ECDC excercise script

Group 1-Spain

- **Start:** Klebsiella pneumoniae is known to cause healthcare-associated infections and is commonly multidrug-resistant. A new variant of K. pneumoniae, designated as hypervirulent K. pneumoniae (hvKP), was first described in 1986 in Taiwan in patients with community-acquired K. pneumoniae infections. The hvKP strains exhibit unique features, such as a striking capacity to cause serious infections in immunocompetent and healthy individuals. Such infections include pyogenic liver abscesses and metastatic infections, such as meningitis and endophthalmitis. hvKP exhibits a hypermucoviscous phenotype that can be identified in the laboratory by a positive “string test.” After this first description of hvKP, additional reports followed and hvKP has been since reported in Asia, South America, North America, the Middle East, Europe, Africa, and Australia. Increasingly, carbapenem resistance in hvKP isolates is being reported, especially from China. Combined with the increased virulence of hvKP strains, the emergence of carbapenem resistance is an additional cause for concern that indicates a need for preparedness.
  - **12 December 2022:** The Spanish Coordinating Centre for Health Alerts and Emergencies at the Ministry of Health, Social Services and Equality is informed by the Hospital of Madrid about two fatal cases of carbapenem-resistant Klebsiella pneumoniae (CRKP) infection in two young, previously healthy adults in the hospital. The patients suffered fulminant sepsis without responding to treatment with a combination of tigecycline and fosfomycin. One of the patients (a 26 yo Spanish football player) was transferred three days ago from Genoa's Hospital, Italy, for rehabilitation and to be closer to his family after a traffic accident whereby he had suffered a fracture of the right femur, multiple rib fractures and a rupture of the spleen. Two days ago while at the Hospital in Madrid, he developed high fever and soon afterwards septic shock, and was transferred to the intensive care unit (ICU) where he died this morning with fulminant sepsis.The other, a 28yo female, also died overnight.
  - **12 December 2022:** **HOSPITAL OF MADRID PRESS STATEMENT: Patients are safe and hospital infection under control.**

    Firstly, we wish to extend our condolences to the family, friends and loved ones of the deceased patients. We want to reassure our patients and the public that our hospital is safe. The infection that spread and proved to be fatal to a handful of our patients, is under control. We have put together a team of experts --- epidemiologists, microbiologists, health-infection experts --- to get to the root of the matter. All our staff - from the Chief of Medical Services to nurses, cleaners and restaurant servers - are trained and well aware on how to prevent the spread of hospital infection. For this particular incident, we have worked with various laboratories, regional public health institutions to identify the source of the infection and how to properly address it. We are continuously working with these institutions to gather more data, to help prevent hospital infection. For interview request, please contact our press office: press@hosp.es or +34 1234 -234

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- **12 December 2022: El PAÍS NEWSPAPER ARTICLE**: Spanish footballer dies from hospital infection Spain national football team member Paul Johnson, died yesterday after a brief stay at the Hospital in Madrid, Spain. The famous 26-year old AC Milan midfielder was initially admitted to a hospital in Genoa, Italy after contracting injuries from a traffic accident. According to anonymous sources, he was then transferred to Hospital in Madrid three days ago and his conditioned worsened. He succumbed to fulminant sepsis at an intensive care unit. According to the same unnamed sources, three patients have died, at the same time in the same Spanish hospital, due to infection acquired during their confinement. The patients were infected with carbapenem-resistant Klebsiella pneumoniae, making it extremely difficult to treat since antibiotics do not work against this infection. Carbapenem is often considered an be an antibiotic of last resort. These infections are usually acquired in hospitals, nursing homes and other health care settings. Healthy patients normally get infected through ventilators, urinary or intravenous catheters and patients who are taking long courses of antibiotics are of particular risk. There were outpouring grief from footballer's family, teammates and football fans worldwide. The footballer is remembered by many as the bright light in an otherwise forgettable World Cup 2018 and it is he that fans expected the future squad to be based around, given the retirement of so many former stars. The hospitals in Italy and Spain have not yet provided comments to the media. Statements from public health authorities are also eagerly awaited."He was so young and very healthy before this terrible accident." says footballer's father, Thomas senior, "it is unacceptable and tragic that hospitals kill you instead of healing."
  - [ ] **What do you think should be done at this point? Should all patient transfers from outside countries be banned to the hospital?**
  - [ ] **What should be the message to the public- is this a problem of only public interest because the case involves a famous footballer?**
  - [ ] **What do you think should be done to examine the extent of hvKp spread in the hospital at this point?**
- **13 December 2022:** A third 43-year-old patient with fulminant meningitis with carbapenems-resistant *Klebsiella pneumoniae* (CRKP) is being treated in the ICU of the same hospital in Madrid. The hospital's clinical microbiology laboratory confirms that the isolate has the same resistance phenotype as the isolates from the other two patients who died. A review of Klebsiella pneumoniae isolates at the laboratory identifies three additional isolates from three different patients in the last fifteen days. The infection prevention and control (IPC) team decides to perform active screening cultures on all patients who have been admitted to the same ICU and other wards where the patients had previously been admitted. Another patients transferred from the Hospital in Genoa, Italy 10 days ago to Spain was a 50-year-old male who suffered from recurrent pelvic osteomyelitis. He was originally hospitalised in a private hospital in Porto but following complications was transferred to the Hospital of Porto and is presenting with the onset of fulminant sepsis, high fever and confusion. He was sharing the ward in the private hospital with 6 other Portuguese nationals and 1 Spanish national and 3 (2 Portuguese, one Spanish) are positive for hvCRKP. Contact precautions have been implemented. The hospital in Porto is asking for further advice on managing these patients.

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- **13 December 2022: Editorial Comment Popular Science Journal:**Cases of CRE-Klebsiella pneumoniae found in Italian hospital: After conducting initial tests, the infection and prevention control team of Geona's Hospital, Italy identified three patients infected with Carbapenam-resistant Klebsiella pneumoniae in its surgical ward. Carbapenam-resistant Klebsiella pneumoniae has also been found in a Madrid's Hospital in Spain where a Spanish footballer and one other patients died according to representatives of said hospital in Madrid. The footballer was of course recently transferred between the two hospitals. So are we now dealing with a multi-country outbreak? Three further cases of infection with Carbapenam-resistant Klebsiella pneumoniae have since been discovered in this same hospital in Genoa. Genoa's hospital specialises in trauma and orthopaedics, has a high turnover of patients and often admits patients from abroad. This heightens the risk of spreading infections like carbapenam-resistant Klebsiella pneumoniae , and other antibiotic-resistant bacteria. These incidents are alarming since antibiotic-resistance already causes 33,000 deaths in the EU alone, according the European Centre for Disease Prevention and Control (ECDC). The EU agency also recently reported 8.9 million healthcare-associated infections occurring each year in both hospitals and long-term care facilities. The emergence of bacteria resistant to multiple groups of antibiotics is particularly concerning, as infections due to these bacteria can be severe, costly and even fatal. Up to 50% of all antibiotic use in European hospitals is unnecessary or inappropriate, the report stated.
- **13 DECEMBER 2021: PUBLIC HEALTH MATTERS Post on Facebook:**Should he stay or should he go? Should we allow this patient from Malta to return to his home country knowing that he has may be carrying an antibiotic-resistant superbug? And if we do how can we expect others not to demand the same treatment? A man admitted to the Galliera hospital in Genoa, Italy after a traffic accident has been exposed to a multi-resistant superbug and now may be a carrier able to spread the disease. During his hospital stay, the Maltese patient was admitted to the same intensive care unit and at the same time as the Spanish football player Susso. The footballer later developed sepsis and acquired an antibiotic-resistant infection from somewhere. One other patient from the same ICU also died. The Maltese patient does not show any symptoms and seems to be recovering well but may still be carrying this deadly disease. After a 14-day confinement, the patient is ready to be released and fly back to Malta. Given the increasing numbers of antibiotic-resistance cases acquired through hospitals and other healthcare facilities, this patient remains a risk to other patients and hospital staff. Carbapenem-resistant bugs, the same bacteria the Maltese patient may be infected with, is known to be the “nightmare bacteria” because it is resistant to almost all antibiotics, extremely difficult to treat and fatal, in most cases. We are risking the lives of many in Malta, a country that already has an increasing number of hospital-acquired antibiotic-resistant cases, if we allow this patient to return. He should stay in Italy until he is completely cured from said bacteria. And that should be a rule applied to all such cases. The solution to antibiotic resistance is as difficult as they come. Experts do not believe that inventing new antibiotics can help – they are very expensive and only perpetuate the cycle of bacteria developing resistance to every new drug. This leaves doctors, hospitals, public health officials with saving the effective antibiotics for when they’re really needed. Concretely speaking, that means improving vaccines uptake (for flu, for example) and clean water to keep people from getting sick in the first place and not prescribing antibiotics for colds.
    - **Do you think more aggressive precautions should be taken? Should the hospital be shut down? Should antimicrobial prophylaxis be administered to patients who are colonized or undergoing risky procedures (i.e. chemotherapy, surgery)**

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- **20 December 2022: GENERAL BULLETIN ALERT FROM THE EUROPEAN CENTER FOR DISEASE PREVENTION AND CONTROL:** A Multi-country outbreak of severe sepsis and multi-organ abscesses with hyper-virulent carbapenem-resistant Klebsiella pneumoniae (hvCRKP) has been reported in Spain, Italy and Greece. Although the situation is rapidly evolving, the following cases have been confirmed since 12 December**: In Spain** two fatal cases of carbapenem-resistant Klebsiella pneumoniae (CRKP) infection in two young, previously healthy adults in the hospital. One patient was transferred three days earlier from the hospital in Genoa 13 December, A third 43-year-old male patient with fulminant meningitis with CRKP is being treated in the ICU of the same hospital in Madrid. A review of Klebsiella pneumoniae isolates at the laboratory identifies three additional isolates from three different patients in the last fifteen days. Screening of all patients admitted in the ICU of the Hospital Universitario identified one more patient carrying carbapenem-resistant Klebsiella pneumoniae. The patient had no active infection. The strain was sent for further testing. **In Italy:** The Hospital in Genoa had three cases with carbapenem resistant Klebsiella pneumoniae sepsis in the surgical ward in the last fifteen days. A businessman, who had transferred three weeks ago from a University Hospital in Bulgaria,a footballer who was transferred to Spain and died, and a third a Maltese national (34-years-old male) who remains in ICU. – Italy has more patients admitted to the same surgical ward as the businessman and the football player, two from Malta, one from Greece, one from Portugal and one from Turkey. The Greek, Portuguese and Turkish patients have since returned home for further treatment and recuperation. **In Greece:** Two Greek patients with pelvic osteomyelitis who underwent treatment in Genoa and were transferred for further care in Athens have developed sepsis due to a hypervirulent, pan-drug resistant strain of *Klebsiella pneumonia*. After extensive screening, of hospitalized patients, an additional 2 patients in the geriatric ward, 1 patient in a surgical ward, and one healthcare worker was found to be positive. Initial genome sequencing of the first available isolates have identified multiple genes associated with a hypervirulent genomic signature (K1-, magA-, rmpA- and rmpA2) and resistance to carbapenems (NDM-1, OXA-48), cephalosporins beta-lactam/beta-lactamase inhibitors (OXA-48) and colistin (mcr-2). Ceftazidime-avibactam (2.5 grams IV infused over 3 hours) + aztreonam 2 grams IV infused over 3 hours) infused together every 8 hours is currently recommended as treatment until further data become available. Any hospital with a recent case of carbapenem and colistin-resistant Klebsiella pneumonia, or patients transferred from the affected hospitals should undertake screening precautions of patients and healthcare worker. Appropriate protective and isolation precautions are recommended for any patient known to be colonised of infected with these Klebsiella pneumoniae strains. Travel should be discouraged. Further data will be communicated as it becomes available.
  - [ ] **How should the treatment recommendations be communicated? Just in the institution, countrywide, or internationally? What needs to be communicated to the public?**
  - [ ] **Your pharmacy reports that ceftazidime-avibactam is out of stock and they have been unsuccessful if finding an alternative supplier**

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- **22 December 2022:** Whole genome sequencing (WGS) of the isolates has been performed at the reference laboratory in Spain. The results from six isolates from separate patients in Spain confirmed that the three initially identified in the ICU (28yo male and 26yo male who both died and the 41yo) shared the same hypervirulent genomic signature. This was K1-, magA-, rmpA- and rmpA2-positive, confirming the hypervirulent phenotype. The isolates were also confirmed as pandrug-resistant, producing the NDM-1 and OXA-48 carbapenemases, and expressing the mcr-2 gene. In silico analysis of multilocus sequence typing (MLST) shows that the strain belongs to sequence type 23 (ST23). By core genome MLST (cgMLST) comparison the three isolates cluster within less than 8 allelic differences. The other three isolates, which were identified later after a wider screen, were confirmed to be carbapenem-resistant but lacked hypervirulence genes and displayed more than 150 allelic differences from the three outbreak-related isolates. No further patients or any staff have been detected in the Spanish hospital with Klebsiella pneumoniae infection or as carriers
  - [ ] **How would this information change your previous recommendations?**
- **26 December 2022:** 14 days after the initial cases were reported in Spain. A Spanish patient in a private hospital in Porto, Portugal has told the hospital that he wishes to return home to his geriatric residential home near Salamanca, Spain. It was confirmed 4 days ago that he is carrying the hvCRKP strain. The nursing home are requesting advice and support from the hospital on what control measures are recommended and for how long these control measures need to be in place. The hospital is unsure what to say and have contacted both Spanish and Portuguese authorities to advise them of the situation.
  - [ ] **Should asymptomatic carriers of hvKP be prevented from returning home, or admission to other healthcare facilities?**
- **3 January 2023** Two patients with upper urinary tract infection and secondary bacteraemia caused by extensively drug-resistant Salmonella enterica serovar Kentucky (producing the VIM-2 carbapenemase) have been identified in Portugal. The first patient was a 38-year-old woman in the postpartum period and the second a 62 year-old man with kidney stones. Both cases were linked to a small outbreak of gastroenteritis in the hospital. An epidemiological investigation has identified a ward nurse carrying this Salmonella strain who had travelled to Bulgaria the previous month to visit her family and on return had an episode of mild self-limiting gastroenteritis.
  - [ ] **Does this new case affect your previous decisions regarding hvKP?**

Group 2-Italy

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- **Start:** Klebsiella pneumoniae is known to cause healthcare-associated infections and is commonly multidrug-resistant. A new variant of K. pneumoniae, designated as hypervirulent K. pneumoniae (hvKP), was first described in 1986 in Taiwan in patients with community-acquired K. pneumoniae infections. The hvKP strains exhibit unique features, such as a striking capacity to cause serious infections in immunocompetent and healthy individuals. Such infections include pyogenic liver abscesses and metastatic infections, such as meningitis and endophthalmitis. hvKP exhibits a hypermucoviscous phenotype that can be identified in the laboratory by a positive “string test.” After this first description of hvKP, additional reports followed and hvKP has been since reported in Asia, South America, North America, the Middle East, Europe, Africa, and Australia. Increasingly, carbapenem resistance in hvKP isolates is being reported, especially from China. Combined with the increased virulence of hvKP strains, the emergence of carbapenem resistance is an additional cause for concern that indicates a need for preparedness.
    - **12- December 2022**: In a Genoa hospital the infection prevention control (IPC) team, in collaboration with the clinical microbiology laboratory, have so far identified three cases with carbapenem resistant Klebsiella pneumoniae sepsis in the surgical ward in the last fifteen days. The first case to be identified was a 57-year-old Italian national, a businessman, who had been transferred three weeks ago from a hospital in Bulgaria, where he was hospitalised after a traffic accident that he suffered during a business trip. The second was the footballer who was transferred to Spain and the third a Maltese national who remains in ICU. However, the Genoa's hospital laboratory has indicated that they believe the isolates from the three patients most likely are not the same strain as one was colistin-resistant but the other two, one of which was the businessman, were colistin-susceptible as indicated by the gradient test (E-test).
        - **What do you think should be done at this point? Should all patient transfers from outside countries be banned to the hospital?**
        - **What should be the message to the public- is this a problem of only public interest because the case involves a famous footballer?**
        - **What do you think should be done to examine the extent of hvKp spread in the hospital at this point?**
    - **13- December 2022** The Genoa's hospital is a specialised hospital with expertise in traumatology and orthopaedics. The orthopaedic ward has 48 beds with a high turnover of admissions. Patients are often being admitted from foreign hospitals to undergo specialised operations. The IPC team has initiated screening within the hospital to identify further cases. Among the patients admitted to the same surgical ward at the same time as the businessman and the football player, two were from Malta, one from Greece, one from Portugal and one from Turkey as well as 20 Italian patients. The Greek, Portuguese and Turkish patients have since returned home for further treatment and recuperation. A Maltese patient has repeatedly requested to transfer from the Genoa's hospital in Italy to one in his home city of Valletta, Malta. His relatives are asking when he will be transferred and are pressing the hospital and the Maltese authorities for an answer. They are threatening to go to the press. Doctors in Genoa confirm there is no medical reason why he cannot be transferred other than they are awaiting the confirmation of whether he is carrying the carbapenem-resistant strain of *Klebsiella pneumoniae* which is expected soon.

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- **13 DECEMBER 2022: PUBLIC HEALTH MATTERS Post on Facebook:**Should he stay or should he go? Should we allow this patient from Malta to return to his home country knowing that he has may be carrying an antibiotic-resistant superbug? And if we do how can we expect others not to demand the same treatment? A man admitted to the Galliera hospital in Genoa, Italy after a traffic accident has been exposed to a multi-resistant superbug and now may be a carrier able to spread the disease. During his hospital stay, the Maltese patient was admitted to the same intensive care unit and at the same time as the Spanish football player Susso. The footballer later developed sepsis and acquired an antibiotic-resistant infection from somewhere. One other patient from the same ICU also died. The Maltese patient does not show any symptoms and seems to be recovering well but may still be carrying this deadly disease. After a 14-day confinement, the patient is ready to be released and fly back to Malta. Given the increasing numbers of antibiotic-resistance cases acquired through hospitals and other healthcare facilities, this patient remains a risk to other patients and hospital staff. Carbapenem-resistant bugs, the same bacteria the Maltese patient may be infected with, is known to be the “nightmare bacteria” because it is resistant to almost all antibiotics, extremely difficult to treat and fatal, in most cases. We are risking the lives of many in Malta, a country that already has an increasing number of hospital-acquired antibiotic-resistant cases, if we allow this patient to return. He should stay in Italy until he is completely cured from said bacteria. And that should be a rule applied to all such cases. The solution to antibiotic resistance is as difficult as they come. Experts do not believe that inventing new antibiotics can help – they are very expensive and only perpetuate the cycle of bacteria developing resistance to every new drug. This leaves doctors, hospitals, public health officials with saving the effective antibiotics for when they’re really needed. Concretely speaking, that means improving vaccines uptake (for flu, for example) and clean water to keep people from getting sick in the first place and not prescribing antibiotics for colds.
    - **Should the patient be allowed to return to Malta? If so, what conditions should be required and who decides?**
    - **What needs to be communicated to the public?**

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    - [ ] **How should the treatment recommendations be communicated? Just in the institution, countrywide, or internationally? What needs to be communicated to the public?**
    - [ ] **Your pharmacy reports that ceftazidime-avibactam is now out of stock and they have been unsuccessful if finding an alternative supplier. Does this change your treatment recommendations?**

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- **22 December 2022 .** A screen of medical staff in the Genoa's hospital has revealed that a Romanian nurse is colonised with the Klebsiella pneumonia strain. This nurse has recently arrived in Italy having previously worked in Romania for several years at the University Hospital in Bucarest. The nurse has been in Italy for approximately three months and is currently working two jobs, one at the Genoa's hospital and one at a private clinic specialising in plastic surgery. A highly respected Croatian plastic surgeon runs this clinic attracting many patients from Italy and Croatia where he has multiple clinicns he visits to conduct surgical procedures. He also has his original clinic in Zagreb which he runs with his partner. Many Polish patients have their initial consultation in this clinic in Zagreb but the procedure is then carried out in the other two clinics before returning to Polam for convalescence.
    - **Should the Ukranian doctor be contacted? What is Italy's obligation to control medical practices in the Ukraine? Should the information be released to the public?**
- **22 December 2022.** Whole genome sequencing (WGS) of the hvCRKP isolates has been performed at the reference laboratory in Italy. All the isolates are K1-, magA-, rmpA- and rmpA2-positive, confirming the hypervirulent phenotype. The isolates are confirmed as pandrug- resistant, producing the NDM-1 and OXA-48 carbapenemases, and expressing the mcr-2 gene. In silico analysis of multilocus sequence typing (MLST) shows that the strain belongs to sequence type 23 (ST23).
- **22 December 2022:** The Maltese patient (60 yo male) is at home in Malta, having recently been in the Genoa's hospital in Italy, recovering from the orthopaedic operation but otherwise in good health. A screening culture is performed and he is positive for CRKP. The isolate is tested by the hospital laboratory and is confirmed to be hvCRKP by the “string test”
    - **How does this new information change previous decisions- i.e. about therapy recommendations, accepting patients from hospitals previously identified to have the hvKP strain?**
- **3 January 2023:** A plastic surgeon who operates a network of private reconstructive (plastic) surgery clinics in Genoa, Italy; Split, Croatia and Kiev, Ukraine is requesting advice and support. He has been advised one of his employees, a nurse working in acute care, has been identified as a carrier of the hvCRKP strain following a screen at the Genoa's Hospital where she also works. He is seeking advice on what measures to take in his clinics. He is also concerned his business may be damaged if news of this incident leaks to the press.
    - **How can the public be appropriately informed without impacting on the business of the plastic surgeon?**
- The wife of the Maltese national (34 yo male), who remains in ICU in the Genoa's hospital, is found to be carrying the hypervirulent CRKP strain by WGS. She is 36 weeks pregnant. It has been a difficult pregnancy and her obstetrician is planning for a caesarian section due to her pre-eclampsia in the coming days. The maternity hospital is looking for advice.
    - **Do you think the patient and newborn should receive prophylactic antibiotics?**
    - **If this case was leaked to the press, what would be your strategy to provide appropriate information?**

Group 3-Greece

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- **Start:** Klebsiella pneumoniae is known to cause healthcare-associated infections and is commonly multidrug-resistant. A new variant of K. pneumoniae, designated as hypervirulent K. pneumoniae (hvKP), was first described in 1986 in Taiwan in patients with community-acquired K. pneumoniae infections. The hvKP strains exhibit unique features, such as a striking capacity to cause serious infections in immunocompetent and healthy individuals. Such infections include pyogenic liver abscesses and metastatic infections, such as meningitis and endophthalmitis. hvKP exhibits a hypermucoviscous phenotype that can be identified in the laboratory by a positive “string test.” After this first description of hvKP, additional reports followed and hvKP has been since reported in Asia, South America, North America, the Middle East, Europe, Africa, and Australia. Increasingly, carbapenem resistance in hvKP isolates is being reported, especially from China. Combined with the increased virulence of hvKP strains, the emergence of carbapenem resistance is an additional cause for concern that indicates a need for preparedness.
  - **12 December 2022:** A Greek male (21-year-old) was transferred 10 days ago from the Genoa's Hospital in Italy. He is suffering from paraplegia after an accident three years ago and has undergone multiple surgical interventions because of recurrent pelvic osteomyelitis. He is now hospitalised in a private hospital in Athens with fulminant sepsis. Active screening with rectal swabs has been initiated. Three patients, one from Albania, one from Montenegro and the third from Athens are sharing the same room and all are positive for hvCRKP. The carriers remain in the same room with dedicated nursing staff (patient and nurse cohorting). Contact precautions are implemented.
  - **12 December 2022:** A second patient transferred from the Hospital in Genoa, Italy to Greece 10 days ago was a 62-year-old male who suffered from recurrent pelvic osteomyelitis. He is currently hospitalised in the ICU in the with fulminant sepsis, high fever and confusion having been transferred from a geriatric medicine ward in the same hospital when he became seriously ill. Active screening with rectal swabs has been initiated.
    - **What do you think should be done at this point? Should all patient transfers from outside countries be banned to the hospital?**
    - **What do you think should be done to examine the extent of hvKp spread in the hospital at this point**
  - **13 December 2022: Editorial Comment Popular Science Journal:**Cases of CRE-Klebsiella pneumoniae found in Italian hospital: After conducting initial tests, the infection and prevention control team of Geona's Hospital, Italy identified three patients infected with Carbapenam-resistant Klebsiella pneumoniae in its surgical ward. Carbapenam-resistant Klebsiella pneumoniae has also been found in a Madrid's Hospital in Spain where a Spanish footballer and one other patients died according to representatives of said hospital in Madrid. The footballer was of course recently transferred between the two hospitals. So are we now dealing with a multi-country outbreak? Three further cases of infection with Carbapenam-resistant Klebsiella pneumoniae have since been discovered in this same hospital in Genoa. Genoa's hospital specialises in trauma and orthopaedics, has a high turnover of patients and often admits patients from abroad. This heightens the risk of spreading infections like carbapenam-resistant Klebsiella pneumoniae , and other antibiotic-resistant bacteria. These incidents are alarming since antibiotic-resistance already causes 33,000 deaths in the EU alone, according the European Centre for Disease Prevention and Control (ECDC). The EU agency also recently reported 8.9 million healthcare-associated infections occurring each year in both hospitals and long-term care facilities. The emergence of bacteria resistant to multiple groups of antibiotics is particularly concerning, as infections due to these bacteria can be severe, costly and even fatal. Up to 50% of all antibiotic use in European hospitals is unnecessary or inappropriate, the report stated.

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- **13 DECEMBER 2022: PUBLIC HEALTH MATTERS Post on Facebook:**Should he stay or should he go? Should we allow this patient from Malta to return to his home country knowing that he has may be carrying an antibiotic-resistant superbug? And if we do how can we expect others not to demand the same treatment? A man admitted to the Galliera hospital in Genoa, Italy after a traffic accident has been exposed to a multi-resistant superbug and now may be a carrier able to spread the disease. During his hospital stay, the Maltese patient was admitted to the same intensive care unit and at the same time as the Spanish football player Susso. The footballer later developed sepsis and acquired an antibiotic-resistant infection from somewhere. One other patient from the same ICU also died. The Maltese patient does not show any symptoms and seems to be recovering well but may still be carrying this deadly disease. After a 14-day confinement, the patient is ready to be released and fly back to Malta. Given the increasing numbers of antibiotic-resistance cases acquired through hospitals and other healthcare facilities, this patient remains a risk to other patients and hospital staff. Carbapenem-resistant bugs, the same bacteria the Maltese patient may be infected with, is known to be the "nightmare bacteria" because it is resistant to almost all antibiotics, extremely difficult to treat and fatal, in most cases. We are risking the lives of many in Malta, a country that already has an increasing number of hospital-acquired antibiotic-resistant cases, if we allow this patient to return. He should stay in Italy until he is completely cured from said bacteria. And that should be a rule applied to all such cases. The solution to antibiotic resistance is as difficult as they come. Experts do not believe that inventing new antibiotics can help – they are very expensive and only perpetuate the cycle of bacteria developing resistance to every new drug. This leaves doctors, hospitals, public health officials with saving the effective antibiotics for when they're really needed. Concretely speaking, that means improving vaccines uptake (for flu, for example) and clean water to keep people from getting sick in the first place and not prescribing antibiotics for colds.
  - [ ] **What do you think should be done at this point? Should all patient transfers from outside countries be banned to the hospital?**
  - [ ] **Should guidelines be developed for diagnosis (i.e. case definition), management and treatment of the infection?**
  - [ ] **How should the treatment recommendations be communicated? Just in the institution, countrywide, or internationally? Should the public be informed?**
- [ ] **20 December 2022**: Three other Greek nationals in the geriatric medicine ward are also found to be positive for hvCRKP by the string test. Contact precautions have been implemented.
- [ ] **20 December 2022** Extensive screening in the University Hospital has identified two cases of hvCRKP colonisation, one in a healthcare worker in a surgical ward and one in a patient in an orthopaedic ward, both by string test. Samples have been sent for whole genome sequencing and results are awaited.

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- **20 December 2022: ALERT FROM THE EUROPEAN CENTER FOR DISEASE PREVENTION AND CONTROL:** A Multi-country outbreak of severe sepsis and multi-organ abscesses with hyper-virulent carbapenem-resistant Klebsiella pneumoniae (hvCRKP) has been reported in Spain, Italy and Greece. Although the situation is rapidly evolving, the following cases have been confirmed since 12 December**: In Spain** two fatal cases of carbapenem-resistant Klebsiella pneumoniae (CRKP) infection in two young, previously healthy adults in the hospital. One patient was transferred three days earlier from the hospital in Genoa 13 December, A third 43-year-old male patient with fulminant meningitis with CRKP is being treated in the ICU of the same hospital in Madrid. A review of Klebsiella pneumoniae isolates at the laboratory identifies three additional isolates from three different patients in the last fifteen days. Screening of all patients admitted in the ICU of the Hospital Universitario identified one more patient carrying carbapenem-resistant Klebsiella pneumoniae. The patient had no active infection. The strain was sent for further testing. **In Italy:** The Hospital in Genoa had three cases with carbapenem resistant Klebsiella pneumoniae sepsis in the surgical ward in the last fifteen days. A businessman, who had transferred three weeks ago from a University Hospital in Bulgaria,a footballer who was transferred to Spain and died, and a third a Maltese national (34-years-old male) who remains in ICU. – Italy has more patients admitted to the same surgical ward as the businessman and the football player, two from Malta, one from Greece, one from Portugal and one from Turkey. The Greek, Portuguese and Turkish patients have since returned home for further treatment and recuperation. **In Greece:** Two Greek patients with pelvic osteomyelitis who underwent treatment in Genoa and were transferred for further care in Athens have developed sepsis due to a hypervirulent, pan-drug resistant strain of *Klebsiella pneumonia*. After extensive screening, of hospitalized patients, an additional 2 patients in the geriatric ward, 1 patient in a surgical ward, and one healthcareworker was found to be positive. Initial genome sequencing of the first available isolates have identified multiple genes associated with a hypervirulent genomic signature (K1-, magA-, rmpA- and rmpA2) and resistance to carbapenems (NDM-1, OXA-48), cephalosporins beta-lactam/beta-lactamase inhibitors (OXA-48) and colistin (mcr-2). Ceftazidime-avibactam (2.5 grams IV infused over 3 hours) + aztreonam 2 grams IV infused over 3 hours) infused together every 8 hours is currently recommended as treatment until further data become available. Any hospital with a recent case of carbapenem and colistin-resistant Klebsiella pneumonia, or patients transferred from the affected hospitals should undertake screening precautions of patients and healthcare workerAppropriate protective and isolation precautions are recommended for any patient known to be colonised of infected with these Klebsiella pneumoniae strains. Travel should be discouragd. Further data will be communicated as it becomes available
  - [ ] **How does this new information change previous decisions- i.e. about therapy recommendations, accepting patients from hospitals previously identified to have the hvKP strain?**
  - [ ] **How should the treatment recommendations be communicated? Just in the institution, countrywide, or internationally? What needs to be communicated to the public?**
  - [ ] **Your pharmacy reports that ceftazidime-avibactam is now out of stock and they have been unsuccessful if finding an alternative supplier**

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- **26 December 2022:** The Greek patient with fulminant sepsis and positive for hvCRKP hospitalised in a private hospital in Athens has sadly died. The Albanian and Montenegran patients who had been sharing the same room and are now carrying the hvCRKP strain are insisting on returning to their home countries immediately and have been in touch directly with their embassies. The private hospital in Athens is looking for advice on what actions to take. The embassies are also seeking information to support their citizens repatriation.
- **26 December 2022**: Whole genome sequencing (WGS) of the hvCRKP Greek isolates has been performed. All the isolates are K1-, magA-, rmpA- and rmpA2-positive, confirming the hypervirulent phenotype. The isolates are confirmed as pandrug- resistant, producing the NDM-1 and OXA-48 carbapenemases, and expressing the mcr-2 gene. In silico analysis of multi locus sequence typing (MLST) shows that the strain belongs to sequence type 23 (ST23).
  - [ ] **Should the patients be allowed to travel?**
  - [ ] **How will the patients be at risk for infection once they return home?**
- Two patients in a geriatric medicine ward, both positive for hvCRKP by the string test with the results from further confirmatory tests linking them to the wider outbreak reported in Italy and Spain awaited, are about to be discharged. One is returning to his village to work in the family hotel and restaurant. The other is returning to his residential home which he shares with 80 other residents over the age of 70.
  - [ ] **Should the patients be allowed to return to return to work or the residential home? If so what type of precautions need to be taken?**
- **3 January 2023:** A plastic surgeon who operates a network of private reconstructive (plastic) surgery clinics in Genoa, Italy; Split, Croatia and Athens Greece is requesting advice and support. He has been advised one of his employees, a nurse working in acute care in an Athens Hospital, has been identified as a carrier of the hvCRKP strain following a screen at the hospital. He is seeking advice on what measures to take in his clinics. He is also concerned his business may be damaged if news of this incident leaks to the press.
  - [ ] **How can the risks be appropriately managed? What type of information would you need to make this decision? Can the public be informed without impacting on the business of the plastic surgeon? How does the fact that this medical provider is performing non-urgent heathcare procedures affect your decisions?**

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