hospitalization. Among 605 patients, 237 (39.2%) developed one or more in-hospital complications.
• Multivariable Cox regression analysis showed that age (HR 1.02 [95% CI 1.00, 1.04]), male sex (HR 1.75 [95% CI 1.17, 2.60]), CRB-65 score 1–2 (HR 2.68 [95% CI 1.56, 4.59]), CRB-65 score 3–4 (HR 5.25 [95% CI 2.05, 13.43]) and FBG ≥7.0 mmol/l (HR 2.30 [95% CI 1.49, 3.55]) were independent predictors for 28-day mortality.
• The OR for 28-day in-hospital complications in those with FBG ≥7.0 mmol/l and 6.1–6.9 mmol/l vs <6.1 mmol/l was 3.99 (95% CI 2.71, 5.88) or 2.61 (95% CI 1.64, 4.41), respectively.

Conclusion:
• FBG ≥7.0 mmol/l at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes. FBG can facilitate the assessment of prognosis and early intervention of hyperglycemia to help improve the overall outcomes in treatment of COVID-19.
Limitation: Retrospective study, authors did not measure HbA1c which helps distinguish patients with poor long-term glycemic control from those with stress hyperglycemia, and lack of information regarding the effect of glucose-lowering treatment on the outcomes.


Definitions:
- mRNA = messenger ribonucleic acid
- PsVNA = Pseudovirion neutralization assay.
- PRNT = plaque reduction neutralization test.
- PRNT$_{80}$ = neutralizing activity capable of reducing infectivity by 80% or more

Background:
- An urgent need for vaccines prompted an international response with more than 120 candidate SARS-CoV-2 vaccines in development
- Candidate vaccine mRNA-1273 encodes the stabilized perfusion SARS-CoV-2 spike protein
  - Lipid nanoparticle-encapsulated, nucleoside-modified mRNA-based vaccine that encodes SARS-CoV-2 spike (S) glycoprotein stabilized in its perfusion conformation
  - S glycoprotein mediates host cell attachment and is required for viral entry and the target for many candidate vaccines
- This is an interim analysis report of findings through day 57

Vaccine:
- mRNA-1273 vaccine candidate was manufactured by Moderna
  - Encodes the S-2P antigen consisting of the SARS-CoV-2 glycoprotein with a transmembrane anchor and an intact S1-S2 cleavage site
- mRNA-1273 vaccine was provided as a sterile liquid for injection at a concentration of 0.5mg/mL and diluted with normal saline to prep for dose administration

Methods:
- Phase 1 clinical trial in healthy adults to evaluate safety and immunogenicity of mRNA-1273
- Dose-escalation, open-label
- Eligible patients: healthy adults age 18 to 55 years who received two injections of trial vaccine 28 days apart at a dose of 25 µg, 100 µg, or 250 µg
  - On the basis of results in groups, further groups were added to the protocol but will be reported in a subsequent publication
- Injection delivered on days 1 and 29 with regular follow-up visits for 7- and 14-days post-vaccination and planned follow-ups on days 57, 119, 209, and 394.
- Participants self-reported local and systemic reactions and adverse events were graded according to a standard toxicity grading scale
- Binding antibody response against S-2P and isolate receptor-binding domain were assessed by ELISA
- Vaccine-induced neutralization activity was assessed by a PsVNA and SARS-CoV-2 PRNT assay

Results:
- 45 participants were enrolled and received first vaccination, 3 (2 in 25µg group and 1 in 250µg group) missed second vaccination
  - 1 due to transient urticaria, 2 due to being isolated for suspected COVID-19
  - No serious adverse events were noted
Mild to moderate solicited systemic adverse events were reported in 5 (25µg group), 10 (100µg group), and 9 (250µg group) patients after first vaccination but were more common after the second vaccination.

- Binding antibody IgG to S-2P increased rapidly after the first vaccination and all participants seroconverted by day 15.
  - Dose-dependent responses to the first and second vaccinations were evident.
  - Receptor-binding domain-specific antibody responses similar in pattern and magnitude.

- Median magnitude of antibody responses after first vaccination of 100µg and 250µg groups was similar to convalescent serum specimens.
  - In all groups, after second vaccination, the median magnitude of antibody response was upper quartile of values in the convalescent serum specimens.
    - TS-2P ELISA at day 57 exceeded the convalescent serum specimens in all groups.

- No participants had detectable PsVNA response before vaccination, after first vaccination PsVNA was detectable in less than half, but was found in all participants after the second vaccination.
  - Lowest responses were in the 25µg group, highest (and similar) in 100µg and 250µg groups.
  - These responses were similar to values in the upper half of the distribution of values for convalescent serum specimens.

- No participants had detectable 80% live-virus neutralization at the highest serum concentration tested in the PRNT assay before vaccination.
  - At day 43, neutralization of SARS-CoV-2 by 80% or more was detected in all participants.
  - PRNT80 average response were generally at or above the values of the three convalescent serum specimens tested.

- 25µg and 100µg dose elicited CD4 T-cell responses that on stimulation by S-specific peptide pools were strongly biased towards Th1 cytokine expression (TNFa > IL-2 > INFy).
- CD8 T-cell response to S-2P were detected at low levels after second vaccination in the 100µg group.

**Conclusions/Limitation:**
- This is an interim report of follow-up of participants through day 57, small study.
- Antibody responses were higher with higher doses, but all had serum-neutralizing activity after the 2nd vaccination.
- More than half of the participants reported adverse events (fatigue, chills, headaches, myalgias, pain at injection site).
  - Systemic adverse events were more common in the highest dose after the 2nd vaccination.
  - 3 patients or 21% in the highest dose reported severe adverse events.
- Durability of the immune response remains unknown.


**Background:**
- Perinatal transmission has been described, unclear if transmission is transplacental, transcervical or environmental exposure.

**Case report:**
- 23 yo G1P0, 35 weeks gestation with severe productive cough, RT-PCR + COVID-19 by blood, NP and vaginal swabs.
- C-section performed due to category III-fetal heart rate tracing, intact amniotic membranes, full isolation, under general anesthesia.
  - Amniotic fluid +COVID-19 RT-PCR.
• Placenta histology: diffuse peri-villous fibrin with infarction, acute and chronic intervillitis, immunostaining positive with antibody against SARS-CoV-2 N-protein

• Neonate: Apgars 4, 2 and 7 at 1, 5 and 10 minutes
  o Blood, NP, rectal and BAL + COVID-19 RT-PCR
  o Received only formula, no breast milk
  o DOL developed irritability, hypotonia, poor feeding, opisthotonos, CSF was negative for SARS-CoV-2 by R-PCR, neonate was improved by 2 months of life

Conclusions/ Limitation:
• Case of transplacental transmission of SARS-CoV-2 during late pregnancy
• Definition of proven neonatal congenital infection: virus detected in amniotic fluid prior to rupture or membranes and in blood drawn early in life

Additional Resources: