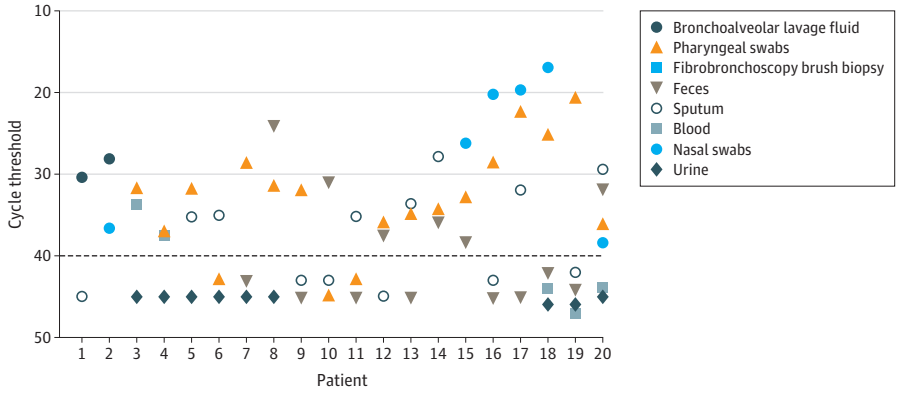
Figure. Severe Acute Respiratory Syndrome Coronavirus 2 Distribution and Shedding Patterns Among 20 Hospitalized Patients



The specimen with a cycle threshold value above the dashed line is interpreted as positive for SARS-CoV-2 RNA; those under, negative.

small. Further investigation of patients with detailed temporal and symptom data and consecutively collected specimens from different sites is warranted.

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Ethics Committee Reviews of Applications for Research Studies at 1 Hospital in China During the 2019 Novel Coronavirus Epidemic

Since December 2019, an epidemic of coronavirus disease 2019 (COVID-19) has spread rapidly from Wuhan, Hubei Province, China.[1] As of March 7, there were 1272 confirmed coronavirus cases in Henan Province (the third-highest in China), which adjoins Hubei Province. Due to the high contagiousness of COVID-19 and the current lack of any effective vaccine or drug, scientists and physicians are conducting a series of clinical studies involving affected patients. In 2016, the World Health Organization (WHO) published "Guidance for Managing Ethical Issues in Infectious Disease"[2] to ensure the scientific validity of and participants' rights and safety in studies conducted during outbreaks. The guidance stated that there is a moral obligation to conduct timely scientific research. The Ethics Committee of the Henan Provincial People's Hospital reviewed the COVID-19 studies from the hospital based on those guidelines.

Methods | Henan Provincial People's Hospital is a designated hospital for COVID-19. The ethics committee designed a review system for research proposals at the beginning of the epidemic, including the use of emergency video conference to review batches of project applications. Electronic documents were formally reviewed by the secretary and sent to members of the committee to review in advance of the

Table 1. Protocols Referred for Modification

Reasons studies needed modifications	No. (%) of studies needing modifications (n = 31)
Lack of statistical basis for sample-size calculation	12 (38.7)
Defective inclusion and exclusion criteria[a]	10 (32.3)
Defective efficacy and safety indicators	8 (25.8)
Study participants' risk minimization criteria insufficient[b]	8 (25.8)
Benefits for future patients or society not described clearly	5 (16.1)
Insufficient team members in key roles	4 (12.9)
Necessary research equipment not available	4 (12.9)
Background evidence not provided sufficiently[c]	3 (9.7)
Operating procedures need improvement[d]	3 (9.7)

[a] Inclusion criteria were too broad, or exclusion criteria were too narrow.

[b] The treatment scheme for expected adverse reactions was incomplete or the criteria for early termination of the study was unclear.

[c] The preclinical data or the mechanism of the drug was not fully provided.

[d] Operating procedures of plasma treatment, cell therapy, traditional Chinese medicine therapy were not standard.

meetings. Applications were voted on by quorum and members proposed clear reasons for the decisions and provided suggestions for revision after full discussion.

We examined all new applications for COVID-19-related studies and meeting minutes from February 2 through March 7, 2020, categorized the study type, determined the approval rate and review time, and summarized the issues in research proposals and informed consent forms consistent with the WHO document. Follow-up reviews of ongoing non-COVID-19 studies are not included in this study.

Results | Ethics review conferences, held once every month in nonepidemic periods, were held 4 times in 35 days. The mean time was 2.13 days from application submissions until an initial review decision was made. For applications that required modifications, the mean time was 1.81 days for the resubmission to be reviewed again.

Forty-one applications were reviewed, including interventional studies (n = 21); diagnostic studies (n = 7); observational studies (n = 10); and other types (n = 3). Six (14.6%) were approved; 4 (9.8%), rejected; and 31 (75.6%), referred for modification.

Of the 4 rejected applications, 2 were denied because 1 involved a new, unapproved interferon-alfa treatment and another involved traditional Chinese medicine with many potential adverse reactions, so the potential risks outweighed benefits. The other 2 studies were denied because the laboratory biosafety level was inadequate, which may have led to virus leakage.

Of the 31 applications that required modifications, the issues with the research proposals and informed consent forms are indicated in **Table 1** and **Table 2**. The most frequent issues with proposals were lack of statistical basis for the sample size calculation and deficiencies in inclusion and exclusion criteria. The most frequent issues with informed consent forms were that patients were not informed of the risks and that compensation was unreasonable.

Table 2. Informed Consent Forms Needing Modification

Reasons informed consent forms needed modifications	No. (%) of studies needing modifications (n = 31)
Research risks not explained completely	13 (41.9)
Compensation of participant not reasonable	13 (41.9)
Misrepresentative language used to induce participation	8 (25.8)
Language barriers	8 (25.8)
Participation steps not described clearly	7 (22.6)
Benefits for participants not described objectively	7 (22.6)
Free items offered by sponsor not declared clearly	6 (19.4)
Alternative treatment strategy not explained sufficiently	5 (16.1)
Responsibility for research-related injuries not declared clearly	5 (16.1)

Discussion | During the outbreak, ethics committee review of COVID-19 studies at 1 hospital were conducted within a few days, more quickly than the 27 ethical reviews organized by the Médecins Sans Frontières ethics review board during the Ebola crisis, with a mean time of 12.4 days to provide a review after the initial request.[3] However, the first-time study approval rate of 14.6 % was lower than 33.4% during the nonepidemic period in 2019 in the Henan Provincial People's Hospital, possibly reflecting researchers' inexperience and the hasty preparation of documents. Review standards were not lowered during the outbreak.

The high frequency of issues with the research proposals and informed consent forms reflect that during an outbreak, researchers may use experimental drugs on affected patients, relax inclusion and exclusion criteria, and fail to offer reasonable compensation or to inform vulnerable patients of trial risks. Because the climate of fear may induce patients to agree to participate in research, the ethics committee paid special attention to such issues.

This study was limited to a small number of studies considered by 1 ethics committee. Future studies of other ethics committees should be conducted.

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Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is highly infectious, with multiple possible routes of transmission.[1-3] Controversy exists regarding whether SARS-CoV-2 can be transmitted in utero from an infected mother to her infant before birth. A series of 9 pregnant women found no mother-child transmission.[4] We report a newborn with elevated IgM antibodies to SARS-CoV-2 born to a mother with coronavirus disease 2019 (COVID-19).

Methods | A mother with COVID-19 and her infant delivered February 22, 2020, at Renmin Hospital, Wuhan, China, were evaluated. The institutional review board of Wuhan University approved the study, and written informed consent was obtained.

Clinical information was obtained from interview of the mother and clinical records. Both mother and infant underwent chest computed tomography (CT); real-time reverse transcriptase–polymerase chain reaction (RT-PCR) for SARS-CoV-2 nucleic acid of nasopharyngeal swabs; and IgM and IgG antibody, cytokine, and other biochemistry tests in blood. The mother also underwent RT-PCR testing of vaginal secretions at delivery. The sensitivity of IgM for SARS-CoV-2 reached 70.2% and specificity was 96.2%. The sensitivity of IgG for SARS-CoV-2 reached 96.1% and specificity was 92.4%.[3]

Results | On January 28, 2020, a 29-year-old primiparous woman (34 weeks 2 days of gestation) suspected of being exposed to SARS-CoV-2 developed a temperature of 37.9° C and nasal congestion, which progressed to respiratory difficulties. On January 31, a chest CT showed patchy ground-glass opacities in the periphery of both lungs. The RT-PCR on a nasopharyngeal swab was positive. On February 2, the patient was admitted to Renmin Hospital and received antiviral, antibiotic, corticosteroid, and oxygen therapies. Results from 4 repeat RT-PCR tests were positive (**Table 1**). On February 21, IgG and IgM antibody levels to SARS-CoV-2 were 107.89 AU/mL and 279.72 AU/mL, respectively (normal IgM and IgG <10 AU/mL). The results of an RT-PCR test of the patient's vaginal secretions were negative.

On February 22, an infant girl was delivered by cesarean in a negative-pressure isolation room. The mother wore an

Table 1. Laboratory Results for the Mother

Time	Laboratory test	Value	Reference range
Feb 2	White blood cell count, $\times 10^9$/L	8.03	3.5-9.5
	Neutrophil count, $\times 10^9$/L	6.57	1.8-6.3
	Neutrophil ratio, %	81.9	40-75
	Lymphocyte count, $\times 10^9$/L	1.08	1.1-3.2
	Lymphocyte ratio, %	13.4	20-50
	C-reactive protein, mg/L	57	0-10
	PCT, ng/mL	0.086	0.1
	ALT, U/L	40	7-40
	AST, U/L	38	13-35
Feb 10	PCR of nasopharyngeal swab	+	–
Feb 19	PCT of nasopharyngeal swab	+	–
	PCR of vaginal secretion	–	–
Feb 21	SARS-CoV-2 IgG, AU/mL	107.89	<10
	SARS-CoV-2 IgM, AU/mL	279.72	<10
Feb 26	PCR of nasopharyngeal swab	+	–
Feb 28	Breast milk	–	–
Feb 29	SARS-CoV-2 IgG, AU/mL	116.30	<10
	SARS-CoV-2 IgM, AU/mL	112.66	<10
Mar 1	PCR of nasopharyngeal swab	+	–

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; PCR, polymerase chain reaction, PCT, procalcitonin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; –, negative; +, positive.