



## COVID-19 y la pandemia global causada por un nuevo coronavirus

COVID-19 and the global pandemic caused by a new coronavirus

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### Resumen

**Introducción:** COVID-19 es una enfermedad respiratoria inédita que se reportó inicialmente como una neumonía atípica en diciembre de 2019. SARS-CoV-2, agente etiológico de esta patología, probablemente originado a partir de un virus de murciélago. La inesperada capacidad de transmisión y patogenicidad que adquirió este coronavirus transformó a COVID-19 en una pandemia de sintomatología variada y compleja. **Objetivo:** Analizar aspectos evolutivos, moleculares, biológicos, inmunológicos y epidemiológicos de esta enfermedad. **Materiales y métodos:** Se realizó una revisión narrativa de literatura científica publicada en *Pubmed*, sobre estos aspectos desde enero 2020. **Resultados:** SARS-CoV-2 es un nuevo coronavirus que utiliza su proteína superficial S para infectar células humanas que exhiben el receptor ACE2. Este patógeno se transmite por secreciones respiratorias e induce un incremento nocivo de mediadores químicos proinflamatorios en individuos vulnerables, reacción inmune conocida como tormenta de citoquinas. Esta respuesta hiper-inflamatoria es la causante de las lesiones alveolares que desencadenan la insuficiencia respiratoria observada en casos severos de COVID-19. **Conclusiones:** En individuos susceptibles, SARS-CoV-2 puede desencadenar una disfunción pulmonar que requiere soporte ventilatorio asistido y tratamiento con inmunosupresores. Se están desarrollando nuevas estrategias terapéuticas y de prevención para disminuir los elevados índices de contagio y la mortalidad asociados con COVID-19.

**Palabras clave:** Betacoronavirus; infecciones por coronavirus; glicoproteína de espiga del coronavirus; síndrome respiratorio agudo grave; inflamación. (Fuente: DeCS, Bireme).

### Abstract

**Introduction:** COVID-19 is a new respiratory disease reported initially as an atypical pneumonia in December 2019. SARS-CoV-2, the etiological agent of this pathology, probably originated from a bat viral pathogen. The unexpected transmission and pathogenicity capacities that this coronavirus acquired turned COVID-19 into a pandemic with a wide and complex arrangement of symptoms. **Objective:** To analyze evolutionary, molecular, biological, immunological and epidemiological aspects of this disease. **Materials and methods:** A narrative review of the literature concerning these topics was conducted, which was published in *Pubmed* mostly from January 2020. **Results:** SARS-CoV-2 is a new coronavirus that uses its surface protein S to infect human cells that exhibit ACE2 receptors. This pathogen is transmitted through respiratory secretions and triggers a harmful increase in pro-inflammatory chemical mediators in vulnerable individuals, an immune reaction known as cytokine storm. This hyper-inflammatory response is the cause of the alveolar lesions behind the respiratory failure observed in severe cases of COVID-19. **Conclusions:** In susceptible individuals, SARS-CoV-2 triggers an acute respiratory distress syndrome that requires assisted ventilatory support and immunomodulatory therapy. New therapeutic and prevention strategies are being developed to reduce the high transmission and mortality rates associated with COVID-19.

**Key words:** Betacoronavirus; coronavirus infections; spike glycoprotein; severe acute respiratory syndrome; inflammation. (Source: DeCS, Bireme).

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Aunque ha habido avances significativos en las áreas descritas anteriormente, virólogos e inmunólogos deben colaborar para enfrentar retos futuros importantes, tales como: (i) caracterizar la estructura ACE2 y su función en la infección de órganos que son frecuentemente lesionados por SARS-CoV-2; (ii) identificar moléculas accesorias de origen celular y viral que contribuyen a la adhesión y penetración de SARS-CoV-2; (iii) descubrir posibles mutaciones del gen humano que codifica ACE2 que incrementan su susceptibilidad al reconocimiento por la proteína viral S; (iv) encontrar y/o diseñar un modelo animal apropiado donde estudiar la dinámica de la interacción entre la proteína S y ACE2; (v) culminar la fase III de pruebas clínicas en humanos donde se pueda cuantificar niveles de inmunogenicidad, de patogenicidad y la dosis efectiva de muchas vacunas que están siendo desarrolladas en la actualidad; y (vi) determinar la duración de la inmunidad inducida por una potencial vacuna.

Contribuciones a corto y largo plazo en las áreas descritas anteriormente acelerarán el desarrollo y uso de métodos preventivos y terapéuticos que protejan eficientemente no sólo a la comunidad en general, sino también al personal de salud, a quienes su trabajo en unidades de cuidado de pacientes con COVID-19 los expone frecuentemente a situaciones de riesgo de contagio.

Los ciclos acelerados de multiplicación y destrucción celular de MERS-CoV, SARS-CoV y SARS-CoV-2 provocan respuestas inflamatorias incontrolables inducidas por una intensa y auto-amplificada tormenta de citoquinas. Se ha demostrado que la insuficiencia respiratoria que desarrollan ciertos pacientes con MERS, SARS y COVID-19 se debe a los efectos adversos de citoquinas inflamatorias que circulan en el cuerpo de pacientes causándoles daño. Sin embargo, las manifestaciones clínicas de COVID-19 son bastante complejas y tienen un desenlace fatal más frecuente en pacientes de edad avanzada, con obesidad y/o con comorbilidades de tipo cardiovascular y respiratoria.

Estudios en el área de la inmunopatología deberán determinar el umbral de citoquinas a partir del cual la tormenta de citoquinas alcanza características perjudiciales de auto-perpetuación y auto-amplificación. De este modo, se haría más fácil diseñar tratamientos que bloqueen citoquinas inflamatorias específicas sin afectar otros

componentes esenciales de las respuestas inmunes, mejorando así el pronóstico de COVID-19. También se debe construir un cuadro clínico individualizado de pacientes, de todas las edades, con y sin comorbilidades, el cual incluya marcadores moleculares y predictores clínicos con la capacidad de pronosticar si un paciente es propenso a desencadenar estas tormentas de citoquinas.

Estudios clínicos de pacientes con COVID-19 bajo soporte ventilatorio han demostrado que agentes inmunosupresores de tipo esteroide pueden atenuar los efectos adversos de citoquinas inflamatorias, mejorando de esta manera los índices de mortalidad de COVID-19. Una perspectiva interesante que se desprende de estas observaciones es investigar si pacientes con enfermedades genéticas autoinmunes de tipo inflamatorio y bajo tratamiento con este tipo de inmunosupresores son menos susceptibles a padecer complicaciones clínicas severas si contraen COVID-19. Por último, se debe descifrar si algunos individuos asintomáticos o con sintomatología leve desarrollaron inmunidad cruzada a partir de encuentros anteriores con otros coronavirus, tal y como lo sugieren algunos reportes.

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