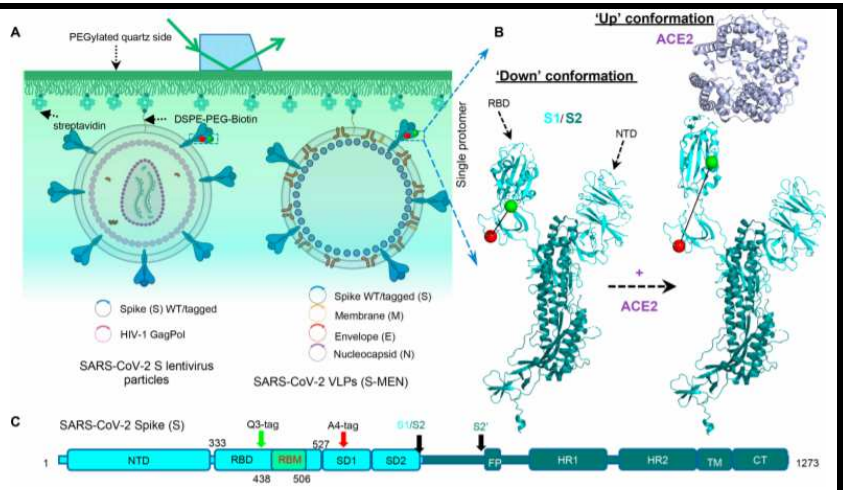
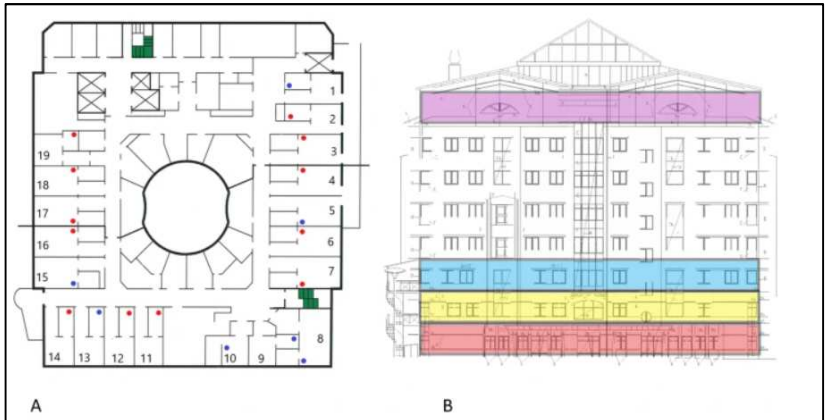
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 16-22.11.2020 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Diez J et al Immunotherapy https://www.biorxiv.org/content/10.1101/2020.04.07.029017v2	Currently available intravenous immunoglobulin contains antibodies reacting against severe acute respiratory syndrome coronavirus 2 antigens	La Grifols, produttrice delle delle immunoglobuline umane Gamunex-C e Flebogamma, riporta i risultati di un test di reattività tramite ELISA contro una serie di betacoronavirus : per quanto riguarda in particolare SARS-CoV-2, si dimostra la reattività di entrambi i prodotti, giustificabile con la cross-reattività dimostrata tra i diversi sottogruppi di coronavirus umani.	Aim: There is a critical need for effective therapies that are immediately available to control the spread of COVID-19 disease. Material & methods: Gamunex R -C and Flebogamma R DIF (Grifols) intravenous immunoglobulin (IVIG) products were tested using ELISA techniques for antibodies against several antigens of human common betacoronaviruses that may crossreact with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Results: Both IVIGs showed consistent reactivity to components of the tested viruses. Positive crossreactivity was seen in SARS-CoV, middle east respiratory syndrome- CoV and SARS-CoV-2. For SARS-CoV-2, positive reactivity was observed at IVIG concentrations ranging from 100 µg/ml with Gamunex-C to 1 mg/ml with Flebogamma 5% DIF. Conclusion: Gamunex-C and Flebogamma DIF contain antibodies reacting against SARS-CoV-2 antigens. Studies to confirm the utility of IVIG preparations for COVID-19 management may be warranted.

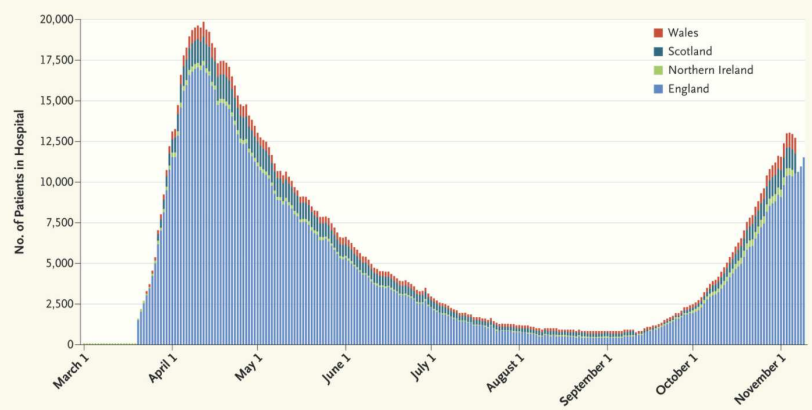
			Table 1. Results of IgG reactivity against different coronaviruses. Concentration denotes the last intravenous immunoglobulin dilution with positive result, or no reactivity even undiluted. N = 1–4 tests. CoV: Coronavirus; HCoV: Human coronavirus; IVIG: Intravenous immunoglobulin; NT: Not tested; RBD: Receptor-binding domain; SARS: Severe acute respiratory syndrome.
Lu M et al Cell https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30618-1?utm_medium=homepage	Real-time Conformational Dynamics of SARS-CoV-2 Spikes on Virus Particles	Variazione conformazionale della proteina S di SARS-CoV-2 al momento dell'interazione col recettore cellulare ACE2, studiata tramite la tecnica biofisica della smFRET e utile ai fini di progettazione di farmaci e vaccini.	SARS-CoV-2 spike (S) mediates viral entry into cells and is critical for vaccine development against COVID-19. Structural studies have revealed distinct conformations of S, but real-time information that connects these structures, is lacking. Here we apply single-molecule Fluorescence (Förster) Resonance Energy Transfer (smFRET) imaging to observe conformational dynamics of S on virus particles. Virus-associated S dynamically samples at least four distinct conformational states. In response to human receptor Angiotensin-Converting Enzyme 2 (hACE2), S opens sequentially into the hACE2-bound S conformation through at least one on-path intermediate. Conformational preferences observed upon expsoure to convalescent plasma or antibodies suggest mechanisms of neutralization involving either competition with hACE2 for binding to the receptor-binding domain (RBD) or allosteric interference with conformational changes required for entry. Our findings inform on mechanisms of S recognition and conformations for immunogen design.

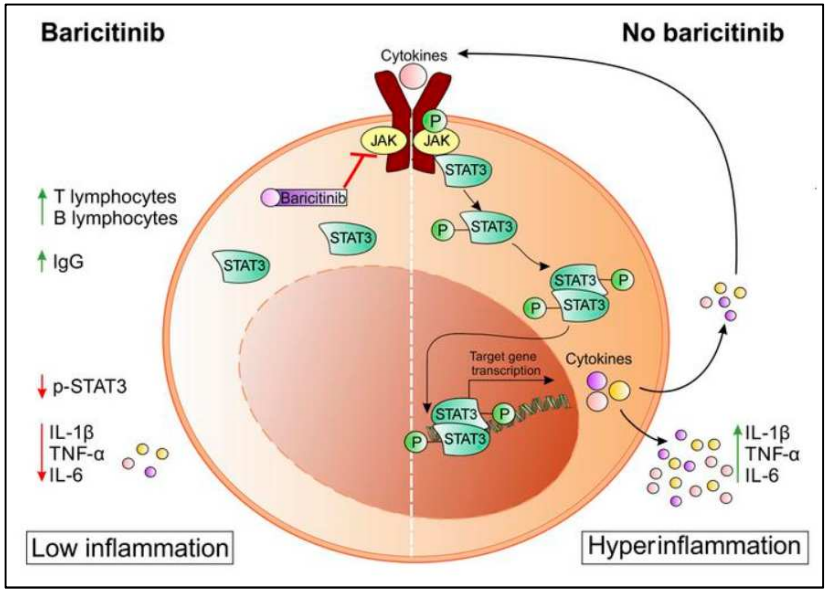
IVIG product	Country of origin of the plasma	Virus and antigen/target							
		HCoV (beta-coronavirus) Undetermined	SARS-CoV Culture lysate	MERS-CoV			SARS-CoV-2		
				N protein	S1 subunit/RBD	S2 subunit	S1 subunit (RV-405200 kit)	S1 subunit (EI-2606-9601-G kit)	Virus lysate
Gamunex-C 10%	USA	Negative	1 mg/ml	100 µg/ml	50 µg/ml	50 µg/ml	100 µg/ml	1 mg/ml	50 mg/ml
Flebogamma 5% DIF	USA	50 mg/ml	10 mg/ml	50 µg/ml	50 µg/ml	50 µg/ml	1 mg/ml	NT	NT
Flebogamma 10% DIF	Spain	100 mg/ml	10 mg/ml	100 µg/ml	50 µg/ml	100 µg/ml	167 µg/ml	10 mg/ml	100 mg/ml
Flebogamma 5% DIF	Czech Republic	50 mg/ml	10 mg/ml	1 mg/ml	1 mg/ml	100 µg/ml	NT	NT	NT
Flebogamma 5% DIF	Germany	100 µg/ml	10 mg/ml	1 mg/ml	1 mg/ml	50 µg/ml	NT	NT	NT

			
Reche PA et al Frontiers in Immunology https://doi.org/10.3389/fimmu.2020.586984	Potential Cross-Reactive Immunity to SARS-CoV-2 From Common Human Pathogens and Vaccines.	Ricerca dell' identità fra peptidi di SARS-CoV-2 e altri 25 patogeni umani o antigeni vaccinali, per prédire cross-reattività : l'unico caso si avrebbe per i vaccini contro difterite-tetano-pertosse.	The recently emerged SARS-CoV-2 causing the ongoing COVID-19 pandemic is particularly virulent in the elderly while children are largely spared. Here, we explored the potential role of cross-reactive immunity acquired from pediatric vaccinations and exposure to common human pathogens in the protection and pathology of COVID-19. To that end, we sought for peptide matches to SARS-CoV-2 (identity >/= 80%, in at least eight residues) in the proteomes of 25 human pathogens and in vaccine antigens, and subsequently predicted their T and B cell reactivity to identify potential cross-reactive epitopes. We found that viruses subject to pediatric vaccinations do not contain cross-reactive epitopes with SARS-CoV-2, precluding that they can provide any general protection against COVID-19. Likewise, common viruses including rhinovirus, respiratory syncytial virus, influenza virus, and several herpesviruses are also poor or null sources of cross-reactive immunity to SARS-CoV-2, discarding that immunological memory against these viruses can have any general protective or pathological role in COVID-19. In contrast, we found combination

			vaccines for treating diphtheria, tetanus, and pertussis infectious diseases (DTP vaccine) to be significant sources of potential cross-reactive immunity to SARS-CoV-2. DTP cross-reactive epitopes with SARS-CoV-2 include numerous CD8 and CD4 T cell epitopes with broad population protection coverage and potentially neutralizing B cell epitopes in SARS-CoV-2 Spike protein. Worldwide, children receive several DTP vaccinations, including three-four doses the first year of life and one at 4-6 years of age. Moreover, a low antigenic Tdap dose is also given at ages 9-14. Thereby, children may well be protected from SARS-CoV-2 through cross-reactive immunity elicited by DTP vaccinations, supporting testing in the general population to prevent COVID-19.
Nissen C et al Scientific Reports https://doi.org/10.1038/s41598-020-76442-2	Long-distance airborne dispersal of SARS-CoV-2 in COVID-19 wards.	Geni di SARS-CoV-2 si trovano a distanza dai pazienti, nei filtri dell'aerazione di una corsia ospedaliera, anche se non si tratterebbe di particelle virali infettanti : il virus si diffonde nell'ambiente anche per via aerea.	Evidence suggests that SARS-CoV-2, as well as other coronaviruses, can be dispersed and potentially transmitted by aerosols directly or via ventilation systems. We therefore investigated ventilation openings in one COVID-19 ward and central ducts that expel indoor air from three COVID-19 wards at Uppsala University Hospital, Sweden, during April and May 2020. Swab samples were taken from individual ceiling ventilation openings and surfaces in central ducts. Samples were subsequently subjected to rRT-PCR targeting the N and E genes of SARS-CoV-2. Central ventilation HEPA filters, located several stories above the wards, were removed and portions analyzed in the same manner. In two subsequent samplings, SARS-CoV-2 N and E genes were detected in seven and four out of 19 room vents, respectively. Central ventilation HEPA exhaust filters from the ward were found positive for both genes in three samples. Corresponding filters from two other, adjacent COVID-19 wards were also found positive. Infective ability of the samples was assessed by inoculation of susceptible cell cultures but could not be determined in these experiments. Detection of SARS-CoV-2 in

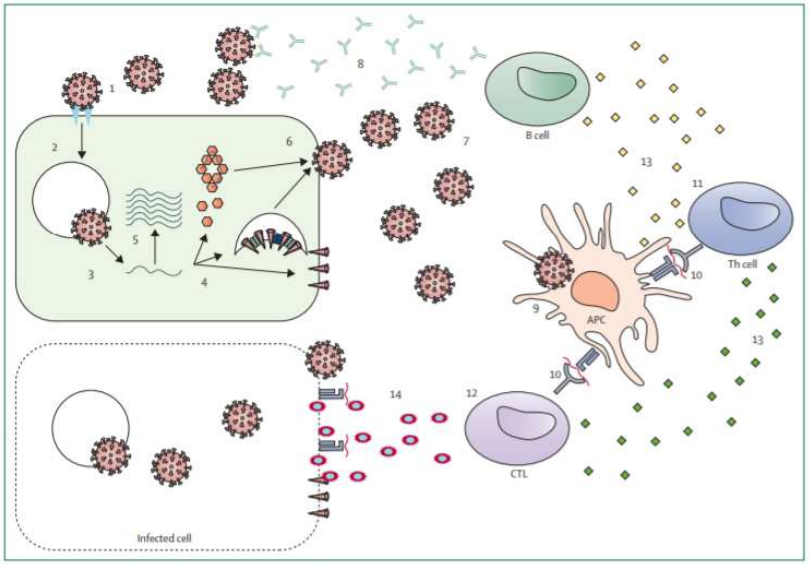
			central ventilation systems, distant from patient areas, indicate that virus can be transported long distances and that droplet transmission alone cannot reasonably explain this, especially considering the relatively low air change rates in these wards. Airborne transmission of SARS-CoV-2 must be taken into consideration for preventive measures.  (**A**) Overview of the 19 investigated COVID-19 ward rooms (ward 1). Dots indicate approximate placing of ceiling vent openings. Red dots indicate openings that where SARS-CoV-2 RNA was detected in at least one of two samplings, blue dots openings negative in both samplings. (**B**) Lateral view of the hospital building. Ward levels: red; COVID-19 outpatient clinic, yellow and blue; COVID-19 wards 1 and 2, with 19 rooms each, purple; eighth floor with central ventilation fans and HEPA filters. Individual ceiling vent openings were investigated on the second-floor ward (yellow) seen in (**A**).
Hunter DJ NEJM https://www.nejm.org/doi/full/10.1056/NEJMp203	Trying to “Protect the NHS” in the United Kingdom	Situazione del servizio sanitario nazionale del Regno Unito (NHS) alla seconda ondata pandemica di COVID-19.	So, as the days shorten, the second wave is breaking on the shores of “the scepter’d isle.” The exhausted NHS workforce is being asked to step up again, and despite government edicts to maintain normal services, much of the NHS may again be repurposed as a Covid service. Large-scale deployment of rapid tests in the hands of local authorities may help the exit from lockdown, but new optimism

2508?query=featured_coronavirus			about vaccines is tempered with realism that a mass rollout will take many months. This is likely to be a winter of discontent. 
Bronte V et al The Journal of Clinical Investigation https://www.jci.org/articles/view/141772/ga	Baricitinib restrains the immune dysregulation in patients with severe COVID-19	Studio osservazionale che confronta 20 pazienti trattati con l'inibitore di JAK1/2 baricitinib e 56 trattati con altri farmaci (mai steroidi) ricoverati per polmonite da SARS-CoV-2. Si evidenzia una riduzione dei livelli di citochine proinfiammatorie (IL-6, IL-1beta, TNF-alfa), una aumentata produzione di anticorpi anti-SARS-CoV-2 e miglioramento clinico.	BACKGROUND. Patients with coronavirus disease 2019 (COVID-19) develop pneumonia generally associated with lymphopenia and a severe inflammatory response due to uncontrolled cytokine release. These mediators are transcriptionally regulated by the JAK/STAT signaling pathways, which can be disabled by small molecules. METHODS. We treated a group of patients (n = 20) with baricitinib according to an off-label use of the drug. The study was designed as an observational, longitudinal trial and approved by the local ethics committee. The patients were treated with 4 mg baricitinib twice daily for 2 days, followed by 4 mg per day for the remaining 7 days. Changes in the immune phenotype and expression of phosphorylated STAT3 (p-STAT3) in blood cells were evaluated and correlated with serum-derived cytokine levels and antibodies against severe acute respiratory syndrome–coronavirus 2 (anti–SARS-CoV-2). In a single treated patient, we also evaluated the alteration of myeloid cell functional activity.

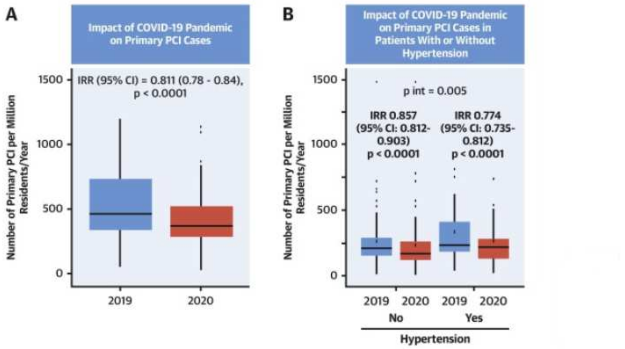
			RESULTS. We provide evidence that patients treated with baricitinib had a marked reduction in serum levels of IL-6, IL-1β, and TNF-α, a rapid recovery of circulating T and B cell frequencies, and increased antibody production against the SARS-CoV-2 spike protein, all of which were clinically associated with a reduction in the need for oxygen therapy and a progressive increase in the P/F (PaO2, oxygen partial pressure/FiO2, fraction of inspired oxygen) ratio. CONCLUSION. These data suggest that baricitinib prevented the progression to a severe, extreme form of the viral disease by modulating the patients' immune landscape and that these changes were associated with a safer, more favorable clinical outcome for patients with COVID-19 pneumonia. 
Callaway E Nature Communications	COVID vaccine excitement builds as Moderna reports third positive result	Commento al comonicato stampa dall'azienda Moderna che ha annunciato che il proprio vaccino a RNA	They say good news comes in threes. For the third time in a week, a coronavirus vaccine developer has reported preliminary results suggesting that its vaccine is highly effective.

https://www.nature.com/articles/d41586-020-03248-7		anti-SARS-CoV-2 mostra un'efficacia del 94%. Ulteriore caratteristica promettente la possibilità di stoccaggio in frigorifero.	Today, biotech company Moderna in Cambridge, Massachusetts, reported that its RNA-based vaccine is more than 94% effective at preventing COVID-19, on the basis of an analysis of 95 cases in its ongoing phase III efficacy trial.
Halstead SB et al The Journal of Infectious Diseases https://academic.oup.com/jid/article/222/12/1946/5891764	COVID-19 Vaccines: Should We Fear ADE?	Gli autori di questo lavoro spiegano perché è improbabile che la vaccinazione contro SARS-CoV-2 scateni una ADE (fenomeno composto da infezione favorita dagli anticorpi diretti contro il patogeno stesso, oppure ipersensibilità da vaccino), come osservato invece per il virus Dengue.	Might COVID-19 vaccines sensitize humans to antibody-dependent enhanced (ADE) breakthrough infections? This is unlikely because coronavirus diseases in humans lack the clinical, epidemiological, biological, or pathological attributes of ADE disease exemplified by dengue viruses (DENV). In contrast to DENV, SARS and MERS CoVs predominantly infect respiratory epithelium, not macrophages. Severe disease centers on older persons with preexisting conditions and not infants or individuals with previous coronavirus infections. Live virus challenge of animals given SARS or MERS vaccines resulted in vaccine hypersensitivity reactions (VAH), similar to those in humans given inactivated measles or respiratory syncytial virus vaccines. Safe and effective COVID-19 vaccines must avoid VAH.
Xuejiao L et al Open Forum Infectious Diseases https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofaa540/5981601	Three-month pulmonary function and radiological outcomes in COVID-19 survivors: a longitudinal patient cohort study	Esiti del follow-up pneumologico e radiologico di 172 persone con storia di polmonite da SARS-CoV-2.	Background : This study aimed to investigate pulmonary function and radiological outcomes in a group of coronavirus disease 2019 (COVID-19) survivors. Methods : 172 COVID-19 survivors in a follow-up clinic in a referral hospital underwent high resolution computed tomography (CT) of the thorax and pulmonary function tests at three month after hospital discharge. Results : The median duration from hospital discharge to radiological and pulmonary function test was 90 (interquartile range=88-95) days. The abnormal pulmonary function was found in 11 (6.40%) patients, and abnormal small airway function (FEF25-75%) in 12 (6.98%). Six (3.49%) patients had obstructive ventilation impairment and six (3.49%) had restrictive ventilatory impairment.

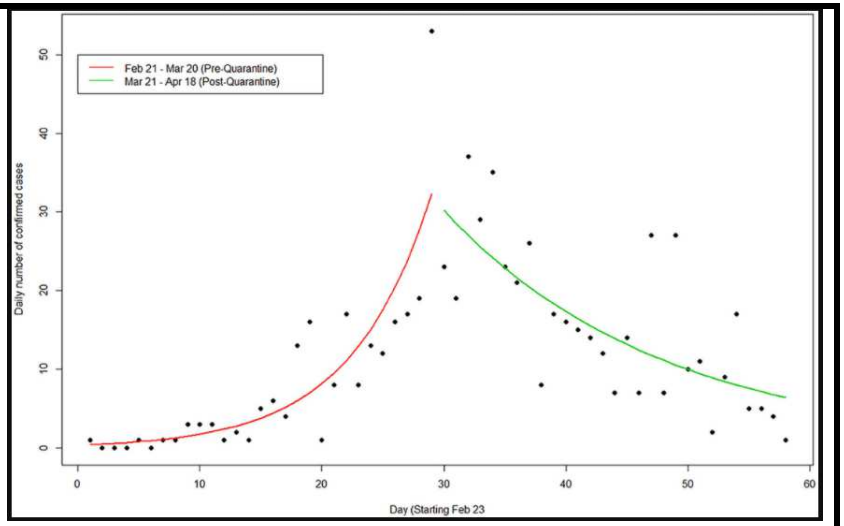
			No significant differences in lung function parameters were observed between the non-severe and severe groups. Of 142 COVID-19 patients performed CT scan, 122 (85.91%) showed residual CT abnormalities and 52 (36.62%) showed chronic and fibrotic changes. The ground-glass opacities absorption in the lungs of severe cases was less satisfactory than that of non-severe patients. The severe paients had higher CT scores than non-severe cases (2.00 versus 0.00, P < 0.001) Conclusion: Of the COVID-19 survivors, 6.40% still present pulmonary function abnormality three month after discharge, which did not vary by disease severity during hospitalization. 85.91% patients had abnormalities on chest CT, with fibrous stripes and ground glass opacity as the most common pattern.
Corominas H et al Clinical Immunology https://www.sciencedirect.com/science/article/pii/S1521661620307919?via%3Dihub	Effectiveness and safety of intravenous tocilizumab to treat COVID-19-associated hyperinflammatory syndrome: Covizumab-6 observational cohort.	Studio osservazionale monocentrico su 104 pazienti ricoverati con infezione da SARS-CoV-2 e trattati co tocilizumab EV, in cui si nota una riduzione di alcuni indici di flogosi nel tempo e una minore mortalità rispetto a quella riportata per questi malati nella stessa regione.	Although the starting event in COVID-19 is a viral infection some patients present with an over-exuberant inflammatory response, leading to acute lung injury (ALI) and adult respiratory distress syndrome (ARDS). Since IL-6 plays a critical role in the inflammatory response, we assessed the efficacy and safety of tocilizumab (TCZ) in this single-centre, observational study in all Covid-19 in-patient with a proven SARS-CoV-2 rapidly progressing infection to prevent ALI and ARDS. 104 patients with COVID-19 treated with TCZ had a lower mortality rate (5·8%) compared with the regional mortality rate (11%), hospitalized patient's mortality (10%), and slightly lower than hospitalized patients treated with our standard of care alone (6%). We found that TCZ rapidly decreased acute phase reactants, ferritin and liver release of proteins. D-Dimer decreased slowly. We did not observe specific safety concerns. Early administration of IL6-R antagonists in COVID-19 patients with impending hyperinflammatory response, may be safe and effective treatment to prevent, ICU admission and further complications.

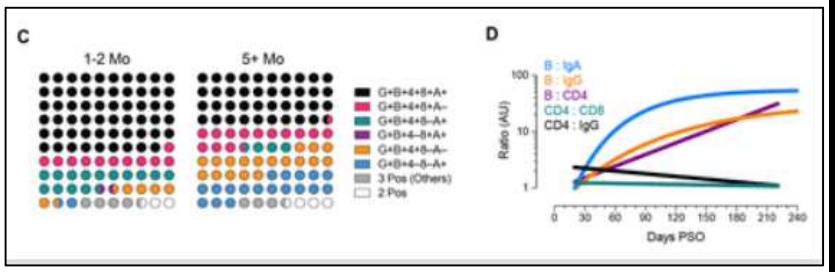
Poland G et al The Lancet https://www.sciencedirect.com/science/article/pii/S0140673620321371	SARS-CoV-2 immunity: review and applications to phase 3 vaccine candidates	Revisione delle conoscenze sulla risposta immunitaria contro SARS-CoV-2 e disamina delle caratteristiche dei principali vaccini attualmente in studio.	Understanding immune responses to severe acute respiratory syndrome coronavirus 2 is crucial to understanding disease pathogenesis and the usefulness of bridge therapies, such as hyperimmune globulin and convalescent human plasma, and to developing vaccines, antivirals, and monoclonal antibodies. A mere 11 months ago, the canvas we call COVID-19 was blank. Scientists around the world have worked collaboratively to fill in this blank canvas. In this Review, we discuss what is currently known about human humoral and cellular immune responses to severe acute respiratory syndrome coronavirus 2 and relate this knowledge to the COVID-19 vaccines currently in phase 3 clinical trials.  ***Figure 2:*** **SARS-CoV-2 infection and the development of immunity** The illustration depicts the major steps in the viral lifecycle and in the development of immune responses. (1) Attachment of the SARS-CoV-2 virion to the cell surface via interactions with the ACE2 cellular receptor. (2) Entry into the cell. Viral proteins can be recognised by pattern recognition receptors (eg, TLR3, TLR4, and TLR7), leading to the release of danger-associated molecular patterns, the inflammatory response, and the activation of innate anti-viral pathways. (3) Membrane fusion and release of RNA into the cell. (4) RNA translation to produce viral proteins. (5) RNA genome is copied and attached to the nucleocapsid protein. (6) Assembly of daughter SARS-CoV-2 virions. (7) Recognition of the spike glycoprotein and nucleocapsid protein (structural proteins) by the B-cell receptor. (8) B cell produces spike glycoprotein-binding antibodies and neutralising antibodies targeting the RBD region of the spike glycoprotein. (9) Viral uptake by APCs. (10) Presentation of antigens, including epitopes from structural and non-structural proteins, to T cells. (11) Activation of Th cells. (12) Activation of CTLs. (13) Th cells produce cytokines (mainly IFNγ, IL-2, and TNFα). (14) CTL recognition and killing of infected cells. ACE2=angiotensin-converting enzyme 2. APC=antigen-presenting cell. CTL=cytotoxic T lymphocyte. RBD=receptor-binding domain. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. Th=T-helper. TLR=toll-like receptor. TNF=tumour necrosis factor.

De Luca G et al Journal of the American College of Cardiology https://www.sciencedirect.com/science/article/abs/pii/S0735109720372399?via%3Dihub	Impact of COVID-19 Pandemic on Mechanical Reperfusion for Patients With STEMI	Ancora un lavoro sui « danni collaterali » da COVID-19 : sulla base dei dati di un ampio registro europeo di procedure di cardiologia interventistica su pazienti con STEMI, si nota una riduzione del numero di interventi e un aumento del tempo « door-to-balloon » (dall'ingresso in ospedale all'inizio della procedura) fra marzo-aprile 2019 e lo stesso periodo nel 2020.	Background : The fear of contagion during the coronavirus disease-2019 (COVID-19) pandemic may have potentially refrained patients with ST-segment elevation myocardial infarction (STEMI) from accessing the emergency system, with subsequent impact on mortality. Objectives : The ISACS-STEMI COVID-19 registry aims to estimate the true impact of the COVID-19 pandemic on the treatment and outcome of patients with STEMI treated by primary percutaneous coronary intervention (PPCI), with identification of "at-risk" patient cohorts for failure to present or delays to treatment. Methods : This retrospective registry was performed in European high-volume PPCI centers and assessed patients with STEMI treated with PPPCI in March/April 2019 and 2020. Main outcomes are the incidences of PPCI, delayed treatment, and in-hospital mortality. Results : A total of 6,609 patients underwent PPCI in 77 centers, located in 18 countries. In 2020, during the pandemic, there was a significant reduction in PPCI as compared with 2019 (incidence rate ratio: 0.811; 95% confidence interval: 0.78 to 0.84; $p < 0.0001$). The heterogeneity among centers was not related to the incidence of death due to COVID-19. A significant interaction was observed for patients with arterial hypertension, who were less frequently admitted in 2020 than in 2019. Furthermore, the pandemic was associated with a significant increase in door-to-balloon and total ischemia times, which may have contributed to the higher mortality during the pandemic. Conclusions : The COVID-19 pandemic had significant impact on the treatment of patients with STEMI, with a 19% reduction in PPCI procedures, especially among patients suffering from hypertension, and a longer delay to treatment, which may have contributed to the increased mortality during the pandemic.

			CENTRAL ILLUSTRATION: Impact of Coronavirus Disease-2019 Pandemic Primary Percutaneous Coronary Intervention Cases, on Time Delays and Mortality 
Biasucci G et al Frontiers in Pediatrics https://doi.org/10.3389/fped.2020.565522	Safe Perinatal Management of Neonates Born to SARS-CoV-2 Positive Mothers at the Epicenter of the Italian Epidemic.	Eperienza dell'Ospedale di Piacenza nella gestione di 15 nascite da madre con infezione da SARS-CoV-2 : protocolli di test, gestione del neonato e outcome.	Introduction: 2019-novel Coronavirus Disease (COVID-19) pandemic has recently struck Northern Italy. Limited data are available about COVID-19 during pregnancy and infancy, mostly from China. Herein, our experience on a safe perinatal management of neonates born to COVID-19 mothers is reported. Method: Since late February through May 15, 2020, 375 pregnant women delivered at our City Hospital in Piacenza, at the epicenter of the Italian epidemic. Of these, 144 were tested via a SARS-CoV-2 quantitative rRT-PCR nasopharyngeal swab prior to delivery, firstly on the basis of epidemiological and clinical criteria, then adopting a universal screening approach. All newborns from SARS-CoV-2 positive mothers were tested via nasopharyngeal swab at birth, on day 3 and/or day 7. In case of positive result, they were re-tested on day 14. Results: Fifteen women tested positive for SARS-CoV-2 infection. All newborns except one were born at term. All of them were non-infected at birth, irrespective of mode of delivery; 13 out 15 remained negative; the two positive neonates became negative by

			day 14 of life. All of them have always remained asymptomatic. All newborns except two were allowed to have immediate bonding, permanent rooming-in, and direct breastfeeding. Conclusions: Our study supports the claim that COVID-19 in pregnancy is not associated with worse clinical outcomes compared to non-COVID-19 pregnant women and/or with higher rates of preterm birth and intrauterine growth restriction. Intrauterine vertical transmission of SARS-CoV-2 seems to be unlikely. Breastfeeding appears to be safe and protective for the neonate, once appropriate preventive measures are adopted.
Kkharroubi S et al Frontiers in Public Health https://doi.org/10.3389/fpubh.2020.549692	Are Lockdown Measures Effective Against COVID-19?	Studio degli effetti del lockdown in Libano.	As the Coronavirus Disease 2019 (COVID-19) pandemic progresses, countries around the world are increasingly implementing a range of responses that are intended to help prevent the transmission of this disease. In the absence of a COVID-19 vaccine, we assess the potential role of containment measures to suppress the virus transmission, thereby slowing down the growth rate of cases and rapidly reducing case incidence. The aim of this study is to show that country lockdown has a critical and significant impact on the pandemic. This is explored using real time incidence data in Lebanon. We analyze COVID-19 cases in Lebanon before and after lockdown measures have been implemented. The findings show that the nationwide lockdown was effective in reducing cases and has been successful in, so far, containing the virus. This study could be an evidence-based call to continue with the lockdown measures, based on real time incidence data. Further research is encouraged.

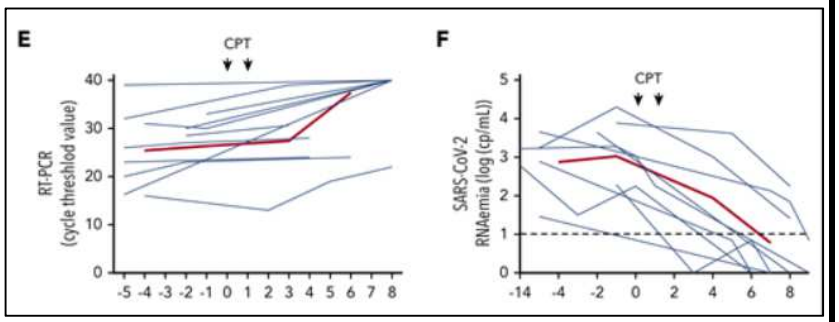
			
Ntoumi F et al Nature https://www.nature.com/articles/d41586-020-03220-5	What if tropical diseases had as much attention as COVID?	Lo sforzo che il mondo ha dedicato alla lotta contro SARS-CoV-2 potrebbe essere messo a frutto, una volta terminata l'emergenza, per contrastare le malattie tropicali neglette, che frattanto non sono scomparse.	All year, COVID-19 has commandeered the world's attention. It is as if no other disease has ever been more important, more contagious or more deadly.
Dan JM et al bioRXiv https://www.biorxiv.org/content/10.1101/2020.11.15.383323v1	Immunological memory to SARS-CoV-2 assessed for greater than six months after infection	Analisi della risposta immunitaria in 185 pazienti con COVID-19, di cui 41 studiati a più di 6 mesi dall'infezione.	Understanding immune memory to SARS-CoV-2 is critical for improving diagnostics and vaccines, and for assessing the likely future course of the pandemic. We analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 185 COVID-19 cases, including 41 cases at ≥6 months post-infection. Spike IgG was relatively stable over 6+ months. Spike-specific memory B cells were more abundant at 6 months than at 1 month. SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a

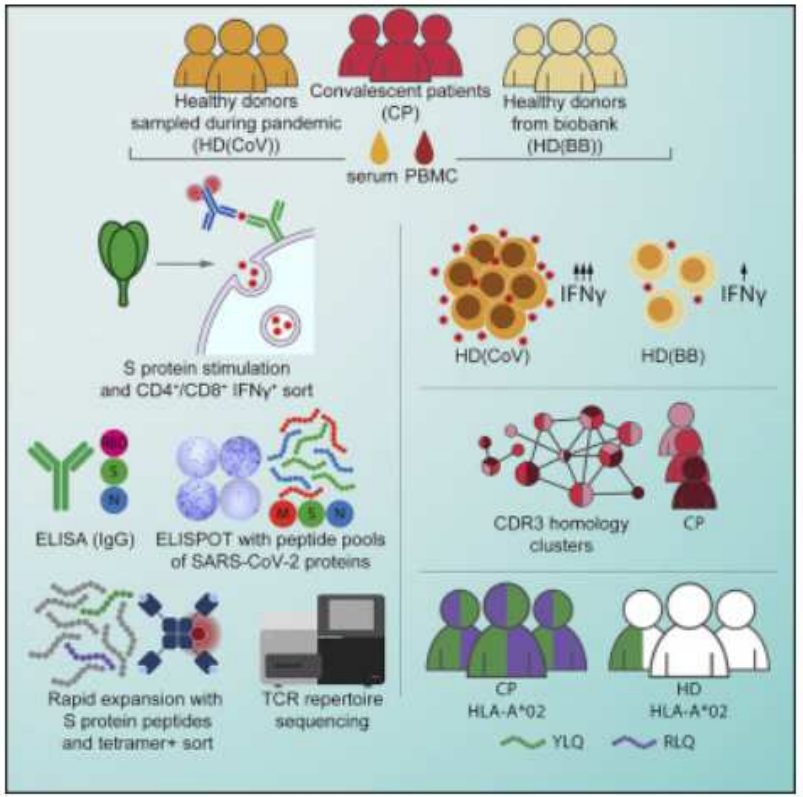
			half-life of 3-5 months. By studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory to SARS-CoV-2 in an integrated manner, we observed that each component of SARS-CoV-2 immune memory exhibited distinct kinetics. 
Cassone A et al Future Microbiology https://www.futuremedicine.com/doi/10.2217/fmb-2020-0247	Chloroquine/hydroxycloroquine and COVID-19: need to know more about	Il ruolo dell'idrossiclorochina contro SARS-CoV-2 merita, secondo gli Autori di questo studio, di essere ancora considerato in studi ben disegnati che pongano l'attenzione su dose e durata della terapia.	Chloroquine and its more soluble hydroxylated derivative (CQ/HCQ), are members of the quinoline class of compounds which have long been used in the treatment of malaria and inflammatory disorders such as rheumatoid arthritis and lupus erythematosus (recently reviewed). They are generally safe, easy to administer and cheap compounds. Since an initial report from Gao et al., these two old drugs have also become the subject of an intense research activity and clinical use for their presumed prophylactic and/or therapeutic efficacy in patients with COVID-19, the pandemic disease caused by the newly emerged coronavirus SARS-CoV-2 (www.who.org). The basic rationale for repurposing CQ/HCQ for COVID-19 treatment stems from an initial hypothesis, raised by some of us and derived from studies on anti-HIV therapy, that CQ could inhibit SARS-CoV-2, that was later verified and has now been confirmed with the new coronavirus. For this and the lack of specific anti-COVID-19 therapies and vaccines, CQ/HCQ were soon proposed and included in Chinese guidelines for COVID-19 treatment, though HCQ is no longer included.

Zhonghua S et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2773060	Diaphragm Pathology in Critically Ill Patients With COVID-19 and Postmortem Findings From 3 Medical Centers	Studio delle biopsie diaframmatiche di 26 pazienti deceduti per COVID-19 e precedentemente sottoposti a ventilazione meccanica, a confronto con 8 pazienti ventilati deceduti per altre cause (3 polmoniti virali). Si dimostra la presenza del recettore ACE2 nel diaframma e la tendenza alla fibrosi nei pazienti COVID-19.	Extrapulmonary manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are now widely recognized and have important clinical implications.To our knowledge, the association of SARS-CoV-2 with the respiratory muscles has not been studied. This is surprising, as the respiratory muscles drive alveolar ventilation and their weakness results in acute respiratory failure. In critically ill patients undergoing ventilation, respiratory muscle weakness prolongs mechanical ventilation and increases mortality. The aim of this study was to investigate the association of severe coronavirus disease 2019 (COVID-19) with the respiratory muscles in critically ill patients and compare the findings with those obtained from non-COVID-19 critically ill patients.
Chan PS et al JAMA https://jamanetwork.com/journals/jamacardiology/fullarticle/2773109	Outcomes for Out-of-Hospital Cardiac Arrest in the United States During the Coronavirus Disease 2019 Pandemic	Confronto degli outcome dell'arresto cardiocircolatorio fuori dall'ospedale fra il periodo pandemico (marzo-aprile 2020) e l'anno precedente in un ampio registro statunitense : minore ripristino del circolo spontaneo e minore sopravvivenza durante la pandemia da COVID-19.	Importance Recent reports from communities severely affected by the coronavirus disease 2019 (COVID-19) pandemic found lower rates of sustained return of spontaneous circulation (ROSC) for out-of-hospital cardiac arrest (OHCA). Whether the pandemic has affected OHCA outcomes more broadly is unknown. Objective To assess the association between the COVID-19 pandemic and OHCA outcomes, including in areas with low and moderate COVID-19 disease burden. Design, Setting, and Participants This study used a large US registry of OHCAs to compare outcomes during the pandemic period of March 16 through April 30, 2020, with those from March 16 through April 30, 2019. Cases were geocoded to US counties, and the COVID-19 mortality rate in each county was categorized as very low (0-25 per million residents), low (26-100 per million residents), moderate (101-250 per million residents), high (251-500 per million residents), or very high (>500 per million residents). As additional

			controls, the study compared OHCA outcomes during the prepandemic period (January through February) and peripandemic period (March 1 through 15). Exposure The COVID-19 pandemic. Main Outcomes and Measures Sustained ROSC (≥20 minutes), survival to discharge, and OHCA incidence. Results A total of 19 303 OHCAs occurred from March 16 through April 30 in both years, with 9863 cases in 2020 (mean [SD] age, 62.6 [19.3] years; 6040 men [61.3%]) and 9440 in 2019 (mean [SD] age, 62.2 [19.2] years; 5922 men [62.7%]). During the pandemic, rates of sustained ROSC were lower than in 2019 (23.0% vs 29.8%; adjusted rate ratio, 0.82 [95% CI, 0.78-0.87]; P < .001). Sustained ROSC rates were lower by between 21% (286 of 1429 [20.0%] in 2020 vs 305 of 1130 [27.0%] in 2019; adjusted RR, 0.79 [95% CI, 0.65-0.97]) and 33% (149 of 863 [17.3%] in 2020 vs 192 of 667 [28.8%] in 2019; adjusted RR, 0.67 [95% CI, 0.56-0.80]) in communities with high or very high COVID-19 mortality, respectively; however, rates of sustained ROSC were also lower by 11% (583 of 2317 [25.2%] in 2020 vs 740 of 2549 [29.0%] in 2019; adjusted RR, 0.89 [95% CI, 0.81-0.98]) to 15% (889 of 3495 [25.4%] in 2020 vs 1109 of 3532 [31.4%] in 2019; adjusted RR, 0.85 [95% CI, 0.78-0.93]) in communities with very low and low COVID-19 mortality. Among emergency medical services agencies with complete data on hospital survival (7085 total patients), survival to discharge was lower during the pandemic compared with 2019 (6.6% vs 9.8%; adjusted RR, 0.83 [95% CI, 0.69-1.00]; P = .048), primarily in communities with moderate to very high COVID-19 mortality (interaction P = .049). Incidence of OHCA was higher than in 2019, but the increase was largely observed in communities with high COVID-19 mortality (adjusted mean difference, 38.6 [95% CI, 37.1-

			40.1] per million residents) and very high COVID-19 mortality (adjusted mean difference, 28.7 [95% CI, 26.7-30.6] per million residents). In contrast, there was no difference in rates of sustained ROSC or survival to discharge during the prepandemic and peripandemic periods in 2020 vs 2019. Conclusions and Relevance Early during the pandemic, rates of sustained ROSC for OHCA were lower throughout the US, even in communities with low COVID-19 mortality rates. Overall survival was lower, primarily in communities with moderate or high COVID-19 mortality.
Hueso T et al Blood https://ashpublications.org/blood/article/136/20/2290/463806/Convalescent-plasma-therapy-for-B-cell-depleted	Convalescent plasma therapy for B-cell–depleted patients with protracted COVID-19	Trattamento di 17 pazienti con grave linfopenia B e persistenza di sintomi da COVID-19 con infusione di plasma prelevato a soggetti guariti.	Anti-CD20 monoclonal antibodies are widely used for the treatment of hematological malignancies or autoimmune disease but may be responsible for a secondary humoral deficiency. In the context of COVID-19 infection, this may prevent the elicitation of a specific SARS-CoV-2 antibody response. We report a series of 17 consecutive patients with profound B-cell lymphopenia and prolonged COVID-19 symptoms, negative immunoglobulin G (IgG)-IgM SARS-CoV-2 serology, and positive RNAemia measured by digital polymerase chain reaction who were treated with 4 units of COVID-19 convalescent plasma. Within 48 hours of transfusion, all but 1 patient experienced an improvement of clinical symptoms. The inflammatory syndrome abated within a week. Only 1 patient who needed mechanical ventilation for severe COVID-19 disease died of bacterial pneumonia. SARS-CoV-2 RNAemia decreased to below the sensitivity threshold in all 9 evaluated patients. In 3 patients, virus-specific T-cell responses were analyzed using T-cell enzyme-linked immunospot assay before convalescent plasma transfusion. All showed a maintained SARS-CoV-2 T-cell response and poor cross-response to other coronaviruses. No adverse event was reported. Convalescent plasma with anti–SARS-CoV-2

			antibodies appears to be a very promising approach in the context of protracted COVID-19 symptoms in patients unable to mount a specific humoral response to SARS-CoV-2.
Shomuradova AS et al Immunity https://www.cell.com/immunity/fulltext/S1074-7613(20)30469-6	SARS-CoV-2 epitopes are recognized by a public and diverse repertoire of human T cell receptors	Dimostrazione delle caratteristiche della risposta T-mediata nei pazienti guariti da infezione da SARS-CoV-2.	Understanding the hallmarks of the immune response to SARS-CoV-2 is critical for fighting the COVID-19 pandemic. We assessed antibody and T cell reactivity in convalescent COVID-19 patients and healthy donors sampled both prior to and during the pandemic. Healthy donors examined during the pandemic exhibited increased numbers of SARS-CoV-2-specific T cells, but no humoral response. Their probable exposure to the virus resulted in either asymptomatic infection without antibody secretion, or activation of pre-existing immunity. In convalescent patients, we observed a public and diverse T cell response to SARS-CoV-2 epitopes, revealing T cell receptor (TCR) motifs with germline-encoded features. Bulk CD4+ and CD8+ T cell responses to the spike glycoprotein were mediated by groups of homologous TCRs, some of them shared across multiple donors. Overall, our results demonstrate that the T cell response to SARS-CoV-2, including the identified set of TCRs, can serve as a useful biomarker for surveying antiviral immunity. 

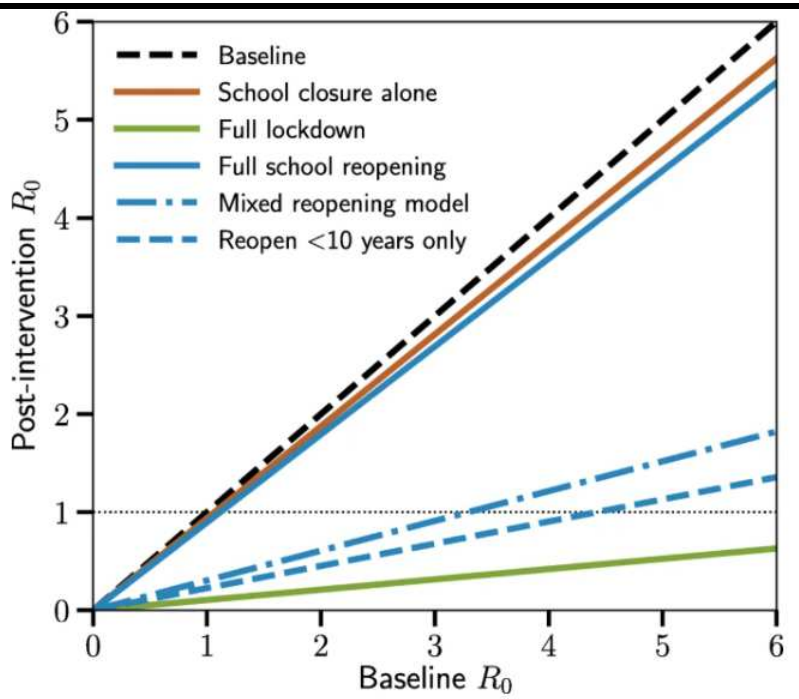
			
Rochwerg B et al BMJ https://www.bmj.com/content/370/bmj.m3379	A living WHO guideline on drugs for covid-19	Linea guida del WHO sull'utilizzo della terapia per COVID-19 : relativamente sconsigliato l'uso di remdesivir nei pazienti ospedalizzati (forse tenendo conto di una carenza a livello internazionale), appoggiati invece gli steroidi per i pazienti gravi.	Clinical question : What is the role of drug interventions in the treatment of patients with covid-19? New recommendation : The latest version of this WHO living guidance focuses on remdesivir, following the 15 October 2020 preprint publication of results from the WHO SOLIDARITY trial. It contains a weak or conditional recommendation against the use of remdesivir in hospitalised patients with covid-19 Recommendations : The first version on this living guidance focused on corticosteroids. The strong recommendation for systemic corticosteroids in patients with severe and critical covid-19, and a

			weak or conditional recommendation against systemic corticosteroids in patients with non-severe covid-19 are unchanged. How this guideline was created WHO has partnered with the non-profit Magic Evidence Ecosystem Foundation (MAGIC) for methodologic support, to develop and disseminate living guidance for covid-19 drug treatments, based on a living systematic review and network analysis. An international standing Guideline Development Group (GDG) of content experts, clinicians, patients, and methodologists produced recommendations following standards for trustworthy guideline development using the GRADE approach. No competing interests were identified for any panel member. Understanding the new recommendation : When moving from evidence to the conditional recommendation against the use of remdesivir in patients with covid-19, the panel emphasised the evidence suggesting no important effect on mortality, need for mechanical ventilation, time to clinical improvement, and other patient-important outcomes. Considering the low or very low certainty evidence for all outcomes, the panel interpreted the evidence as not proving that remdesivir is ineffective; rather, there is no evidence based on currently available data that it does improve patient-important outcomes. The panel placed low value on small and uncertain benefits in the presence of the remaining possibility of important harms. In addition, the panel considered contextual factors such as resources, feasibility, acceptability, and equity for countries and health care systems. Updates This is a living guideline. It replaces an earlier version published on 4 September 2020 and the BMJ Rapid Recommendations on remdesivir published on 2 July 2020, and the previous version can be found as a data supplement. Future updates

			are planned to cover hydroxychloroquine and lopinavir-rotinavir. New recommendations will be published as updates to this guideline.
Cevik M et al The Lancet https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30172-5/fulltext	SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis	Revisione delle conoscenze sullo shedding virale nelle principali malattie da Coronavirus conosciute : sulla base di 79 studi su SARS-CoV-2, durata media dell'eliminazione del virus dalle alte vie aeree 17 giorni, massima 83 giorni.	Background : Viral load kinetics and duration of viral shedding are important determinants for disease transmission. We aimed to characterise viral load dynamics, duration of viral RNA shedding, and viable virus shedding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in various body fluids, and to compare SARS-CoV-2, SARS-CoV, and Middle East respiratory syndrome coronavirus (MERS-CoV) viral dynamics. Methods : In this systematic review and meta-analysis, we searched databases, including MEDLINE, Embase, Europe PubMed Central, medRxiv, and bioRxiv, and the grey literature, for research articles published between Jan 1, 2003, and June 6, 2020. We included case series (with five or more participants), cohort studies, and randomised controlled trials that reported SARS-CoV-2, SARS-CoV, or MERS-CoV infection, and reported viral load kinetics, duration of viral shedding, or viable virus. Two authors independently extracted data from published studies, or contacted authors to request data, and assessed study quality and risk of bias using the Joanna Briggs Institute Critical Appraisal Checklist tools. We calculated the mean duration of viral shedding and 95% CIs for every study included and applied the random-effects model to estimate a pooled effect size. We used a weighted meta-regression with an unrestricted maximum likelihood model to assess the effect of potential moderators on the pooled effect size. This study is registered with PROSPERO, CRD42020181914. Findings : 79 studies (5340 individuals) on SARS-CoV-2, eight studies (1858 individuals) on SARS-CoV, and 11 studies (799 individuals) on

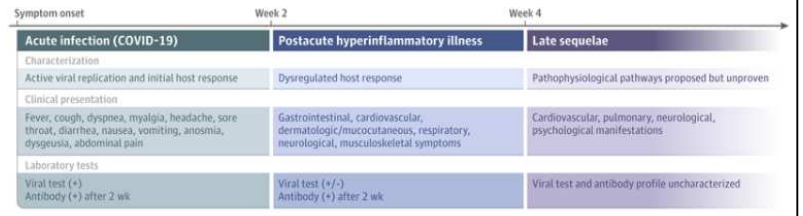
			MERS-CoV were included. Mean duration of SARS-CoV-2 RNA shedding was 17·0 days (95% CI 15·5–18·6; 43 studies, 3229 individuals) in upper respiratory tract, 14·6 days (9·3–20·0; seven studies, 260 individuals) in lower respiratory tract, 17·2 days (14·4–20·1; 13 studies, 586 individuals) in stool, and 16·6 days (3·6–29·7; two studies, 108 individuals) in serum samples. Maximum shedding duration was 83 days in the upper respiratory tract, 59 days in the lower respiratory tract, 126 days in stools, and 60 days in serum. Pooled mean SARS-CoV-2 shedding duration was positively associated with age (slope 0·304 [95% CI 0·115–0·493]; p=0·0016). No study detected live virus beyond day 9 of illness, despite persistently high viral loads, which were inferred from cycle threshold values. SARS-CoV-2 viral load in the upper respiratory tract appeared to peak in the first week of illness, whereas that of SARS-CoV peaked at days 10–14 and that of MERS-CoV peaked at days 7–10. Interpretation : Although SARS-CoV-2 RNA shedding in respiratory and stool samples can be prolonged, duration of viable virus is relatively short-lived. SARS-CoV-2 titres in the upper respiratory tract peak in the first week of illness. Early case finding and isolation, and public education on the spectrum of illness and period of infectiousness are key to the effective containment of SARS-CoV-2.
Lee B et al BMC Public Health https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-020-09799-8	Modeling the impact of school reopening on SARS-CoV-2 transmission using contact structure data from Shanghai.	Modello matematico basato su dati di contact tracing eseguito a Shanghai, utilizzato per prédire l'impatto dell'apertura delle scuole sulla diffusione di SARS-CoV-2 : rilevante impatto della presenza di	BACKGROUND: Mathematical modeling studies have suggested that pre-emptive school closures alone have little overall impact on SARS-CoV-2 transmission, but reopening schools in the background of community contact reduction presents a unique scenario that has not been fully assessed. METHODS: We adapted a previously published model using contact information from Shanghai to model school reopening under various conditions. We investigated different strategies by combining the contact patterns observed

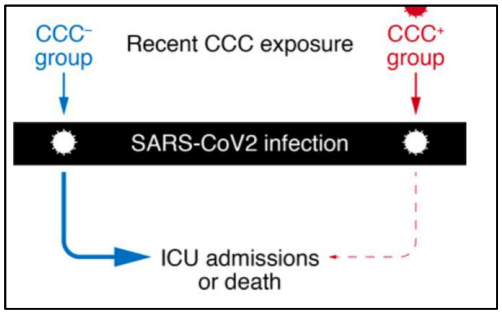
		misure di isolamento fra alunni e persone adulte.	between different age groups during both baseline and "lockdown" periods. We also tested the robustness of our strategy to the assumption of lower susceptibility to infection in children under age 15 years. RESULTS: We find that reopening schools for all children would maintain a post-intervention R0 < 1 up to a baseline R0 of approximately 3.3 provided that daily contacts among children 10-19 years are reduced to 33% of baseline. This finding was robust to various estimates of susceptibility to infection in children relative to adults (up to 50%) and to estimates of various levels of concomitant reopening in the rest of the community (up to 40%). However, full school reopening without any degree of contact reduction in the school setting returned R0 virtually back to baseline, highlighting the importance of mitigation measures. CONCLUSIONS: These results, based on contact structure data from Shanghai, suggest that schools can reopen with proper precautions during conditions of extreme contact reduction and during conditions of reasonable levels of reopening in the rest of the community.

			 Effects of school reopening during community "lockdown." Post-intervention R_0 as a function of baseline R_0 under various conditions are shown. Dashed black line: Baseline, represents all contact patterns pre-pandemic. Solid orange line: School closure alone, represents community pre-pandemic contact patterns but with contacts among children 0–19 years removed to simulate full school closure. Solid green line: Full "lockdown," represents full contact suppression during pandemic conditions. Solid blue line: Full school reopening, represents full "lockdown" conditions but with re-incorporation of all contacts among children 0–19 years according to baseline contact patterns to simulate return to full school attendance. Interrupted blue line: Mixed reopening model, simulates the effect of re-incorporating full contact patterns for children 0–9 years with reduction in contacts in children 10–19 years to 33% of baseline. Dashed blue line: Reopen < 10 years only, simulates the effect of re-incorporating baseline contact patterns for children 0–9 years only
Wang Y et al Experimental and Therapeutic Medicine	Lactoferrin for the treatment of COVID-19 (Review).	La lattoferrina, che ha acquisito popolarità tra le persone comuni per la prevenzione e cura di COVID-19, è una glicoproteina legante il ferro	The coronavirus disease 2019 (COVID-19) outbreak was caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The clinical outcomes of elderly individuals and those with underlying diseases affected by COVID-19 are serious, and may result in acute respiratory distress syndrome (ARDS) and even

https://doi.org/10.3892/etm.2020.9402		con prorpietà antinfiammatorie la cui attività contro SARS-CoV-2 non è tuttavia supportata da studi rigorosi.	mortality. Currently, the clinical treatments for COVID-19 mostly involve symptom alleviation measures and non-specific broad spectrum antiviral drugs, as highly effective antiviral drugs and vaccines are not yet available. Lactoferrin (LF) is a safe iron-binding glycoprotein that is present in the milk of the majority of mammals and exhibits broad-spectrum antiviral activity, including against coronaviruses. In addition, LF also exhibits anti-inflammatory, anti-infective and immune-regulating properties, which are in line with the treatment requirements for SARS-CoV-2 infection. Therefore, the use of LF may be of value in the prevention and/or management of COVID-19. The aim of the present review was to summarize the previous reports on the antiviral properties of LF and compare these with the characteristics of SARS-CoV-2 infection, in order to determine whether LF could be used to assist in the prevention of COVID-19 and to investigate the possible underlying mechanisms governing its mode of action.
De Morais HA et al Frontiers in Veterinary Science https://doi.org/10.3389/fvets.2020.591216	Natural Infection by SARS-CoV-2 in Companion Animals: A Review of Case Reports and Current Evidence of Their Role in the Epidemiology of COVID-19.	Revisione dei casi di infezione da SARS-CoV-2 negli animali da compagnia : nessuna infezione descritta da animale a uomo, incerto significato della diffusione del virus fra gli animali.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for the coronavirus disease 2019 (COVID-19), is the causative infectious agent of the current pandemic. As researchers and health professionals are still learning the capabilities of this virus, public health concerns arise regarding the zoonotic potential of SARS-CoV-2. With millions of people detected with SARS-CoV-2 worldwide, reports of companion animals possibly infected with the virus started to emerge. Therefore, our aim is to review reported cases of animals naturally infected with SARS-CoV-2, particularly companion pets, shedding light on the role of these animals in the epidemiology of COVID-19.

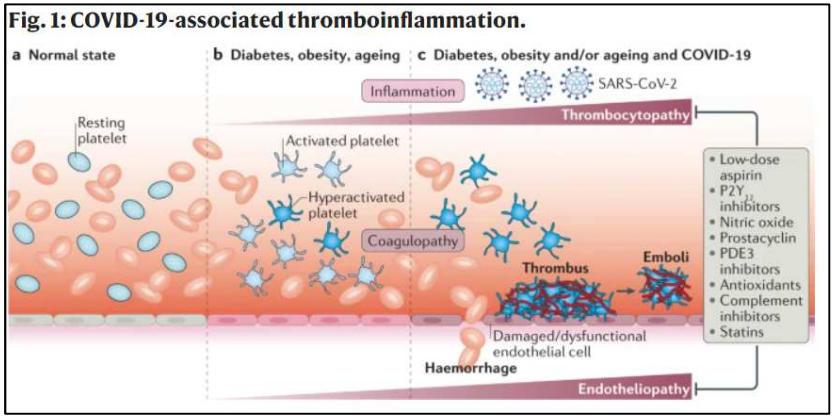
Rochford- Brennan H et al HRB Open Research https://doi.org/10.12688/hrbopenres.13063.2	Giving voice to those directly affected by the COVID-19 pandemic - the experience and reflections of a person with dementia.	Cosa significa l'isolamento nel corso della pandemia da COVID-19 per una persona affetta da demenza ?	The coronavirus disease 2019 (COVID-19) pandemic presents unprecedented challenges to society. Behind the daily tally of deaths and cases of infection are individuals and families who are experiencing the ultimate consequence of this disease. Every aspect of our lives has been affected and these affects are amplified for those who have to cocoon and have conditions such as dementia. There is little opportunity to directly hear the experience of those 'vulnerable adults' who have been self-isolating for many weeks now. This letter takes the form of a reflective conversation with a person living with dementia. Honouring the principles of public and patient involvement (PPI), it is an attempt to give voice to the experience of one of the many thousands of vulnerable people during the COVID-19 pandemic. As well as describing the effect on her daily life, Helen describes what supports would help at this time. While the focus of attention at the moment is rightly on dealing with the effects of the virus in nursing homes, the many thousands of people living with dementia in the community should not be forgotten.
Datta SD et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2773338	A Proposed Framework and Timeline of the Spectrum of Disease Due to SARS-CoV-2 Infection Illness Beyond Acute Infection and Public Health Implications	Disamina delle fasi dell'infezione da SARS-CoV-2, incluse le sequele post-acuzie (fasi non invariabilmente presenti in ogni individuo).	Although much of the response to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has focused on acute coronavirus disease 2019 (COVID-19) illness, accumulating evidence demonstrates morbidity beyond acute SARS-CoV-2 infection.At least 2 other periods of illness appear to be temporally associated with SARS-CoV-2 infection: a rare postacute hyperinflammatory illness and late inflammatory and virological sequelae. These 3 illness periods not only define the temporal course of SARS-CoV-2 infection at the population level but also capture distinct phases of host-viral interaction.

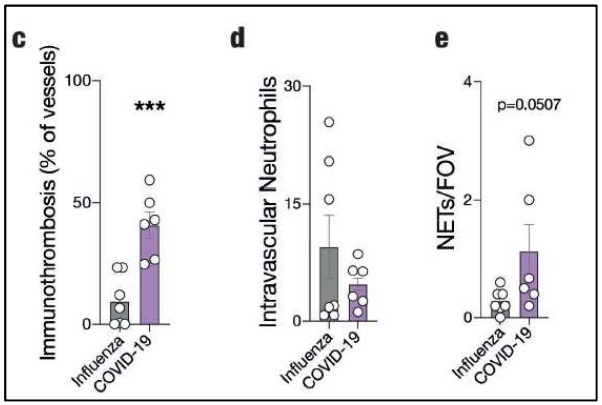
			Figure. Proposed Population-Based Framework for Symptomatic SARS-CoV-2 Infection[a]  COVID-19 indicates coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. [a]The population-based framework refers to the fact that these illnesses are observed at the population level and not necessarily in any given individual.
Al- Salameh A et al International Journal of Obesity https://www.nature.com/articles/s41366-020-00721-1	The association between body mass index class and coronavirus disease 2019 outcomes	Il sovrappeso è associato alla degenza in rianimazione ma non al decesso in questo studio retrospettivo su 433 pazienti ricoverati per COVID-19 in Francia.	Background/Objectives : A growing body of data suggests that obesity influences coronavirus disease 2019 (COVID-19). Our study's primary objective was to assess the association between body mass index (BMI) categories and critical forms of COVID-19. Subjects/Methods : Data on consecutive adult patients hospitalized with laboratory-confirmed COVID-19 at Amiens University Hospital (Amiens, France) were extracted retrospectively. The association between BMI categories and the composite primary endpoint (admission to the intensive care unit or death) was probed in a logistic regression analysis. Results : In total, 433 patients were included, and BMI data were available for 329: 20 were underweight (6.1%), 95 have a normal weight (28.9%), 90 were overweight (27.4%), and 124 were obese (37.7%). The BMI category was associated with the primary endpoint in the fully adjusted model; the odds ratio (OR) [95% confidence interval (CI)] for overweight and obesity were respectively 1.58 [0.77–3.24] and 2.58 [1.28–5.31]. The ORs [95% CI] for ICU admission were similar for overweight (3.16 [1.29–8.06]) and obesity (3.05 [1.25–7.82]) in the fully adjusted model. The unadjusted ORs for death were similar in all BMI categories while obesity only was associated with higher risk after adjustment.

			Conclusions : Our results suggest that overweight (and not only obesity) is associated with ICU admission, but overweight is not associated with death.
Meyerholz D et al Journal of Clinical Investigation https://www.jci.org/articles/view/144807?utm_source=TrendMD&utm_medium=cpc&utm_campaign=J_Clin_Invest_TrendMD_0	Does common cold coronavirus infection protect against severe SARS-CoV2 disease?	Commento ad un articolo (precedentemente presentato nella nostra bibliografia) che riporta migliore decorso clinico nei pazienti con COVID-19 e recente infezione da Coronavirus minori : significato e possibili spiegazioni.	The coronavirus disease 2019 (COVID 19) pandemic continues to cause morbidity and mortality. Since severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was identified as the cause for COVID 19, some have questioned whether exposure to seasonal common cold coronaviruses (CCCs) could provide tangible protection against SARS-CoV-2 infection or disease. In this issue of the JCI, Sager, et al. examined SARS-CoV-2 infections and outcomes from patients previously tested for CCC as part of a comprehensive respiratory panel using PCR and were segregated into negative (CCC–) or positive (CCC+) exposure. No differences were seen between groups in terms of susceptibility to SARS-CoV-2 infection. However, hospitalized patients with a documented history of CCC+ infection had lower rates of ICU admissions and higher rates of survival than hospitalized CCC– patients. While these findings are associative and not causative, they highlight evidence suggesting that previous CCC+ infection may influence the disease course of SARS-CoV-2 infection. 

Capalbo C et al International Journal of Environmental Research https://doi.org/10.3390/ijerph17228461	No Evidence of SARS-CoV-2 Circulation in Rome (Italy) during the Pre-Pandemic Period: Results of a Retrospective Surveillance.	Esaminando retrospettivamente i 166 casi di infezione respiratoria acuta (SARI) di origine non influenzale sottoposti a tampone nasofaringeo in un pronto soccorso di Roma tra novembre 2019 e marzo 2020, in nessun caso la ricerca di SARS-CoV-2 eseguita a posteriori sul tampone ha dato esito positivo : il virus non sembrava circolare prima dei report ufficiali.	In March 2020, the World Health Organization (WHO) declared that the COVID-19 outbreak recorded over the previous months could be characterized as a pandemic. The first known Italian SARS-CoV-2 positive case was reported on 21 February. In some countries, cases of suspected "COVID-19-like pneumonia" had been reported earlier than those officially accepted by health authorities. This has led many investigators to check preserved biological or environmental samples to see whether the virus was detectable on dates prior to those officially stated. With regard to Italy, the results of a microbiological screening in sewage samples collected between the end of February and the beginning of April 2020 from wastewaters in Milan (Northern Italy) and Rome (Central Italy) showed presence of SARS-CoV-2. In the present study, we evaluated, by means of a standardized diagnostic method, the SARS-CoV-2 infection prevalence amongst patients affected by severe acute respiratory syndrome (SARI) in an academic hospital located in Central Italy during the period of 1 November 2019-1 March 2020. Overall, the number of emergency room (ER) visits during the investigated period was 13,843. Of these, 1208 had an influenza-like syndrome, but only 166 matched the definition of SARI as stated in the study protocol. A total of 52 SARI cases were laboratory confirmed as influenza: 26 as a type B virus, 25 as a type A, and 1 as both viruses. Although about 17% of the total sample had laboratory or radiological data compatible with COVID-19, all the nasopharyngeal swabs stored underwent SARS-CoV-2 RT-PCR and tested negative. Based on our result, it is confirmed that the COVID-19 pandemic spread did not start prior to the "official" onset in central Italy. Routine monitoring of SARI causative agents at the local level is critical for reporting epidemiologic and etiologic trends that may differ from one country to another and also among different

			influenza seasons. This has a practical impact on prevention and control strategies.
The Centers for Disease Control and Prevention https://www.cdc.gov/coronavirus/2019-ncov/more/masking-science-sars-cov2.html	Scientific Brief: Community Use of Cloth Masks to Control the Spread of SARS-CoV-2	Il CDC argomenta il supporto all'utilizzo della mascherina multistrato, non valvolata, come forma di protezione dall'infezione da SARS-CoV-2 per tutta la popolazione.	Experimental and epidemiological data support community masking to reduce the spread of SARS-CoV-2. The prevention benefit of masking is derived from the combination of source control and personal protection for the mask wearer. The relationship between source control and personal protection is likely complementary and possibly synergistic14, so that individual benefit increases with increasing community mask use. Further research is needed to expand the evidence base for the protective effect of cloth masks and in particular to identify the combinations of materials that maximize both their blocking and filtering effectiveness, as well as fit, comfort, durability, and consumer appeal. Adopting universal masking policies can help avert future lockdowns, especially if combined with other non-pharmaceutical interventions such as social distancing, hand hygiene, and adequate ventilation.
Gu SX et al Nature Reviews Cardiology https://doi.org/10.1038/s41569-020-00469-1	Thrombocytopathy and endotheliopathy: crucial contributors to COVID-19 thromboinflammation.	Interazione fra disfunzione endoteliale, piastrinopatia e attivazione della cascata coagulativa nella patogenesi del danno da SARS-CoV-2.	The core pathology of coronavirus disease 2019 (COVID-19) is infection of airway cells by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that results in excessive inflammation and respiratory disease, with cytokine storm and acute respiratory distress syndrome implicated in the most severe cases. Thrombotic complications are a major cause of morbidity and mortality in patients with COVID-19. Patients with pre-existing cardiovascular disease and/or traditional cardiovascular risk factors, including obesity, diabetes mellitus, hypertension and advanced age, are at the highest risk of death from COVID-19. In this Review, we summarize new lines of evidence that point to both platelet and

			endothelial dysfunction as essential components of COVID-19 pathology and describe the mechanisms that might account for the contribution of cardiovascular risk factors to the most severe outcomes in COVID-19. We highlight the distinct contributions of coagulopathy, thrombocytopathy and endotheliopathy to the pathogenesis of COVID-19 and discuss potential therapeutic strategies in the management of patients with COVD-19. Harnessing the expertise of the biomedical and clinical communities is imperative to expand the available therapeutics beyond anticoagulants and to target both thrombocytopathy and endotheliopathy. Only with such collaborative efforts can we better prepare for further waves and for future coronavirus-related pandemics. **Fig. 1: COVID-19-associated thromboinflammation.** 
Nicolai L et al Journal of Thrombosis and Haemostasis	Vascular neutrophilic inflammation and immunothrombosis distinguish severe COVID-19 from influenza pneumonia.	L'attivazione intravascolare dei neutrofili, richiamati dai monociti, sarebbe uno dei fattori scatenanti la trombosi nell'infezione grave da SARS-CoV-2,	OBJECTIVE: Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can lead to severe pneumonia, but also thrombotic complications and non-pulmonary organ failure. Recent studies suggest intravascular neutrophil activation and subsequent immune cell triggered immunothrombosis as a central pathomechanism linking the heterogenous clinical picture of

https://doi.org/10.1111/jth.15179		mentre è un fenomeno meno evidente nella polmonite influenzale, come dimostrato dal confronto autoptico fra 7 pazienti con COVID-19 e 6 con influenza.	Coronavirus Disease 2019 (COVID-19). We sought to study whether immunothrombosis is a pathognomonic factor in COVID-19 or a general feature of (viral) pneumonia, as well as to better understand its upstream regulation. APPROACH AND RESULTS: By comparing histopathological specimens of SARS-CoV-2 with influenza affected lungs, we show that vascular neutrophil recruitment, NETosis, and subsequent immunothrombosis are typical features of severe COVID-19, but less prominent in influenza pneumonia. Activated neutrophils were typically found in physical association with monocytes. To explore this further, we combined clinical data of COVID-19 cases with comprehensive immune cell phenotyping and bronchoalveolar lavage fluid scRNA-seq data. We show that a HLADR(low) CD9(low) monocyte population expands in severe COVID-19, which releases neutrophil chemokines in the lung, and might in turn explain neutrophil expansion and pulmonary recruitment in the late stages of severe COVID-19. CONCLUSIONS: In summary, our data underline an innate immune cell axis causing vascular inflammation and immunothrombosis in severe SARS-CoV-2 infection. 

Hopewell PC et al Emerging Infectious Diseases https://doi.org/10.3201/eid2703.203456	Parallels and Mutual Lessons in Tuberculosis and COVID-19 Transmission, Prevention, and Control.	Alcune delle strategie messe in atto per il contenimento dell'infezione da SARS-CoV-2 potrebbero essere applicate alla lotta contro la tubercolosi, malattia che a propria volta ha insegnato molto alla comunità scientifica in termini di misure di isolamento, contact tracing e ruolo degli asintomatici nella diffusione dei patogeni respiratori.	The coronavirus disease (COVID-19) pandemic has had unprecedented negative effects on global health and economies, drawing attention and resources from many other public health services. To minimize negative effects, the parallels, lessons, and resources from existing public health programs need to be identified and used. Often underappreciated synergies relating to COVID-19 are with tuberculosis (TB). COVID-19 and TB share commonalities in transmission and public health response: case finding, contact identification, and evaluation. Data supporting interventions for either disease are, understandably, vastly different, given the diseases' different histories. However, many of the evolving issues affecting these diseases are increasingly similar. As previously done for TB, all aspects of congregate investigations and preventive and therapeutic measures for COVID-19 must be prospectively studied for optimal evidence-based interventions. New attention garnered by the pandemic can ensure that knowledge and investment can benefit both COVID-19 response and traditional public health programs such as TB programs.