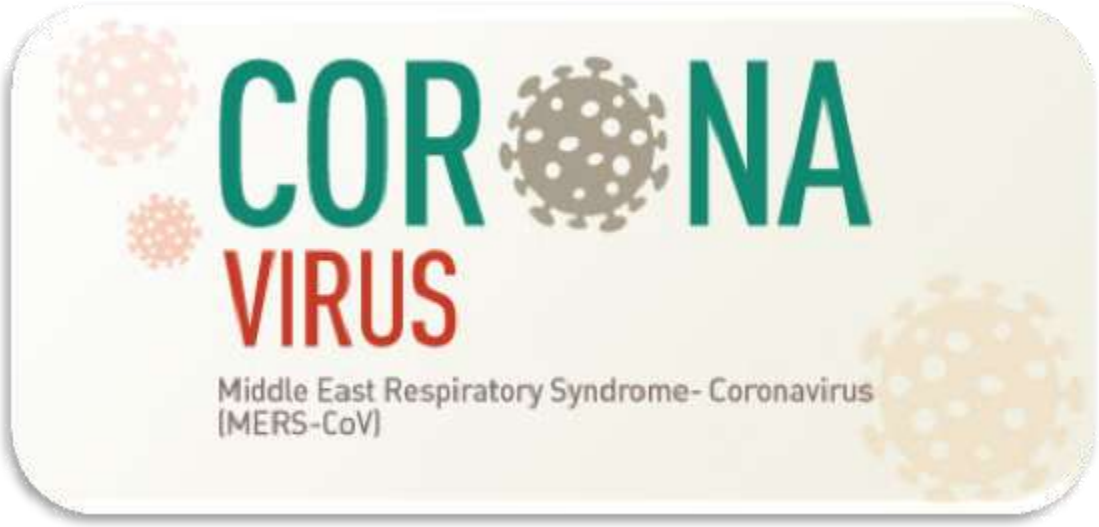
King Saud University
College of Science
Second semester
1437 / 2016

A research for Course (450 MIC)



Done By:

Amjad Al-Otaibi	432202389
Najd Al-Bakheet	433925234
Rahma Mansour	433201676
Wafa Al-Adwani	432202146

Supervised by : Miss. Reham Mosleh Alahmadi

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1 Topic. (Corona virus)

2 Introduction:

2.1 History of the disease.

The history of human coronaviruses began in 1965 when Tyrrell and Bynoe (1) found that they could passage a virus named B814. It was found in human embryonic tracheal organ cultures obtained from the respiratory tract of an adult with a common cold. The presence of an infectious agent was demonstrated by inoculating the medium from these cultures intranasally in human volunteers; colds were produced in a significant proportion of subjects, but Tyrrell and Bynoe were unable to grow the agent in tissue culture at that time. At about the same time, Hamre and Procknow (2) were able to grow a virus with unusual properties in tissue culture from samples obtained from medical students with colds. Both B814 and Hamre's virus, which she called 229E, were ether-sensitive and therefore presumably required a lipid-containing coat for infectivity, but these 2 viruses were not related to any known myxo- or paramyxoviruses. While working in the laboratory of Robert Chanock at the National Institutes of Health, McIntosh et al (3) reported the recovery of multiple strains of ether-sensitive agents from the human respiratory tract by using a technique similar to that of Tyrrell and Bynoe. These viruses were termed “OC” to designate that they were grown in organ cultures. Within the same time frame, Almeida and Tyrrell (4) performed electron microscopy on fluids from organ cultures infected with B814 and found particles that resembled the infectious bronchitis virus of chickens. The particles were medium sized (80–150 nm), pleomorphic, membrane-coated, and covered with widely spaced club-shaped surface projections. The 229E agent identified by Hamre and Procknow and the previous OC viruses identified by McIntosh et al had a similar morphology(Fig.1).

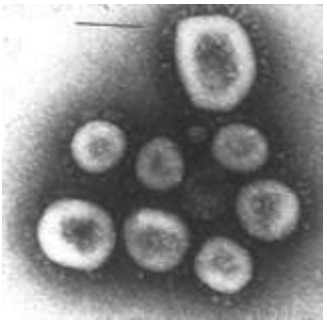


Figure 1

In the late 1960s, Tyrrell was leading a group of virologists working with the human strains and a number of animal viruses. These included infectious bronchitis virus, mouse hepatitis virus and transmissible gastroenteritis virus of swine, all of which had been demonstrated to be morphologically the same as seen through electron microscopy (5,6). This new group of viruses was named coronavirus (corona denoting the crown-like appearance of the surface projections) and was later officially accepted as a new genus of viruses (7).

Ongoing research using serologic techniques has resulted in a considerable amount of information regarding the epidemiology of the human respiratory coronaviruses. It was found that in temperate climates, respiratory coronavirus infections occur more often in the winter and spring than in the summer and fall. Data revealed that coronavirus infections contribute as much as 35% of the total respiratory viral activity during epidemics. Overall, he proportion of adult colds produced by coronaviruses was estimated at 15% (8).

In the 3 decades after discovery, human strains OC43 and 229E were studied exclusively, largely because they were the easiest ones to work with. OC43, adapted to growth in suckling mouse brain and subsequently to tissue culture, was found to be closely related to mouse hepatitis virus. Strain 229E was grown in tissue culture directly from clinical samples. The 2 viruses demonstrated periodicity, with large epidemics occurring at 2- to 3-year intervals (9). Strain 229E tended to be epidemic throughout the United States, whereas strain OC43 was more predisposed to localized outbreaks. As with many other respiratory viruses, reinfection was common (10). Infection could occur at any age, but it was most common in children.

Despite the extensive focus placed exclusively on strains 229E and OC43, it was clear that there were other coronavirus strains as well. As shown by Bradburne (11), coronavirus strain B814 was not serologically identical with either OC43 or 229E. Contributing to the various strain differences in the family of coronaviruses, McIntosh et al (12) found that 3 of the 6 strains previously identified were only distantly related to OC43 or 229E.

Epidemiologic and volunteer inoculation studies found that respiratory coronaviruses were associated with a variety of respiratory illnesses; however, their pathogenicity was considered to be low (13,14). The predominant illness associated with infections was an upper respiratory infection with occasional cases of pneumonia in infants and young adults (15,16). These viruses were also shown to be able to produce asthma exacerbations in children as well as chronic bronchitis in adults and the elderly (17-18).

While research was proceeding to explore the pathogenicity and epidemiology of the human coronaviruses, the number and importance of animal coronaviruses were growing rapidly. Coronaviruses were described that caused disease in multiple animal species, including rats, mice, chickens, turkeys, calves, dogs, cats, rabbits and pigs. Animal studies included, but were not limited to, research that focused on respiratory disorders. Study focus included disorders such as gastroenteritis, hepatitis and encephalitis in mice; pneumonitis and sialodacryoadenitis in rats; and infectious peritonitis in cats. Interest peaked particularly regarding areas of encephalitis produced by mouse hepatitis virus and peritonitis produced by infectious peritonitis virus in cats.

Pathogenesis of these disease states was various and complex, demonstrating that the genus as a whole was capable of a wide variety of disease mechanisms (20). Human and animal coronaviruses were segregated into 3 broad groups based on their antigenic and genetic makeup. Group I contained virus 229E and other viruses, group II contained virus OC43 and group III was made up of avian infectious bronchitis virus and a number of related avian viruses (21).

2.2 Introduction of the virus.

Coronaviruses cause infections in a wide variety of animals, resulting in respiratory, enteric, hepatic, and neurological diseases of various levels of severity. Based on genotypic and serological characterization, coronaviruses traditionally were classified into three distinct groups, groups 1, 2, and 3. Recently, the Coronavirus Study Group of the International Committee for Taxonomy of Viruses has renamed the traditional group 1, 2, and 3 coronaviruses as Alphacoronavirus, Betacoronavirus, and Gammacoronavirus, respectively.

The recent severe acute respiratory syndrome (SARS) epidemic due to SARS coronavirus (SARS-CoV) and the identification of SARS-related coronaviruses (SARSr-CoVs) from Himalayan palm civets and horseshoe bats in mainland China have led to a boost in interest in the study of coronaviruses in both humans and animals. Before the SARS epidemic in 2003, there were only 19 known coronaviruses, including 2 human, 13 mammalian, and 4 avian coronaviruses. After the SARS epidemic, more than 20 additional novel coronaviruses have been described with complete genome sequences. These include 3 human coronaviruses, 15 mammalian coronaviruses, and 4 avian coronaviruses. For human coronaviruses, human coronavirus NL63 (HCoV-NL63) (an alphacoronavirus) and human coronavirus HKU1 (HCoV-HKU1) (a betacoronavirus) have been discovered in addition to the two previously known human coronaviruses, human coronavirus 229E (HCoV-229E) (an alphacoronavirus) and human coronavirus OC43 (HCoV-OC43) (a betacoronavirus), as well as SARS-CoV (a betacoronavirus). While HCoV-229E and HCoV-OC43 were thought to account for 5 to 30% of human respiratory tract infections, HCoV-NL63 and HCoV-HKU1 often were detected in <5% of respiratory tract samples. Outbreaks due to HCoV-OC43 also have been reported. Nevertheless, the different HCoVs often cocirculate, with one or two HCoVs being predominant depending on the geographical area and year.

Coronaviruses are unique in having a high frequency of homologous RNA recombination, which is a result of random template switching during RNA replication that is thought to be mediated by a copy-choice mechanism. Their tendency for recombination and high mutation rates may allow them to adapt to new hosts and ecological niches.

During our previous investigations on the molecular epidemiology of HCoV-HKU1, we documented the first evidence for natural recombination in coronavirus associated with human infection, resulting in the generation of different HCoV-HKU1 genotypes. Since some strains of HCoV-HKU1 were found to display incongruent phylogenetic relationships upon the analysis of the RNA-dependent RNA polymerase (RdRp), spike (S), and nucleocapsid (N) genes, recombination events were suspected and later

confirmed with the complete genome sequencing of 22 strains of HCoV-HKU1 and recombination analysis.

Although HCoV-OC43 is thought to be the most commonly encountered human coronavirus, no similar molecular epidemiology studies have been performed, and little is known about its evolution among humans. Only five complete genome sequences of HCoV-OC43, two from the same American Type Culture Collection (ATCC) strain, VR759, that was isolated in 1967, one Paris strain that was isolated in 2001, and two Belgium strains detected in 2003 and 2004, were available in GenBank. In this study, we investigate the presence of different genotypes among HCoV-OC43 strains and identify potential recombination events that lead to the generation of novel genotypes, a situation analogous to that observed for HCoV-HKU1. HCoV-OC43 detected from the nasopharyngeal aspirates (NPAs) from 29 patients with respiratory tract infections from 2004 to 2011 were subjected to complete RdRp, S, and N gene sequencing and analysis. The clinical characteristics of patients also were analyzed in relation to molecular epidemiology results. As initial analyses showed the presence of potential recombination events, two complete genomes of HCoV-OC43 were selected for sequencing and further analysis. The emergence of a novel genotype of HCoV-OC43 through recombination and the evolution of different HCoV-OC43 genotypes also was described (22).

2.3 The distribution of this disease.

More than 475 people have died from Middle East respiratory syndrome (MERS), which first appeared in 2012 in Saudi Arabia and then in other countries in the Middle East, Africa, Asia, and Europe. In April 2014, the first American was hospitalized for MERS in Indiana and another case was reported in Florida. Both had just returned from Saudi Arabia. In May 2015, there was an outbreak of MERS in Korea which was the largest outbreak outside of the Arabian peninsula. People also died from a severe acute respiratory syndrome (SARS) outbreak in 2003. As of 2015, there were no further reports of cases of SARS. Both MERS and SARS are types of coronaviruses (23).

2.4 Epidemic.

The epidemiology of coronavirus colds has been little studied. Waves of infection pass through communities during the winter months, and often cause small outbreaks in families, schools, etc. Immunity does not persist, and subjects may be re-infected, sometimes within a year. The pattern thus differs from that of rhinovirus infections, which peak in the fall and spring and generally elicit long-lasting immunity. About one in five colds is due to coronaviruses. The rate of transmission of coronavirus infections has not been studied in detail. The virus is usually transmitted via inhalation of contaminated droplets, but it may also be transmitted by the hands to the mucosa of the nose or eyes (24).

In September 2012, a novel coronavirus infection was reported in ProMed Mail, an internet-based reporting system that helps disseminate information about infectious disease outbreaks worldwide. The virus was isolated from the sputum of a man in Jeddah, Saudi Arabia, who was admitted to a hospital with pneumonia and acute kidney injury in June 2012. Shortly thereafter, a report appeared of an almost identical virus detected in a patient in Qatar with acute respiratory syndrome and acute kidney injury; the patient had traveled recently to Saudi Arabia.

Subsequent cases and clusters of infections have been reported. Since April 2012, at least 1630 cases of MERS-CoV infection have been reported. The actual number of cases is likely to be higher. The median age is 48 years (range 9 months to 94 years) and 64 percent of cases have been male.

The number of cases in the Middle East increased dramatically in March and April 2014 then declined sharply in mid-May 2014. A smaller increase in cases occurred during March and April 2013. An outbreak of more than 180 cases occurred in South Korea in May and June 2015; the index case had recently traveled to several countries in the Arabian Peninsula (25).

3 Classification of the virus:

3.1 Order.

Virus; ssRNA positive-strand viruses (26).

3.2 Family.

The coronaviruses were originally grouped into the family Coronaviridae (24).

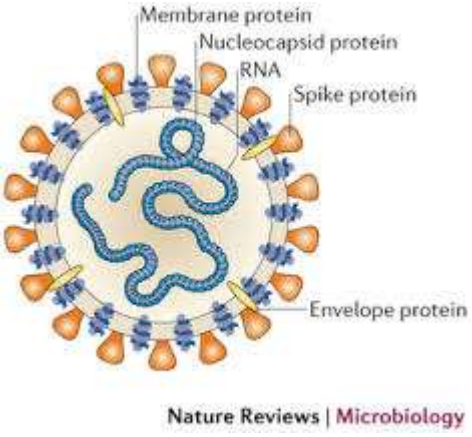
3.3 Genus.

- Genus: Alphacoronavirus; type species: Alphacoronavirus 1
- Genus Betacoronavirus; type species: Murine coronavirus
- Genus Gammacoronavirus; type species: Avian coronavirus
- Genus Deltacoronavirus; type species: Bulbul coronavirus HKU11

(27)

4 structure and genome:

4.1 Shape.



4.2 Size.

The genomic size of corona viruses ranges from approximately 26 to 32 kilobases, the largest for an RNA virus (28,29) .

4.3 Enveloped.

Corona viruses are enveloped viruses with a positive-sense single-stranded RNAgenome and with a nucleocapsid of helical symmetry(28,29).

4.4 Nucleic acid.

is a positive-stranded RNA virus that is infectious to cats worldwide(28,29) .

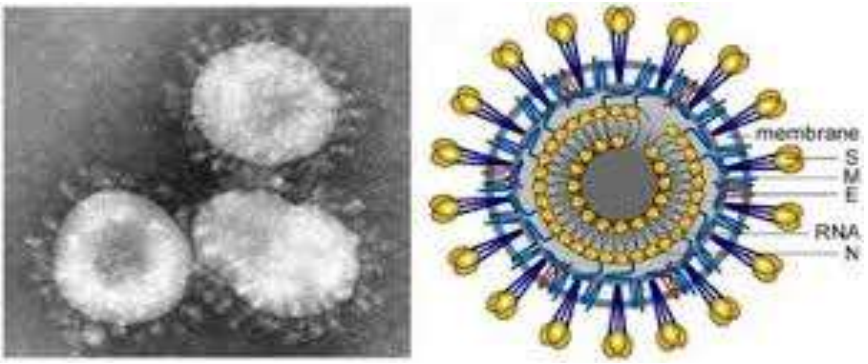
5 Protein (Virulence Factors):

5.1 Structural proteins.

Proteins that contribute to the overall structure of all corona viruses are the spike (S), envelope (E), membrane (M) and nucleocapsid (N). In the specific case of the SARS

corona virus, a defined receptor-binding domain on S mediates the attachment of the virus to its cellular receptor, angiotensin-converting enzyme 2 (ACE2). Some corona viruses (specifically the members of Betacoronavirus subgroup A) also have a shorter spike-like protein called hemagglutinin esterase (HE)(30).

A



B

Figure 2

Figure 2: Coronavirus particle. (A) Model of a Coronavirus particle. The virion membrane contains the spike (S), envelope (E) and matrix (M) proteins. The RNA genome is associated with nucleocapsid protein N (31). (B) Electron microscopy showing the typical coronavirus "crown" of the S proteins (picture taken by H.R. Gelderblom, Robert Koch-Institute).

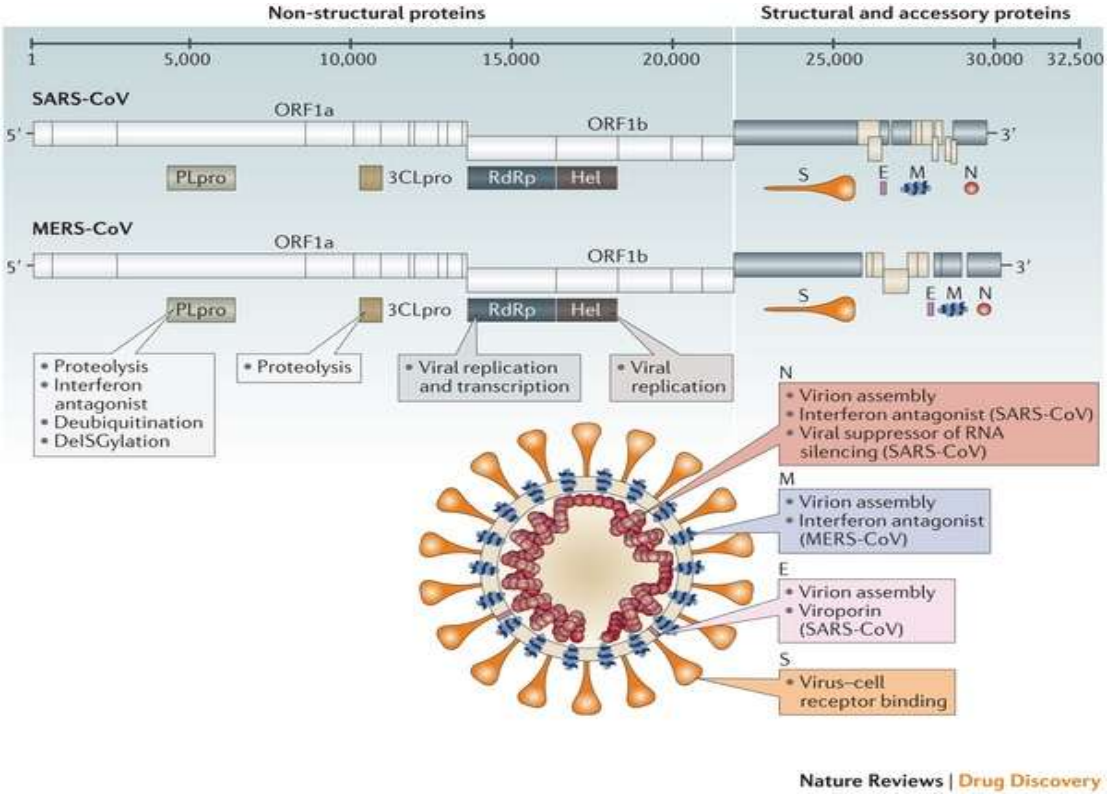
Most of the remaining one-third of the genome encodes 4 structural proteins. The spike (S) protein is the major surface protein (Fig. 2.1A). Neutralizing antibodies are directed against the S protein and it is responsible for virus entry and host range. The envelope protein (E) is an integral membrane protein and is involved in virus formation and budding. The matrix protein M is the most abundant structural protein in the virion whose C-terminus is located at the inside of the virus particle where it interacts with the helical nucleocapsid protein (N), which in turn is associated with the viral genome. The M protein is not transported via the Golgi apparatus to the cell membrane, but rather stays at the endoplasmatic reticulum during the whole infection cycle. There the first steps of virus assembly are initiated by interactions of the M and N protein.

Interspersed between these structural genes are eight accessory genes (Fig. 2.2B), marked in red). The encoded proteins share little amino acid identity between genera, formally termed "groups", of coronaviruses and are therefore called "group-specific". These

proteins are not generally required for virus replication in vitro but are thought to have important roles in replication in the natural host . Figure 1.2: Genome organization and generation of subgenomic RNAs of SARS-CoV. (A) Organization of the SARS-CoV genome. The replicase genes (ORF1a, ORF1b, green) make up twothird of the whole genome. Common to all coronaviruses ORFs encoding for the structural proteins are located downstream of ORF1a/b in the order S (spike), E (envelope), M (membrane) and N (nucleocapsid) protein (highlighted in blue). Interspersed between the structural genes are the genes coding for group-specific accessory proteins (red). (B) A negative-strand copy of the full-length RNA genome serves as template for genome replication (a). Subgenomic mRNAs for translation are transcribed from discontinuously transcribed negative-strand subgenomic RNAs. The viral polymerase starts transcription at the genomes 3' end (b) and stops at one of the transcription regulatory sequences (TRS) located upstream of each ORF. Then the newly synthesized strand dissociates from the template strand and fuses to the first TRS at the genomes 5' end (c). Transcription is continued through the leader sequence of the genome (d). The negative-strand subgenomic RNAs of various lengths are template for transcription of subgenomic mRNAs (e).(32)

5.2 Non- Structural proteins.

The first open reading frame, ORF1ab, makes up two-thirds of its 29.7 kb genome and codes for proteins contributing to virus replication. Almost all of these proteins are not packaged into virions and therefore called non-structural proteins (nsp).



Wafa Al-Adwani

6 Transmission of Corona virus:

The ways that human coronaviruses spread from an infected person to others through:

• The air by coughing and sneezing.

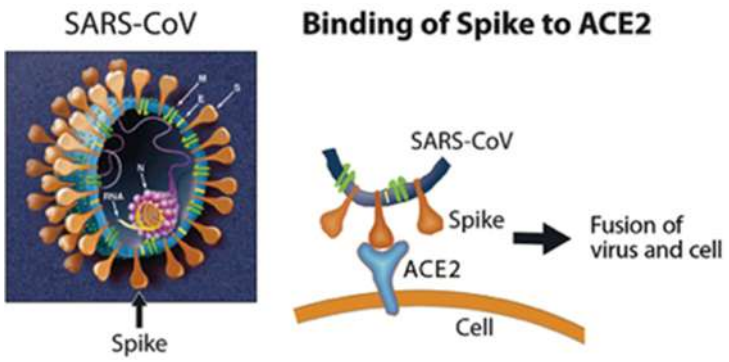
• Close personal contact, such as touching or shaking hands.

• These viruses may also spread by touching contaminated objects or surfaces then touching your mouth, nose, or eyes (33).

The virus that causes SARS is thought to be transmitted most readily by respiratory droplets produced when an infected person coughs or sneezes. Droplet spread can happen when droplets from the cough or sneeze of an infected person are propelled a short distance through the air and deposited on the mucous membranes of the mouth, nose, or eyes of persons who are nearby. The virus also can spread when a person touches a surface or object contaminated with infectious droplets and then touches his or her mouth, nose, or eye(s). In addition, it is possible that the SARS virus might spread more broadly through the air or by other ways that are not now known. People usually get infected with common human coronaviruses in the fall and winter. However, you can get infected at any time of the year (34).

7 Penetration and the target organ:

The penetration of the virus is through fusion of virus into the cytoplasm of the cell host. The envelope spike (S) glycoprotein is responsible for CoV cell entry. The S mediates both attachment of CoV particles to cell surface receptor molecules (ACE2 receptor) as well as membrane penetration by fusion. Receptor-binding domains (RBD) have been identified in the S of diverse CoV; they usually contain antigenic determinants targeted by antibodies that neutralize CoV infections. To penetrate host cells, the CoV can use various cell surface molecules (35).



The lungs are the target organ of infection, the lower respiratory tract, the brain is also infected in some patients. Brain infection may result in long-term neurological sequelae, but little is known about the pathogenesis of SARS-CoV in this organ.

The SARS coronavirus targets the epithelial cells of the respiratory tract, resulting in diffuse alveolar damage. Several organs/cell types may be infected in the course of the illness, including mucosal cells of the intestines, tubular epithelial cells of the kidneys, neurons of the brain, and several types of immune cells, and certain organs may suffer from indirect injury. Coronaviruses mainly target epithelial cells but they also infect macrophages and other widely distributed cells (36).

Rahma Mansour

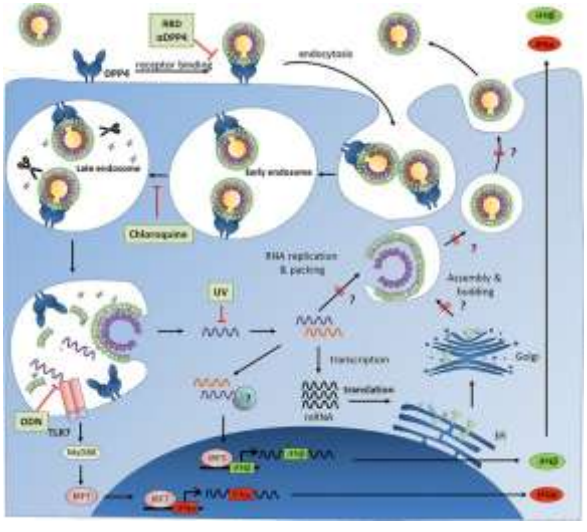
8 Replication cycle (the main site):

1- with their S-protein, coronavirus bind on cell surface molecules.

2- So far, it is not clear whether the virus get into the host cell by fusion of viral and cell membrane or by receptor mediated endocytosis in the virus.

3- Since corona virus have a single strand positive RNA, they can directly produce their proteins and new genome in the cytoplasm .at first, the virus synthesize its RNA polymerase that only recognize and produce viral RNAs. This enzyme synthesize the minus strand using the positive strand as template.

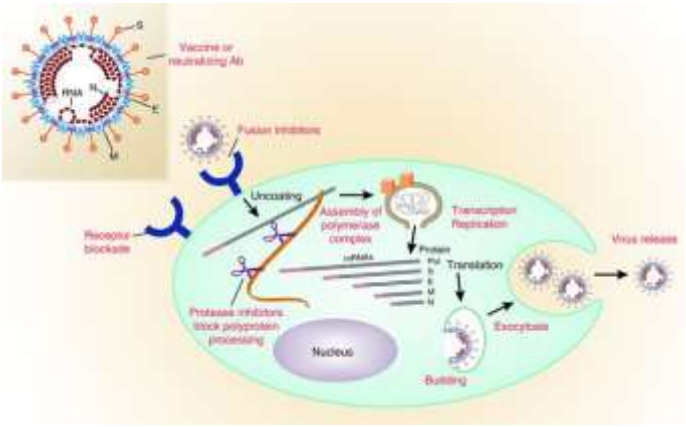
4- Subsequently, this minus strand serves as template to transcribe smaller sub genomic positive RNAs which are used to synthesize all other proteins. Furthermore, this minus strand serves for replication of new positive stranded RNA genomes.



Model of coronavirus replication. After receptor interaction and fusion of viral and plasma membranes, virus-specific RNA and proteins are synthesized, probably entirely in the cytoplasm. Expression of coronaviruses starts with translation of two polyproteins, pp1a and pp1ab, which undergo translational proteolytic processing into the proteins that form the replicase complex. This complex is used to transcribe a 3′-coterminal set of nested subgenomic mRNAs, as well as genomic RNA, that have a common 5′ "leader" sequence derived from the 5′ end of the genome. Proteins are translated from the 5′ end of each mRNA. New virions are assembled by budding into intracellular membranes and released through vesicles by the cell secretory mechanisms. RER, rough endoplasmic reticulum; ER/GIC, endoplasmic reticulum/Golgi intermediate compartment (37).

9 Assembly and egressions:

The protein N binds genomic RNA and the protein M is integrated into membrane of the endoplasmic reticulum like the envelope protein S and HE. After binding. Assembled nucleocapsid with helical twisted RNA budd into the ER lumen and are encased with its membrane. These viral progeny are finally transported by Golgi vesicles to the cell membrane and are exocytosed into the extracellular space.



The assembly of this complex. Viral mRNAs made by discontinuous transcription are shown in the cytoplasm with the protein that each encodes indicated at the right. The common 70 base long leader sequence on the 5′ end of each mRNA is shown in red.

Budding and exocytosis are processes essential to virus replication that may be targets for development of antiviral drugs. M, membrane protein required for virus budding; S, viral spike glycoprotein that has receptor binding and membrane fusion activities; E, small membrane protein that plays a role in coronavirus assembly; N, nucleocapsid phosphoprotein associated with viral RNA inside the virion (38).

Najd Al-Bakheet

10 Symptoms:

The symptoms of coronavirus runny nose, sore throat, cough, headache and chills. The incubation period is about two to seven days.

Clinical Spectrum of Illness: Fever, myalgia, headache and shortness of breath. The patient might shed infectious virus even when there are no apparent symptoms (39).

11 Diagnosis and cytopathic effect:

Diagnosis:

-Doctor Questionnaire:

Travel - Workplace - Direct contact with infected individuals.

-Chest x-rays: used to find atypical pneumonia or respiratory distress syndrome.

-The main test for coronavirus is a screening PCR tests, ELISA test followed by a more specific confirmatory test (40)

Cytopathic effect:

Certain organs of SARS victims, such as the lungs and intestines, have been extensively studied and the pathological lesions of SARS in these organs are fairly well known. By contrast, the pathology of other organs is incompletely described, and imperfectly known. For ease of reference, the major pathological findings for each organ are summarized in Table 1 Major Pathological Findings in Various Organs and Tissue (41).

Organs/tissue	Pathology
Respiratory tract	Diffuse alveolar damage with varying degrees of acute exudative features including edema and hyaline membranes, organization, and fibrosis. Macrophagic or mixed cellular infiltration, multinuclear giant cells, atypical reactive pneumocytes, and vascular injury
Spleen and lymph nodes	Lymphocyte depletion in spleen and lymph nodes with architectural disruption.
Urogenital tract	Kidneys: acute tubular necrosis.
Central nervous system	Edema and degeneration of neurons
Adrenal gland	Necrosis and infiltration of monocytes and lymphocytes
Thyroid gland	Destruction of follicular epithelial cells, several apoptotic cells
Testes	Germ cell destruction, apoptotic spermatogenetic cells
Heart	Edema and atrophy of myocardial fibers

Table 1

12 Control the virus and prevention:

Currently, there is no vaccine to prevent MERS-CoV infection. The U.S. National Institutes of Health is exploring the possibility of developing one.

CDC routinely advises that people help protect themselves from respiratory illnesses by taking everyday preventive actions:

- Wash your hands often with soap and water for 20 seconds, and help young children do the same. If soap and water are not available, use an alcohol-based hand sanitizer.

- Cover your nose and mouth with a tissue when you cough or sneeze, then throw the tissue in the trash.
- Avoid touching your eyes, nose and mouth with unwashed hands.
- Avoid personal contact, such as kissing, or sharing cups or eating utensils, with sick people.
- Clean and disinfect frequently touched surfaces and objects, such as doorknobs. (42).

13 Treatment:

There is no specific antiviral treatment recommended for MERS-CoV infection. Individuals with MERS can seek medical care to help relieve symptoms. For severe cases, current treatment includes care to support vital organ functions.

13.1 vaccine.

Currently, there is no vaccine.

13.2 medication.

You treat a coronavirus infection the same way you treat a cold:

• Get plenty of rest.

• Drink fluids.

• Take over-the-counter medicine for sore throat and fever (but don't give aspirin to children or teens younger than 19; use ibuprofen or acetaminophen instead).

(43).

Najd Al-Bakheet

14 Host Immune Defense :

The innate immune response is a coordinated series of signaling pathways in all nucleated cells that function to thwart an invading pathogen's replication and disease potential. From interferon (IFN) induction and secretion to the recruitment of macrophages and DCs to sites of infection, the system functions to restrict tissue tropism and spread, dampen virus replication efficiency, and eliminate virally infected cells (reviewed in references 44-46). In addition to IFN regulatory factor 3 (IRF3) in the IFN pathway, another critical signaling protein for the innate immune response is nuclear factor of kappa light polypeptide gene enhancer in B cells (NF-κB). NF-κB is activated during viral infection from the sensing of viral replication products and via cytokine secretion from macrophages and DCs (47). This leads to a broad induction of the innate immune response while also fine-tuning the response to remove virus while not harming the cells .

The modulation of these pathways is critical for virus survival, as evidenced by the many viruses that express proteins that block various key effector proteins in these pathways and from the increased disease severity noted in many gene knockout animals. Protein products from many viruses including the NSP1, ORF6, and N proteins from SARS-CoV (48-53), the NS1 protein from influenza virus (54,55), the VP35 and VP24 proteins from Ebola virus (56,57), the leader protein from picornaviruses (59,60), and the V proteins from Nipah and Hendra viruses (58,59) have each been identified as being immunomodulating proteins. Each protein blocks one or more key signaling proteins in

the IFN and NF-κB pathways to enhance viral replication and pathogenesis. The influenza virus NS1 protein affects the IRF3 signaling pathway as well as mRNA stability and trafficking (47,43). In contrast, VP35 from Ebola virus and ORF6 from SARS-CoV block nuclear import (41,43), while the V proteins from Nipah and Hendra viruses induce signal transducer and activator of transcription (STAT) protein degradation (59). Picornavirus leader blocks by binding to promoter regions of IFN genes via a zinc finger domain and inhibits transcription (43-45). Each protein antagonizes the innate immune response but uses different tools and targets to achieve these goals. An understanding of how each antagonist affects the innate immune response illuminates key interactions between the host signaling pathway components and the virus. In addition, these studies pinpoint key host cell components that function to regulate virus replication and pathogenesis, providing novel targets for the development of antiviral compounds .

15 Genetic (Gene Mutation):

Mutations in the ORF 3c/ORF 7b genes are proposed to play a role in the occurrence of the fatal FIPV biotype. Here, we investigated 282 tissue specimens from 28 cats that succumbed to FIP. Within one cat, viral sequences from different organs were similar or identical, whereas greater discrepancies were found comparing sequences from various cats. Eleven of the cats exhibited deletions in the 3c gene, resulting in truncated amino acid sequences. The 7b gene was affected by deletions only in one cat. In three of the FIP cats, coronavirus isolates with both intact 3c genes as well as 7b genes of full length could also be detected. Thus, deletions or stop codons in the 3c sequence seem to be a frequent but not compelling feature of FIPVs.Coronaviruses also cause a range of diseases in farm animals and domesticated pets, some of which can be serious and are a threat to the farming industry. Economically significant coronaviruses of farm animals include porcine coronavirus (transmissible gastroenteritis coronavirus, TGE) and bovine coronavirus, which both result in diarrhea in young animals. Feline Coronavirus: two forms, Feline enteric coronavirus is a pathogen of minor clinical significance, but spontaneous mutation of this virus can result in feline infectious peritonitis (FIP), a disease associated with high mortality. Similarly, there are two types of coronavirus that

infect ferrets: Ferret enteric coronavirus causes a gastrointestinal syndrome known as epizootic catarrhal enteritis (ECE), and a more lethal systemic version of the virus (like FIP in cats) known in ferrets as ferret systemic coronavirus (FSC). There are two types of canine coronavirus (CCoV), one that causes mild gastrointestinal disease and one that has been found to cause respiratory disease. Mouse hepatitis virus (MHV) is a coronavirus that causes an epidemic murine illness with high mortality, especially among colonies of laboratory mice (60).

Wafa Al-Adwani

16 Recent discoveries:

The field of coronavirology has advanced significantly in recent years. The SARS epidemic was a dramatic reminder that animal coronaviruses are potential threats to the human population, although the exact mechanism of species-to-species spread of the SARS coronavirus remains obscure. NL63 has been identified in many countries. This virus and the related viruses NL and HCoV-NH are likely the cause of a substantial proportion of respiratory tract disease in infants and children. The impact of HKU1 is not yet known. It seems clear that the coronaviruses infecting humans and causing respiratory disease are heterogeneous and quite widely distributed among groups I and II. It may be that some of the newer coronaviruses represent strains similar to the original B814 and OC strains that could not be further characterized in the 1960s. Additional human coronavirus strains will very likely be discovered, which stresses the need for further investigation into the virology and etiology of these infectious organisms (61).

Amjad Al-Otaibi

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