COVID-19 UPDATES
April 27, 2020

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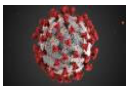

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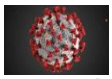

CDC Update

Watch for symptoms

People with COVID-19 have had a wide range of symptoms reported – ranging from mild symptoms to severe illness.

These symptoms may appear **2-14 days after exposure to the virus:**

- Fever
- Cough
- Shortness of breath or difficulty breathing
- Chills
- Repeated shaking with chills
- Muscle pain
- Headache
- Sore throat
- New loss of taste or smell

When to Seek Medical Attention

If you have any of these **emergency warning signs*** for COVID-19 get **medical attention immediately:**

- Trouble breathing
- Persistent pain or pressure in the chest
- New confusion or inability to arouse
- Bluish lips or face

*This list is not all inclusive. Please consult your medical provider for any other symptoms that are severe or concerning to you.

Call 911 if you have a medical emergency: Notify the operator that you have, or think you might have, COVID-19. If possible, put on a cloth face covering before medical help arrives.

CDC.gov

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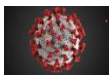
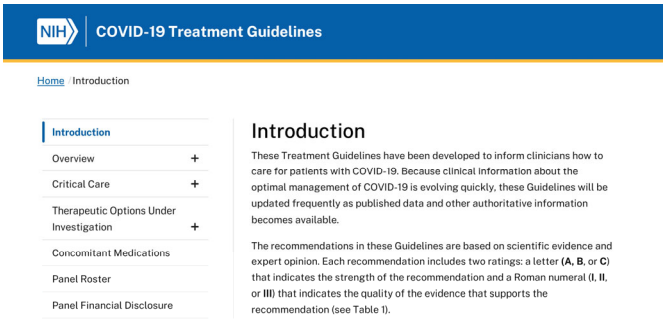


NIH Guidelines



NIH | COVID-19 Treatment Guidelines

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Introduction

These Treatment Guidelines have been developed to inform clinicians how to care for patients with COVID-19. Because clinical information about the optimal management of COVID-19 is evolving quickly, these Guidelines will be updated frequently as published data and other authoritative information becomes available.

The recommendations in these Guidelines are based on scientific evidence and expert opinion. Each recommendation includes two ratings: a letter (**A**, **B**, or **C**) that indicates the strength of the recommendation and a Roman numeral (**I**, **II**, or **III**) that indicates the quality of the evidence that supports the recommendation (see Table 1).

- A, for strong recommendations;
- B, for moderate recommendations and;
- C, for optional recommendations.

The guidance also stratifies evidence quality into three levels, including:

- I, for evidence validated by one or more randomized trials with clinical outcomes and/or validated laboratory endpoints;
- II, for evidence validated by one or more well-designed, nonrandomized trials or observational cohort studies and;
- III, for expert opinions.

https:www.covid19treatmentguidelines.nih.gov/

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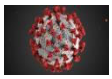

Younger patients with MAFLD are at increased risk of severe COVID-19 illness: A multicenter preliminary analysis

Table 1. Association between the presence of MAFLD and COVID-19 severity in younger and older patients.

	Younger patients			Elderly patients		
	OR	95% CI	*P*	OR	95% CI	*P*
60 years as the cut-off	n=253 [72(28.5%) MAFLD, 34(13.4%) severe cases]			n=74 [21(28.4%) MAFLD, 25(33.8%) severe cases]		
Unadjusted	3.97	1.89-8.35	< 0.001	0.72	0.24-2.15	0.55
Adjusted model I	3.25	1.47-7.16	0.003	0.75	0.25-2.28	0.61
Adjusted model II	2.49	1.04-5.96	0.04	0.45	0.13-1.59	0.22
Adjusted model III	2.67	1.13-6.34	0.03	0.61	0.18-2.03	0.42
55 years as the cut-off	n=199 [56(28.1%) MAFLD, 21(10.6%) severe cases]			n=128 [37(28.9%) MAFLD, 38(29.7%) severe cases]		
Unadjusted	6.48	2.45-17.1	< 0.001	1.00	0.44-2.31	0.99
Adjusted model I	5.02	1.81-13.90	0.002	1.02	0.44-2.39	0.96
Adjusted model II	3.10	1.01-9.56	0.05	0.77	0.30-1.99	0.60
Adjusted model III	3.63	1.20-10.95	0.02	0.91	0.37-2.28	0.85
65 years as the cut-off	n=276 [80(29.0%) MAFLD, 41(14.9%) severe cases]			n=51 [13(25.5%) MAFLD, 18(35.3%) severe cases]		
Unadjusted	3.13	1.59-6.18	0.001	0.76	0.20-2.94	0.69
Adjusted model I	2.69	1.31-5.53	0.01	0.75	0.19-2.94	0.68
Adjusted model II	2.22	1.02-4.86	0.04	0.33	0.07-1.69	0.19
Adjusted model III	2.41	1.12-5.22	0.03	0.59	0.13-2.64	0.49

Data are presented as odds ratios (ORs) and 95% confidence intervals (CIs) measured by univariable and multivariable logistic regression analyses.
Model I: adjusted for age and sex.
Model II: adjusted for age, sex, smoking, obesity, diabetes mellitus and hypertension.

- In patients aged younger than 60 years, a **more than two-fold higher prevalence of severe COVID-19 was observed in MAFLD patients** compared to those without; this association remained significant after adjusting for age, sex, smoking status, overweight, diabetes, and hypertension (adjusted-OR 2.67, 95%CI 1.13-6.34, P=0.03).
- **MAFLD was not associated** with disease severity in multivariable analysis in elderly patients (P >0.05). We performed sensitivity analysis by setting a cut-off point other than 60 years to define younger and elderly patients. Similar results were observed at cut-offs using 55 and 65 years.

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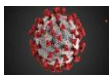

COVID-19 Antibody testing: Information that Would be Useful

- The presence of antibodies confirms exposure
- The presence of antibodies confirms immunity (neutralizing antibodies)
- Antibodies can complement RNA testing to confirm early infection
- The absence of antibodies excludes exposure
- The titer of antibodies predicts severity

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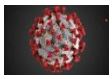

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

- This study investigates the dynamics of total antibody (Ab), IgM and IgG antibody against SARS-CoV-2 in serial blood samples collected from 173 confirmed COVID-19 patients
- COVID -19 Case defined as:
  - Acute respiratory infection syndromes and/or abnormalities in chest CT images accompanied by detectable SARSCoV-2 RNA in respiratory sample since illness onset for at least one time
- The Ab, IgM antibody and IgG antibody against SARS-CoV-2 in plasma samples were tested using enzyme linked immunoassay.
  - The Ag was the receptor binding domain (RBD) of the spike protein of SARS-CoV-2
- The specificity of the assays for Ab, IgM and IgG was determined as 99.1% (211/213), 98.6% (210/213) and 99.0% (195/197) by testing of samples collected from healthy individuals prior to the pandemic

2020 Mar 28. pii: ciaa344. doi: 10.1093/cid/ciaa344. [Epub ahead of print]

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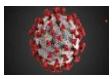

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

Table 2. Performance of different detections in samples at different time since onset of patients.

Days after onset	n	RNA		Ab		IgM		IgG		RNA+Ab	
		n(+)	Sensitivity (%, 95%CI)	n(+)	Sensitivity (%, 95%CI)	n(+)	Sensitivity (%, 95%CI)	n(+)	Sensitivity (%, 95%CI)	n(+)	Sensitivity (%, 95%CI)
Total	173	112[$]	67.1 (59.4, 74.1)	161	93.1 (88.2, 96.4)	143	82.7 (76.2, 88)	112	64.7 (57.1, 71.8)	172	99.4 (96.8, 100.0)
1-7	94	58[$]	66.7 (55.7, 76.4)	36	38.3 (28.5, 48.9)	27	28.7 (19.9, 39.0)	18	19.1 (11.8, 28.6)	74	78.7 (69.1, 86.5)
8-14	135	67[$]	54.0 (44.8, 63.0)	121	89.6 (83.2, 94.2)	99	73.3 (65.0, 80.6)	73	54.1 (45.3, 62.7)	131	97.0 (92.6, 99.2)
15-39	90	25[$]	45.5 (32.0, 59.5)	90	100.0 (96.0, 100.0)	83*	94.3 (87.2, 98.1)	71#	79.8 (69.9, 87.6)	90	100.0 (96.0, 100.0)

[*] Two patients missed IgM tests due to inadequate plasma samples. [#] One patient missed IgG tests due to inadequate plasma samples. [$] There were 7, 11 and 35 patients had not been performed RNA testing during the 1-7 onset day, 8-14 onset day and 15-39 onset day, respectively.

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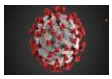

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

- **The seroconversion rate for Ab, IgM and IgG was 93.1%, 82.7% and 64.7%**, respectively.
- **The median seroconversion time for Ab, IgM and then IgG were day-11, day-12 and day-14, separately.**
- **The presence of antibodies was <40%** among patients within 1-week since onset, and rapidly increased to 100.0% (Ab), 94.3% (IgM) and 79.8% (IgG) since day-15 after onset.
- **RNA detectability decreased from 66.7%** (58/87) **before day-7** to **45.5%** (25/55) day **15-39**.
- Combining RNA and antibody detections significantly improved the sensitivity of pathogenic diagnosis for COVID-19 ($p<0.001$), even in early phase of 1-week since onset ($p=0.007$).
- Moreover, a higher titer of Ab was independently associated with a worse clinical classification ($p=0.006$)

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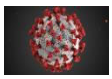

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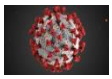

EUROIMMUN: COVID-19 Antibody Test Limitations

Anti-SARS-CoV-2 ELISA (IgGA) and Anti-SARS-CoV-2 ELISA (IgG)

- This test has not been reviewed by the FDA.
- Results from antibody testing should not be used as a sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
- Negative results do not rule out SARS CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic should be considered to rule out infection in these individuals.
- Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.
- Not for the screening of donated blood

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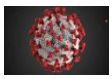

EUROIMMUN

Clinical performance

Diagnostic sensitivity: The sensitivity was determined by investigating 9 samples from 8 European patients, using the Anti-SARS-CoV-2 ELISA (IgA) and the Anti-SARS-CoV-2 ELISA (IgG). In these patients, infections with SARS-CoV-2 had been confirmed by RT-PCR test [4] based on one sample each, taken at the early phase of infection. The serological test was performed on samples taken at a later stage of infection. The tables show the results with respect to specific antibodies of classes IgA and IgG. The determined sensitivities are shown in two groups, i.e. the early samples (< 10 days after onset of symptoms) and the later samples (> 10 days after onset of symptoms). The two lines marked in grey show two samples from one patient over the course of time.

Sample	Days after symptom onset	Disease severity	EUROIMMUN Anti-SARS-CoV-2 ELISA			
			IgA (ratio) pos.: ≥ 1.1 borderl.: 0.8 – 1.0	IgA Results	IgG (ratio) pos.: ≥ 1.1 borderl.: 0.8 – 1.0	IgG Results
< 10 days after onset of symptoms						
1	4	mild	0.2	neg.	0.1	neg.
2	7	severe	7.2	pos.	4.4	pos.
3	8	severe	2.0	pos.	0.3	neg.
4	8	severe	0.2	neg.	0.8	borderl.
> 10 days after onset of symptoms						
5	13	mild	2.3	pos.	0.3	neg.
6	13	mild	2.1	pos.	1.3	pos.
7	16	mild	8.5	pos.	6.7	pos.
8	18	mild	2.7	pos.	1.9	pos.
9	32	mild	1.8	pos.	1.1	pos.

Group	EUROIMMUN Anti-SARS-CoV-2 ELISA IgA			
	positive	borderline	negative	Sensitivity
< 10 days after onset of symptoms	2	0	2	50.0%
> 10 days after onset of symptoms	5	0	0	100%

Group	EUROIMMUN Anti-SARS-CoV-2 ELISA IgA & IgG combined			
	positive	borderline	negative	Sensitivity
< 10 days after onset of symptoms	2	1	1	66.7%
> 10 days after onset of symptoms	5	0	0	100%

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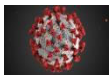

ARS-CoV-2 IgG (Abbott)

- **This test has not been reviewed by the FDA.**
- **This test is for clinical laboratory use only. It is not for home use.**
- **Not for the screening of donated blood.**
- **Results should be used in conjunction with other data; e.g., symptoms, results of other tests, and clinical impressions.**
- **Immunocompromised patients who have COVID-19 may have a delayed antibody response and produce levels of antibody which may not be detected as positive by the assay.**
- **Potentially interfering disease states and other cross reactants have been evaluated and are represented in the SPECIFIC PERFORMANCE CHARACTERISTICS section of this package insert.**
- **Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as SARS-CoV-2 IgG that employ mouse monoclonal antibodies.**
- **Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed.**

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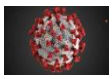

SARS-CoV-2 IgG (Abbott)

Clinical Performance

A study was performed to determine the clinical performance of the SARS-CoV-2 IgG assay.

To estimate the positive percent agreement (PPA), 122 serum and plasma specimens were collected at different times from 31 subjects who tested positive for SARS-CoV-2 by a polymerase chain reaction (PCR) method and who also presented with COVID-19 symptoms. Each specimen was tested using the SARS-CoV-2 IgG assay. The PPA and the 95% confidence interval (CI) were calculated.

To estimate the negative percent agreement (NPA), 1070 serum and plasma specimens from subjects assumed to be negative for SARS-CoV-2 were tested. Of the 1070 specimens, 997 specimens were collected prior to September 2019 (pre-COVID-19 outbreak). An additional 73 specimens were collected in 2020 from subjects who were exhibiting signs of respiratory illness but tested negative for SARS-CoV-2 by a PCR method. All 1070 specimens were tested using the SARS-CoV-2 IgG assay. The NPA and the 95% CI were calculated.

The results of both groups are presented in the following 2 tables.

Positive Agreement by Days Post-Symptom Onset

Days Post-Symptom Onset	n	Positive	Negative	PPA (95% CI)
< 3	5	0	5	0.00% (0.00, 52.18)
3 - 7	10	5	5	50.00% (18.71, 81.29)
8 - 13	34	31	3	91.18% (76.32, 98.14)
≥ 14	**73**	**73**	**0**	**100.00% (95.07, 100.00)**

Negative Agreement by Category

Category	n	Positive	Negative	NPA (95% CI)
Pre-COVID-19 Outbreak	997	4	993	99.60% (98.98, 99.89)
Other Respiratory Illness	73	0	73	100.00% (95.07, 100.00)
Total	**1070**	**4**	**1066**	**99.63% (99.05, 99.90)**

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