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Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know

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1 Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know

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29 Glossary of terms

- 30 • 2019-nCoV: 2019-novel coronavirus (previous name for COVID-19 and SARS-CoV-2)
- 31 • Basic Reproduction Number: estimate of number of individuals who will become
- 32 infected from a single person in a population where all individuals are susceptible
- 33 • CDC: US Centers for Disease Control and Prevention
- 34 • COVID-19: Coronavirus Disease 2019 (previously called 2019 novel coronavirus (2019-
- 35 CoV) - illness caused by SARS-CoV-2
- 36 • MERS: Middle East respiratory syndrome
- 37 • MERS-CoV: Middle East respiratory syndrome coronavirus – virus that causes Middle
- 38 East respiratory syndrome (MERS)
- 39 • N95 respirator: respiratory protective device that removes at least 95 percent of very
- 40 small (0.3 micron) test particles, also called N95 filtering facepiece respirator
- 41 • SARS: severe acute respiratory syndrome
- 42 • SARS-CoV: severe acute respiratory syndrome coronavirus – virus that caused severe
- 43 acute respiratory syndrome (SARS)
- 44 • SARS-CoV-2: severe acute respiratory syndrome coronavirus-2 virus (current name of
- 45 the novel coronavirus, according to International Committee on Taxonomy of Viruses) –
- 46 virus that causes COVID-19
- 47 • WHO – World Health Organization

48

49 **Abstract**

50 Coronavirus Disease 2019 (COVID-19) is an emerging disease with a rapid increase in
51 cases and deaths since its first identification in Wuhan, China, in December 2019. Limited data
52 are available about COVID-19 during pregnancy; however, information on illnesses associated
53 with other highly pathogenic coronaviruses (i.e., severe acute respiratory syndrome (SARS) and
54 the Middle East respiratory syndrome (MERS)) might provide insights into COVID-19's effects
55 during pregnancy.

56 Coronaviruses cause illness ranging in severity from the common cold to severe
57 respiratory illness and death. Currently the primary epidemiologic risk factors for COVID-19
58 include travel from mainland China (especially Hubei Province) or close contact with infected
59 individuals within 14 days of symptom onset. Data suggest an incubation period of ~5 days
60 (range-2-14 days). Average age of hospitalized patients has been 49-56 years, with a third to half
61 with an underlying illness. Children have been rarely reported. Men were more frequent among
62 hospitalized cases (54-73%). Frequent manifestations include fever, cough, myalgia, headache,
63 and diarrhea. Abnormal testing includes abnormalities on chest radiographic imaging,
64 lymphopenia, leukopenia and thrombocytopenia. Initial reports suggest that acute respiratory
65 distress syndrome (ARDS) develops in 17-29% of hospitalized patients. Overall case fatality rate
66 appears to be ~1%; however, early data may overestimate this rate. In two reports describing 18
67 pregnancies with COVID-19, all were infected in the third trimester, and clinical findings were
68 similar to those in non-pregnant adults. Fetal distress and preterm delivery were seen in some
69 cases. All but two pregnancies were cesarean deliveries, and testing for SARS-CoV-2 was
70 negative on all babies tested.

71 Data on SARS and MERS in pregnancy are sparse. For SARS, the largest series of 12
72 pregnancies had a case-fatality rate of 25%. Complications included ARDS in four, disseminated
73 intravascular coagulopathy in three, renal failure in three, secondary bacterial pneumonia in two,
74 and sepsis in two patients. Mechanical ventilation was three times more likely among pregnant
75 compared to nonpregnant women. Among seven first-trimester infections, four ended in
76 spontaneous abortion. Four of five women with SARS after 24 weeks gestation delivered
77 preterm. For MERS-CoV, there were 13 case reports in pregnant women, of which two were
78 asymptomatic, identified as part of a contact investigation; three patients (23%) died. Two
79 pregnancies ended in fetal demise and two were born preterm. No evidence of *in utero*
80 transmission was seen in SARS or MERS.

81 Currently, no coronavirus-specific treatments have been approved by the US Food and
82 Drug Administration. Because COVID-19 might increase the risk for pregnancy complications,
83 management should optimally be in a health care facility with close maternal and fetal
84 monitoring. Principles of management of COVID-19 in pregnancy include early isolation,
85 aggressive infection control procedures, oxygen therapy, avoidance of fluid overload, empiric
86 antibiotics (secondary to bacterial infection risk), SARS-CoV-2 and co-infection testing, fetal
87 and uterine contraction monitoring, early mechanical ventilation for progressive respiratory
88 failure, individualized delivery planning, and a team-based approach with multi-specialty
89 consultations.

90 Information on the COVID-19 is increasing rapidly. Clinicians should continue to follow
91 the CDC website to stay up-to-date with the latest information.
92 <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>

93

94 Emerging infections have been shown to have an important impact on pregnant women
95 and their fetuses,¹ with the increased risk of complications in pregnant women with the 2009
96 pandemic H1N1 influenza virus² and the severe fetal effects of Zika virus as recent examples.^{3,4}
97 The emergence of a coronavirus not previously seen in humans, first reported in Wuhan, China,
98 on December 31, 2019, has attracted much interest throughout the world. Since then, the number
99 of reported cases has increased rapidly, with more than 51,800 laboratory-confirmed cases and
100 1,600 deaths as of February 16, 2020. In addition to China, cases have spread to 25 other
101 countries (Figure 1) including 15 cases in the United States. Initial outbreak data from China
102 show a near exponential growth of reported cases.⁵ Reported numbers are likely underestimates
103 of the true numbers since milder cases are less likely to be reported. On January 30, 2020, the
104 World Health Organization declared the outbreak as a Public Health Emergency of International
105 Concern; on January 31, 2020, the United States declared a public health emergency, and the
106 Centers for Disease Control and Prevention (CDC) issued a federal quarantine for 195
107 Americans who traveled from Wuhan, China, its first federal quarantine in more than 50 years.
108 On February 11, the new coronavirus disease (previously referred to as 2019 novel coronavirus
109 (2019-nCoV)) received an official name from the World Health Organization (WHO),
110 Coronavirus Disease 19 (COVID-19) (Figure 2).⁶ The International Committee on Taxonomy of
111 Viruses has proposed SARS-CoV-2 as the name of the virus that causes COVID-19.⁷

112 Coronaviruses are single-stranded RNA, nonsegmented, enveloped viruses, which cause
113 illness ranging in severity from the common cold to severe and fatal illness. The term
114 coronavirus derives from the Latin word “corona”, which means crown or “halo”; that
115 designation arises from the appearance of coronavirus virions viewed by electron microscopy,
116 where the virus particles display a crown-like fringe typically referred to as “spikes” (Figure 3).

117 In the past two decades, two other coronaviruses that cause severe respiratory illness in humans
118 have emerged: severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East
119 respiratory syndrome coronavirus (MERS-CoV). With the emergence of SARS-CoV-2, a third
120 coronavirus that can cause severe respiratory illness has been identified. In a short period of
121 time, this novel coronavirus has caused more cases of illness than were reported for MERS and
122 SARS combined. Here we summarize what is currently known about COVID-19 and what this
123 means for practicing obstetricians and their pregnant patients. Since so little is currently known
124 about COVID-19 in pregnancy, we also review available information on the effects of SARS and
125 MERS during pregnancy to inform care of pregnant women with COVID-19 until additional data
126 on pregnant women and their fetuses become available.

127

128 **SARS and its effects on pregnant women**

129 Severe acute respiratory syndrome (SARS) is caused by the SARS-coronavirus (SARS-
130 CoV). Reports of the emergence of SARS-CoV appeared in February of 2003, with the first
131 cases observed in Guangdong Province in China. The virus spread to nearly 30 countries
132 throughout the world, resulting in more than 8000 cases and 770 deaths.⁸ The outbreak was
133 brought under control after public health control measures to reduce contact with infected
134 persons were put into place, and no cases have been seen since 2004. Manifestations of SARS
135 consist of fever, chills, headache, malaise, and myalgia. Diarrhea was seen in some patients.
136 Pneumonia was nearly always seen in patients diagnosed with SARS, with mechanical
137 ventilation being required in 10-20% of cases. Case fatality rate was estimated at 9-10% (Table).

138 The natural reservoir for SARS-CoV is believed to be bats; however, some evidence
139 supported civet cats or raccoon dogs as possible intermediate sources of these illnesses.⁸ SARS is
140 transmitted by close person-to-person contact through contact of the mucus membranes of the
141 respiratory tract with respiratory droplets formed when an infected person coughs or sneezes.
142 Fecal-oral transmission and transmission via fomites have also been reported.⁸ Airborne spread
143 due to inhalation of small particle aerosols may also be possible. Transmission in health care
144 settings was frequently seen during the 2003 outbreak, with superspreading (when a single
145 patient transmits infection to a disproportionate number of contacts) reported.⁹ The incubation
146 period was estimated at a mean of 4.6 days, with a range of 2-14 days. Transmission appeared to
147 occur most often during the second week of illness when viral excretion is highest; there is no
148 evidence that a person with SARS is contagious before symptom onset.

149 The largest case series of pregnant women with SARS was from the 2003 outbreak in
150 Hong Kong, in which 12 pregnant women were identified.¹⁰ The case-fatality rate was 25% (3
151 deaths). Clinical and laboratory findings were similar to those seen in the non-pregnant
152 population. Pneumonia on chest radiograph or CT was seen in all patients. Major medical
153 complications included adult respiratory distress syndrome in four, disseminated intravascular
154 coagulopathy (DIC) in three, renal failure in three, secondary bacterial pneumonia in two, and
155 sepsis in two patients.

156 Pregnancy outcomes varied by trimester of presentation.¹⁰ Among the seven women who
157 became ill in the first trimester, four had a spontaneous abortion, two had pregnancy terminations
158 for social reasons after recovery from SARS, and one delivered a full-term healthy infant.
159 Among the five women who presented after 24 weeks gestation, four delivered preterm. Three
160 women delivered by cesarean delivery due to deteriorating maternal condition from their SARS

161 illness at 26, 28 and 32 weeks gestation.¹¹ These babies had birth weights appropriate for
162 gestational age. Two of the infants had respiratory distress syndrome requiring surfactant (born
163 at 26 and 28 weeks gestation), with one later developing bronchopulmonary dysplasia.
164 Gastrointestinal complications were observed in two infants, including a jejunal perforation in an
165 infant delivered at 26 weeks and necrotizing enterocolitis with ileal perforation in an infant
166 delivered at 28 weeks gestation. Whether these gastrointestinal complications were related to
167 complications from SARS or its treatment or if they were secondary to preterm delivery is
168 unknown.¹¹ The two infants who were delivered after their mothers' recovery from SARS had
169 intrauterine growth restriction. No clinical, radiologic, or laboratory evidence for transmission
170 from mother to fetus was observed, despite laboratory testing of different specimens.^{12,13}

171 A matched case-control study¹⁴ compared 10 of the 12 pregnant women noted above (two
172 were excluded because they were unable to be matched) to 40 non-pregnant women with SARS.
173 Women were matched on sex, age, timing of contracting SARS, health care worker status,
174 underlying illness and whether the woman resided in a housing area where there was a large
175 outbreak. Pregnancy appeared to have no effect on clinical symptoms or time to presentation
176 after symptom onset. However, complications and adverse outcomes were more common among
177 pregnant women: women who were pregnant had a longer hospital stay, were statistically
178 significantly more likely to develop renal failure, sepsis, and DIC, and were more likely to
179 require intensive care unit admission. Forty percent of pregnant women required mechanical
180 ventilation, compared to 13% of non-pregnant patients ($p=0.07$). Pregnant women were also
181 significantly more likely to die ($p=0.01$).

182 We identified five reports of additional cases of SARS during pregnancy treated in Hong
183 Kong ($n=2$), United States ($n=2$), and Canada ($n=1$).¹⁵⁻¹⁹ Two of the five women required

184 mechanical ventilation, one required hemodialysis for acute renal failure, and one had seizures
185 and positive cerebrospinal fluid for SARS-CoV, suggestive of a central nervous system infection.
186 All patients recovered from their illness. In one case, the pregnancy was terminated at the
187 mother's request; the remaining pregnancies ended in liveborn infants (two at term and two
188 preterm). Testing of neonatal specimens for SARS-CoV RNA was negative.

189 Several hospitals in Toronto and Hong Kong reported measures instituted on obstetrics
190 services during the SARS outbreak to decrease transmission to pregnant women, their families,
191 community members and health care workers.^{20,21} For example, all hospital staff, patients, and
192 visitors were screened for symptoms at the hospital entrance and wore N95 respirators. Visitors
193 were limited to one per patient on labor and delivery, with no visitors allowed in the postpartum
194 ward. Postpartum stays were reduced in length with a postpartum nurse home visit added.
195 Postpartum patients were asked to observe a 10-day home quarantine. Health care workers were
196 asked to observe a work quarantine in which they were asked to go directly from home to work
197 and vice versa to minimize interaction in the community. Obstetric services considered to be
198 non-essential such as routine ultrasound and prenatal diagnosis were suspended. Although the
199 impact of these interventions was not evaluated, there may be some relevant lessons learned
200 from these experiences during SARS that could help inform the approach to COVID-19.

201

202 **MERS and its effects on pregnant women**

203 Middle East Respiratory Syndrome (MERS) is a respiratory illness caused by MERS-
204 CoV. The illness was first identified in Saudi Arabia in 2012, with spread to other countries in
205 the Arabian peninsula and eventually to countries outside the Arabian peninsula, including the

206 United States.^{22,23} The largest outbreak outside the Arabian Peninsula was in the Republic of
207 Korea in 2015. Nearly 2,500 cases of MERS-CoV illness and over 860 deaths have been
208 reported with continuing reports into the present. The manifestations of MERS include severe
209 respiratory illness characterized by fever, cough, and shortness of breath. Some patients also
210 have diarrhea. The case fatality rate is estimated to be 35-40 percent. Patients who developed
211 MERS were more likely to be older (median age is 50 years) with about two-thirds of patients
212 being male. Patients with MERS were also more likely to have an underlying illness. Some
213 patients with MERS-CoV infection have been asymptomatic (identified through contact
214 investigations). The mean incubation period is 5.2 days, with a range of 2-13 days. As with
215 SARS, MERS is mainly spread person-to-person through close contact, with transmission in
216 health care settings, and superspreading events have been observed. However, since 2016, the
217 number of cases of MERS-CoV has been dramatically reduced after public health efforts to
218 prevent MERS-CoV transmission were put into place.²⁴

219 Information on MERS among pregnant women is limited. We identified reports of 13
220 cases of pregnant women with MERS from several countries, including Saudi Arabia (8), Korea
221 (2), Jordan (1), United Arab Emirates (1), and Philippines (1).^{13,25-31} Two women were
222 asymptomatic, identified as part of a contact investigation. Among the 11 symptomatic women,
223 manifestations were similar to those seen in non-pregnant patients with MERS. Seven of 13
224 patients were admitted to an intensive care unit for respiratory deterioration or ARDS, five
225 required ventilator support, three died, and eight recovered. Among the three deaths, the mothers
226 died 8-25 days post-delivery. Both babies born to asymptomatic women were born healthy at
227 term; among those who were symptomatic, there was one intrauterine fetal demise, one stillbirth,

228 one baby delivered at 25 weeks who died 4 hours after birth, two healthy preterm infants and five
229 healthy term infants (infant status was not mentioned for one).

230

231 **Coronavirus Disease 2019 (COVID-19)**

232 Clinical, epidemiologic, and viral characteristics

233 Respiratory illness caused by a novel coronavirus (now referred to as SARS-CoV-2) was
234 first noted in December of 2019 in Wuhan, Hubei Province, China. The WHO China Country
235 office was notified of an outbreak of pneumonia of unknown etiology on December 31, 2019
236 (Figure 2). Between December 31, 2019 and January 3, 2020, 44 cases were reported to the
237 WHO. On January 7, 2020, Chinese authorities identified a novel coronavirus as the cause. The
238 virus has quickly spread first through Wuhan and subsequently to other areas of China and other
239 countries in the world (Figure 1). Early data suggested an association between the Huanan
240 Seafood Wholesale Market and COVID-19 with 27 of 41 cases in one report³² and 26 of 47 in
241 another report³³ with epidemiologic links to the market, leading to closure of the market on
242 January 1, 2020. Given that the earliest case reported (illness onset on December 1, 2019)³² did
243 not have exposure to the market raises the possibility that the initial emergence into humans
244 occurred elsewhere. However, sampling of the market's environment supports the market's
245 importance in early transmission of the virus. Later cases were much less likely to have visited
246 the market, supporting the role of person-to-person transmission in later cases.

247 The SARS-CoV-2 is a betacoronavirus similar to SARS-CoV and MERS-CoV (Table).
248 Sequencing data show that the SARS-CoV-2 is most closely related to coronaviruses found in
249 bats, with more than 85% nucleotide identity with a bat SARS-like CoV.^{34,35} The virus has 79%

250 nucleotide identity to SARS-CoV and about 50% to MERS-CoV.³⁵ Bats appear to be the natural
251 reservoirs of both SARS-CoV and MERS-CoV. The emergence of these viruses in humans has
252 been attributed to host switching: the virus “jumped” from an intermediary host species (e.g.,
253 civet cats for SARS-CoV and dromedary camels for MERS-CoV) to humans. An intermediary
254 host species is thought to be likely for SARS-CoV-2,³⁵ although it has been yet to be identified.
255 Sequence data that show a high degree (>99.98%) of similarity of the virus among different
256 patients, suggesting a recent emergence in humans.

257 Clinical manifestations of COVID-19 are similar to those with SARS and MERS (Table).
258 Studies of hospitalized patients with COVID-19 show that patients commonly develop severe
259 pneumonia with 23-32% admitted to the intensive care unit and 17-29% of cases progressing to
260 acute respiratory distress syndrome (ARDS).^{32,36,37} Among hospitalized patients, 4-15% have
261 died.^{32,36,37} Overall case fatality ratio estimates (including asymptomatic and symptomatic
262 infections) appear to be in the range of 1% (95% confidence interval 0.5-4%),³⁸ although these
263 estimates should be considered preliminary. Average age of hospitalized patients was 49-56
264 years, with 32-51% having an underlying illness. Most (54-73%) patients were men. Children
265 with COVID-19 appear to be rarely identified, with only 28 children reported as of January 30,
266 2020 (<1% of total), and most of those identified had mild symptoms.³⁹ No pregnant women
267 were reported in any of these initial cohorts. Common manifestations among hospitalized
268 patients were fever (83-100%), cough (59-82%), myalgia (11-35%), headache (7-8%), and
269 diarrhea (2-10%). All patients had abnormalities on radiographic imaging of the chest.

270 Person-to-person transmission of SARS-CoV-2 is thought to be similar to transmission of
271 influenza and other respiratory pathogens; respiratory droplets are formed when an infected
272 person coughs or sneezes and these droplets are inhaled by close contacts, generally within 6

273 feet. It is unclear if infection can be transmitted from fomites. Fecal-oral transmission might be
274 possible, given that SARS-CoV-2 has been identified in stool specimens⁴⁰ and SARS-CoV might
275 have been transmitted in this manner.⁴¹ The basic reproduction number, R_0 (the average number
276 of people who will become infected from a single infected person in a population where all
277 persons are susceptible) is affected by factors such as the duration of infectivity, the
278 transmissibility of the pathogen, and the number of susceptible contacts. Measles, which is
279 highly infective, has a R_0 of 12-18, while 2009 H1N1 influenza and SARS have an R_0 of 1.2-1.6
280 and 2-5, respectively.⁴² Current estimates of R_0 for SARS-CoV-2 places it at 2.2 (95% CI, 1.4 to
281 3.9)³³ As with SARS and MERS, nosocomial transmission is playing a key role in transmission,
282 presumed to be responsible for infection of 29% of affected health professionals and 12% of
283 hospitalized patients in a recent study.³⁷

284

285 **Implications of COVID-19 for pregnant women**

286 In the midst of a rapidly evolving outbreak that could have significant effects on our
287 public health and medical infrastructure, the unique needs of pregnant women should be included
288 in preparedness and response plans. In previous outbreaks, clinicians have at times been reluctant
289 to treat or vaccinate pregnant women because of concerns for fetal safety.⁴³ It is critical that
290 pregnant women not be denied potentially life-saving interventions in the context of a serious
291 infectious disease threat unless there is a compelling reason to exclude them. As with all
292 decisions regarding treatment during pregnancy, carefully weighing of the benefits of
293 interventions for the mother and fetus with potential risks is necessary. As surveillance systems
294 for cases of COVID-19 are established, it is essential that information on pregnancy status, as
295 well as maternal and fetal outcomes, be collected and reported.

296 Susceptibility to and severity of COVID-19 in pregnancy

297 Although data are limited, there is no evidence from other severe coronavirus infections
298 (SARS or MERS) that pregnant women are more susceptible to infection with coronavirus. Thus
299 far, in this outbreak of novel coronavirus infection, more men have been affected than
300 women.^{32,33,36,37} This observed gender difference could be due to differences in reporting,
301 susceptibility, exposure, or recognition and diagnosis of infection. There are no data to inform
302 whether pregnancy increases susceptibility to COVID-19.

303 Previous data on SARS and MERS suggest that clinical findings during pregnancy can
304 range from no symptoms to severe disease and death. The most common symptoms of COVID-
305 19 are fever and cough, with more than 80% of hospitalized patients presenting with these
306 symptoms.³⁶ In a recent study by Chen et al.⁴⁴, nine women diagnosed with COVID-19 during
307 the third trimester of pregnancy were reported. In this small series, clinical presentation was
308 similar to that seen in nonpregnant adults, with fever in seven, cough in four, myalgia in three,
309 and sore throat and malaise each in two women. Five had lymphopenia. All had pneumonia, but
310 none required mechanical ventilation, and none died. All women had a cesarean delivery, and
311 Apgars were 8-9 at 1 minute and 9-10 at 5 minutes. In a second series of nine pregnancies with
312 ten infants (one set of twins) reported by Zhu et al.,⁴⁵ symptom onset was before delivery (1-6
313 days) in four, on the day of delivery in two, and after delivery (1-3 days) in three cases. Clinical
314 presentation of COVID-19 was similar to that seen in nonpregnant patients. Among the nine
315 pregnancies, intrauterine fetal distress was noted in six, seven were cesarean deliveries, and six
316 infants were born preterm. Based on these limited reports, and the available data from other
317 respiratory pathogens such as SARS and influenza, it is unknown whether pregnant women with
318 COVID-19 will experience more severe disease.

319 Travel guidance for pregnant women

320 Travel recommendations have been instituted to limit exposure to persons in the United
321 States. All persons, including pregnant women, should not travel to China. On February 2, 2020,
322 the U.S. State Department upgraded their travel advisory to level 4, the highest level of travel
323 advisory. Obstetric providers should obtain a detailed travel history for all patients and should
324 specifically ask about travel in the past 14 days to areas experiencing widespread transmission of
325 SARS-CoV-2. Currently this is limited to China, but this situation is rapidly evolving and
326 obstetricians should stay alert to the global situation by consulting the CDC website and
327 following media coverage.

328 Vaccination in pregnancy

329 There is currently no vaccine to prevent COVID-19. Since posting of a SARS-CoV-2
330 virus genetic sequence online on January 10, 2020, multiple organizations, including the
331 National Institutes of Health, have been working to rapidly develop a COVID-19 vaccine.
332 Development of this vaccine builds on and benefits from work on SARS and MERS vaccines.⁴⁶
333 However, it is not known how quickly a safe and effective vaccine may be readily available.

334 Infection control measures and diagnostic testing

335 All patients, including pregnant women, should be evaluated for fever and signs and
336 symptoms of a respiratory infection. Ideally, screening procedures begin before arrival on a labor
337 and delivery unit or prenatal care clinic. For example, when scheduling appointments, patients
338 should be instructed what to do if they have respiratory symptoms on the day of their
339 appointment or if a patient calls triage prior to presentation, respiratory signs and symptoms
340 should be assessed over the telephone. Those patients with respiratory symptoms should be

341 separated from other waiting patients and a facemask should be placed on them. Patients who
342 meet criteria for a Person Under Investigation (Box 1) should be immediately placed in an
343 Airborne Infection Isolation Rooms (single-patient rooms at negative pressure). Once in
344 isolation, the patient's facemask may be removed. Health care personnel should adhere to
345 standard, contact and airborne precautions. Infection control personnel and local/state health
346 departments should be notified immediately; local/state health departments can help to arrange
347 testing of relevant specimens (upper and lower respiratory specimens and serum are currently
348 recommended; other specimens [stool and urine] may also be sent).

349 Management of COVID-19 in pregnancy

350 General principles regarding management of COVID-10 during pregnancy include early
351 isolation, aggressive infection control procedures, testing for SARS-CoV-2 and co-infection,
352 oxygen therapy as needed, avoidance of fluid overload, empiric antibiotics (due to secondary
353 bacterial infection risk), fetal and uterine contraction monitoring, early mechanical ventilation
354 for progressive respiratory failure, individualized delivery planning, and a team-based approach
355 with multi-specialty consultations (Box 2). Team-based management is recommended for
356 pregnancies managed in a health care facility and should include a determination of the optimal
357 clinical unit on which to provide care. Ability to provide surveillance for early detection of a
358 worsening maternal course of illness, as well as an ability to monitor for evidence of obstetric
359 complications (e.g., preterm labor or fetal compromise), are needed.

360 Changes in fetal heart rate pattern may be an early indicator of maternal respiratory
361 deterioration. Based on experience with SARS and MERS, severe respiratory failure might occur
362 in pregnant women, and in the most severe cases, mechanical ventilation might not be sufficient
363 to support adequate oxygenation. If that occurs, limited literature suggests a potential role of

364 extracorporeal membrane oxygenation (ECMO) in pregnancy; use should only be considered in
365 centers that have experience with this technique.⁴⁷ Whether delivery provides benefit to a
366 critically ill mother is unknown; decisions regarding delivery should consider the gestational age
367 of the fetus and should be made in conjunction with the neonatologist.⁴⁸

368 There are currently no antiviral medications approved by the US Food and Drug
369 Administration for treatment of COVID-19, although broad-spectrum antivirals used in animal
370 models of MERS are being evaluated for activity against SARS-CoV-2.⁴⁶ Corticosteroids for the
371 treatment of coronavirus-associated pneumonia should be avoided unless other indications are
372 present because they were not shown to be beneficial in MERS and could lead to delayed
373 MERS-CoV clearance.⁴⁹ Therefore, decisions about the use of corticosteroids for fetal lung
374 maturity should be made in consultation with infectious disease specialists and maternal-fetal
375 medicine consultants. All guidance should be considered subject to revision as additional data on
376 pregnant women with COVID-19 become available.

377 Care of infants born to mothers with COVID-19

378 Although the limited experience with newborn evaluations after delivery with SARS and
379 MERS has not identified cases of maternal-to-fetal transmission, reports have appeared in the
380 media of a 30-hour infant who was diagnosed with COVID-19, suggesting the possibility of *in*
381 *utero* transmission.⁵⁰ However, insufficient information is included in media reports to rule out
382 perinatal or postnatal modes of transmission. Data from the recent case series published by Chen
383 et al.⁴⁴ and Zhu et al.⁴⁵ of 18 women (19 infants) infected in the third trimester of pregnancy with
384 SARS-CoV-2 identified no laboratory evidence of vertical transmission. Testing of amniotic
385 fluid, cord blood, and neonatal throat swab samples was negative for SARS-CoV-2 in the six
386 patients reported by Chen et al.⁴⁴ In the report by Zhu et al.,⁴⁵ some infants were symptomatic

387 (shortness of breath in six, cyanosis in three, gastric bleeding in two, and one baby died of
388 multiple organ failure and DIC); however, throat swab testing of all infants was negative for
389 SARS-CoV-2, suggesting that these neonatal complications might not be related intrauterine
390 transmission. Thus, at this time, it is unknown if SARS-CoV-2 can be transmitted from mother-
391 to-fetus. Given the current lack of information, it seems reasonable to assume that a newborn
392 born to a mother with COVID-19 at delivery could possibly be infected, either *in utero* or
393 perinatally, and thus should be placed in isolation to avoid exposure to other newborns. Although
394 the ideal setting for a healthy infant is within a healthy mother's room, temporary separation of
395 an ill mother and her infant, as was recommended during pandemic H1N1,⁵¹ seems prudent.
396 Whether COVID-19 can be transmitted through breastmilk is unknown. We are aware of a single
397 report of SARS-CoV testing of breastmilk in a mother who had recovered from SARS and no
398 viral RNA was detected; however, the specimen was collected ~130 days after illness onset.¹⁵
399 SARS-CoV antibodies were seen in breastmilk of that patient,¹⁵ but not in another patient who
400 was infected at 7 weeks gestation with breastmilk tested at postpartum days 12 and 30.¹⁶
401 Breastmilk was tested for SARS-CoV-2 in six of the mothers reported by Chen et al.⁴⁴; all
402 specimens were negative. Until additional data are available, mothers who intend to breastfeed
403 and are well enough to express breastmilk should be encouraged to do so; breastfeeding can be
404 instituted after she is no longer considered infectious. No data are available to guide length of
405 separation and will need to be decided on a case-by-case basis after discussion between infection
406 control experts and neonatologists.

407

408 **Conclusions**

409 The COVID-19 outbreak is rapidly increasing in number of cases, deaths, and countries
410 affected. Much is unknown about the virus and its effects, including its modes of transmission,
411 the basic reproduction number, risk factors for illness, and case fatality rate. Although cases are
412 primarily in China, it is highly likely that there will be additional global spread of the virus. At
413 the present time, limited data are available on pregnant women with COVID-19 on which to base
414 recommendations for pregnancy-specific care; however, early reports and lessons from SARS,
415 MERS, and other respiratory infections suggest that pregnant women could have a severe clinical
416 course. Surveillance systems for cases of COVID-19 need to include information on pregnancy
417 status, as well as maternal and fetal outcomes. It is important to be vigilant about the spread of
418 the disease and be able to provide rapid implementation of outbreak control and management
419 measures once the virus reaches a community. Standard interventions to manage any severe
420 respiratory infection is the foundation of care for any pregnant woman with COVID-19 and
421 should be implemented aggressively in a team-based care model.

422

Table – Comparison of Characteristics of Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Coronavirus Disease 2019 (COVID-19)

Characteristics	Severe Acute Respiratory Syndrome	Middle East Respiratory Syndrome	Coronavirus Disease-2019
First patients reported	Guangdong, China, November 2002	Zarga, Jordan, April 2012 and Jeddah, Saudi Arabia, June 2012	Wuhan, China, December 2019
Virus	SARS-CoV	MERS-CoV	SARS-CoV-2
Type of coronavirus	betacoronavirus	betacoronavirus	betacoronavirus
Host cell receptor	Angiotensin converting enzyme 2	Dipeptidyl peptidase 4	structural analysis suggests Angiotensin converting enzyme 2 receptor ⁵²
Sequence similarity	reference		79% to SARS-CoV, 50% to MERS-CoV ³⁵
Animal hosts	Bats (natural reservoir), masked palm civet and raccoon dogs may be intermediate hosts	Bats (natural reservoir), dromedary camel (intermediate host)	Bats, animal sold at the seafood market in Wuhan might represent an intermediate host ³⁵
Incubation period			
Mean (95% CI: days)	4.6 (3.8-5.8)	5.2 (1.9-14.7)	5.2 days (95% confidence interval [CI], 4.1 to 7.0); 95th percentile of the distribution was 12.5 days ³³
Range (days)	2-14	2-13	2-14
Time from illness onset until hospitalization	2-8 days	0-16 days	12.5 days (mean) (95% CI, 10.3 to 14.8) - onset before January 1 9.1 days (mean); 95% CI, 8.6 to 9.7 (onset January 1-11) ³³
Basic reproduction number (R ₀) **	2-3	<1	2.2 (95% CI, 1.4 to 3.9) ³³
Patient characteristics			
Adults	93%	98%	Nearly all reported patients are adults
Children	5-7%	2%	Children have been infrequently reported (<1% of cases) ³⁹
Age range (years)	1-91	1-94	10-89 years
Average age (years)	Mean 39.9	Median 50	59 years (median) ³³
Sex ratio (M:F)	43%:57%	64.5%:35.5%	56%:44% ³³
Mortality			
Case fatality rate overall	9.6%	35-40%	Initial estimate is

			1% ³⁸
Clinical Manifestations			From hospitalized patients ^{32,36,37}
Fever	99-100%	98%	83-100%
Cough	62-100%	83%	59-82%
Myalgia	45-61%	32%	11-35%
Headache	20-56%	11%	7-8%
Diarrhea	20-25%	26%	2-10%
Laboratory findings			
Radiographic abnormalities on chest imaging	94-100%	90-100%	100%
Leukopenia	25-35%	14%	9-25%
Lymphopenia	65-85%	32%	35-70%
Thrombocytopenia	40-45%	36%	5-12%

*Modified from Rasmussen et al.²³

**Basic reproduction number – defined as average number of people who will become infected from a single infected person

Abbreviations: SARS-CoV, severe acute respiratory syndrome coronavirus; MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2

Box 1

Criteria to Guide Evaluation of Persons Under Investigation for Coronavirus Disease 2019 (COVID-19)

Clinical Features	AND	Epidemiologic Risk
Fever* or signs/symptoms of lower respiratory illness (e.g., cough or shortness of breath)	AND	Any person, including health care workers, who has had close contact** with a laboratory-confirmed COVID-19 patient within 14 days of symptom onset
Fever* and signs/symptoms of a lower respiratory illness (e.g., cough or shortness of breath)	AND	A history of travel from Hubei Province China within 14 days of symptom onset
Fever* and signs/symptoms of a lower respiratory illness (e.g., cough or shortness of breath) requiring hospitalization	AND	A history of travel from mainland China within 14 days of symptom onset

*Fever may be subjective or confirmed

**Close contact is defined as:

a) being within ~6 feet (2 meters) of a COVID-19 case for a prolonged period of time while not wearing recommended personal protective equipment (e.g., gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection); close contact can occur while caring for, living with, visiting, or sharing a health care waiting area or room with a COVID-19 case

OR

b) having direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on) while not wearing recommended personal protective equipment.

The criteria are intended to serve as guidance for evaluation. Patients should be evaluated and discussed with public health departments on a case-by-case basis if their clinical presentation or exposure history is equivocal (e.g., uncertain travel or exposure).

From: <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html#foot1>

Box 2

Principles for Management of Pregnant Women with Confirmed or Suspected Coronavirus Disease 2019 (COVID-19)^{48,53,54}

- Patients with respiratory symptoms should adhere to respiratory hygiene, cough etiquette, and hand hygiene. Ensure rapid triage of pregnant patients with respiratory symptoms. Patients with respiratory symptoms should wear a facemask and wait in a separate, well ventilated waiting area at least 6 feet from other people.
- Confirmed and suspected cases of COVID-19 should be isolated as soon as possible in an Airborne Infection Isolation Room (AIIR). If an AIIR is not available, consider transfer to a hospital with an AIIR.
- Implement CDC infection prevention and control procedures for healthcare providers including standard, contact, and airborne precautions. Eye protection and properly-fitted N95 respirators should be used. Provide additional staff training in correct use of personal protective equipment (PPE) including correct donning, doffing and disposal of PPE.
- Contact hospital infection personnel.
- In coordination with local/state health department, collect and send relevant specimens for diagnostic SARS-CoV-2 testing.
- Limit visitor and health care personnel access to patient rooms with a confirmed or suspected case.
- Pregnancy should be considered a potentially increased risk condition and monitored closely including fetal heart rate and contraction monitoring.
- Consider early oxygen therapy (target O₂ saturations $\geq 95\%$ and/or pO₂ ≥ 70 mmHg). Consider early mechanical ventilation with evidence of advancing respiratory failure. Non-invasive ventilation techniques may have a small increased risk of aspiration in pregnancy.
- Use intravenous fluids conservatively unless cardiovascular instability is present.
- Screen for other viral respiratory infections and bacterial infections (due to risk of co-infections).
- Consider empiric antimicrobial therapy (because of risk for superimposed bacterial infections).
- Consider empiric treatment for influenza, pending diagnostic testing.
- Do not routinely use corticosteroids. Use of steroids to promote fetal maturity with anticipated preterm delivery can be considered on individual basis.
- If septic shock is suspected, institute prompt, targeted management.
- Delivery and pregnancy termination decisions should be based on gestational age, maternal condition, and fetal stability, and maternal wishes.
- Consult with specialists in obstetrics, maternal-fetal medicine, neonatology, intensive care, anesthesia, and nursing.
- Communicate with patients and families regarding diagnosis, clinical status and management wishes.

*All guidance should be considered subject to revision as additional data on pregnant women with COVID-19 become available.

Figure Legends:

Figure 1: Global map of confirmed Coronavirus Disease 2019 (COVID-19) cases (as of February 14, 2020) – from

<https://www.cdc.gov/coronavirus/2019-ncov/locations-confirmed-cases.html>

Figure 2: Timeline showing key events in the Coronavirus Disease 2019 (COVID-19) outbreak - - December 1, 2019 through February 15, 2020. Abbreviations: CDC – Centers for Disease Control and Prevention, COVID-19 - Coronavirus Disease 2019, US – United States, WHO – World Health Organization

Figure 3: Illustration of the causative virion for Coronavirus Disease (COVID-19). Credit to CDC/ Alissa Eckert, MS – Obtained from CDC’s Public Health Image Library.

<https://phil.cdc.gov/Details.aspx?pid=23312>

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