Acute and Chronic Infections of the Gastrointestinal Tract

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Question 1: Is there an indication for postoperative antibiotic prophylaxis in visceral surgery?

Eckmann: Perioperative antibiotic prophylaxis (PAP) has one aim: to prevent a postoperative wound infection. To reach that goal, high tissue concentration of the administered antibiotic(s) should be achieved during the procedure and not before or after the operation. Therefore, a postoperative continuation of PAP cannot be useful, although it is still often prescribed by surgeons. To the best of my knowledge, there is no data showing any superiority of postoperative prophylaxis in comparison to regimen where PAP was completely discontinued postoperatively. Postoperative antibiotic prophylaxis should be avoided.

Keck: Meta-analyses of different surgical procedures demonstrate no effect of extended PAP after wound closure. Prolongation of antibiotic treatment is necessary when administered in a therapeutic fashion (peritonitis, perforation), however, not as postoperative antibiotic prophylaxis.

Rodloff: In general, it has been shown that there is no indication for prolonged PAP since antibiotics only prior to surgery or in the early phase of surgery are effective in preventing postoperative wound infections. When the wound is sutured, exogenous bacteria cannot invade the vulnerable tissue any longer.

On the other hand, one has to clearly distinguish between preoperative prophylaxis and the necessity of therapy for an established infection that has been recognized during the surgical procedure.

Schlöricke/Hoffmann: Cultural factors have been proposed as important drivers of inappropriate antibiotic prescribing

within community care. These studies have identified the cultural anthropological dimension of uncertainty avoidance (UA) as being particularly relevant in explaining why doctors in some European countries have a greater propensity to prescribe antibiotics for predominantly viral conditions, such as colds, flu, and sore throat, in the face of clear scientific evidence. UA is described in the Geert Hofstede model of cultural dimension as a construct estimating the extent to which a society tolerates uncertainty and ambiguity. Such cultures often try to counteract the unease created by situations of uncertainty through the adoption of dogmatic and excessive measure, even when there is no evidence of cost-effectiveness or risk attenuation. There is no evidence to support postoperative prophylaxis.

Question 2: Do we need antibiotic therapy in acute cholecystitis?

Eckmann: That depends on the individual case: In perforated, gangrenous cholecystitis as well as in immunocompromised patients, a short-term therapy (3–5 days) might be useful postoperatively after cholecystectomy in order to treat an infection of the abdominal cavity and/or to avoid septic complications. According to the results of the AC/DC (acute cholecystitis/delayed cholecystectomy) trial, most of the cases with acute cholecystitis and without substantial comorbidity should be treated surgically with cholecystectomy within 24 h after admission. Usually, these patients do not need additional antibiotic therapy beside the perioperative single shot. Nevertheless, patients with ASA (American Society of Anesthesiologists) score III and IV do have higher postoperative complication rates. In this subcollective, a conservative approach with antibiotics can be beneficial.

Keck: Apart from perioperative prophylaxis, antibiotic chemotherapy for acute cholecystitis cannot be recommended for the general case. On the contrary, all efforts have pursued the aim that the patient is operated soon. From recent studies (AC/DC) there is level 1 evidence that operation should be preferred before chemotherapeutic treatment of acute cholecystitis. Again, antibiotic treatment in severe cases after the operation might be necessary due to peritonitis or sepsis. Only for the rare case of inoperability due to severe comorbidities, antibiotic therapy and a therapeutic interventional transhepatic puncture and drainage of the gallbladder may be an option.

Rodloff: Once the gallbladder has been surgically removed, it seems unnecessary to administer supportive antimicrobial therapy. However, if the cholecystitis has inflamed the adjacent tissue and a local peritonitis is apparent, antibiotic therapy against enterobacteriaceae, enterococci, and anaerobes might be helpful. Due to the risk for *Candida* infection in the upper gastrointestinal tract, surgery should be included.

Schlörcke/Hoffmann: PAP in patients with acute cholecystitis is undisputed and supported by level 1 evidence. Elevated laboratory parameters indicative of systemic inflammation, intraoperative findings, and the patient's comorbidities are parameters that must be taken into account in the decision for or against a postoperative antibiotic therapy in acute cholecystitis.

In patients with a mild or moderate cholecystitis (grades I and II), a continuation of the antibiotic therapy is not necessary. Patients with a high risk due to immunosuppression (corticosteroids, diabetes mellitus, and active malignancy) and with a moderate cholecystitis may need a continuation of the antibiotic therapy. The decision should be made on an individual basis.

Patients with a severe acute cholecystitis (grade III) who also have systemic inflammatory response syndrome (SIRS) and multiple-organ failure (MOF) must be treated with antibiotic therapy after the operation.

Question 3: When should antimicrobial therapy in necrotizing pancreatitis be started, when should it be stopped?

Eckmann: A decade ago, the majority of colleagues administered antibiotics in patients with severe necrotizing pancreatitis soon after the admission in order to prevent septic complications and to reduce mortality. 'This party is over' since it has been shown in large trials that a prophylactic approach did not influence morbidity and mortality but promoted the development of antibiotic resistance. Today, antimicrobial therapy should be initiated only if an infection is microbiologically proven, which usually occurs 2–3 weeks

after the disease has started. Usually, a course of 7 days is effective in most of the patients. If the antibiotics have not shown any effect so far they will not work after an additional 5–7 days.

Keck: In fact, too many patients with a necrotizing pancreatitis on the intensive care unit (ICU) are treated with antimicrobial chemotherapy. Meta-analyses did not show an advantage of prophylactic antibiotic treatment of necrotizing acute pancreatitis with regard to septic complications or survival. If there are signs of infection of the pancreatic necrosis, such as septic deterioration of the patient or air in the tissue on CT imaging, antibiotic treatment after bacterial culture from the peripancreatic fluid or a fine-needle aspiration of the pancreas should be performed. Today, necrotizing pancreatitis is often treated by minimally invasive techniques such as retroperitoneal necrosectomy or endoscopic transgastric necrosectomy. Both procedures offer the opportunity to obtain microbiological samples. In infected necrotizing pancreatitis, there is a clear indication for antimicrobial chemotherapy.

We do not have any data as to how long we should treat a polymicrobial infection in patients with necrotizing pancreatitis. Naturally, we must let us guide by the clinical picture of the patient. With the declining of the infection parameters, the indication of antibiotic therapy has to be considered daily. With a deterioration of the patient, new or repeated microbiological cultures during a phase of discontinuation of antibiotic treatment might clarify the need for a shift of antibiotic therapy or the need for antifungal therapy.

Rodloff: In the past, study results in necrotizing pancreatitis have been controversially discussed to which extent antibiotic chemotherapy may be helpful.

Prior to therapy, a fine-needle aspiration of the possibly infected tissue should be performed to guide antimicrobial therapy. Uninfected necrosis did not seem to necessitate chemotherapy.

Schlörcke/Hoffmann: There is an ongoing discussion on antibiotic prophylaxis in necrotizing pancreatitis. Different guidelines recommend the initiation of antibiotic therapy in patients with infected necrosis. Theoretically, the individual outcome of the patient may be worsened by the selection of Gram-positive or -negative bacteria because of unnecessary antibiotic therapy. Another remark is the development of fungal infections during the course of broad-spectrum antibiotic therapy.

From our point of view, a broad-spectrum antibiotic therapy must be initiated together with the stabilization of the patient. Together with antibiotic coverage, a retroperitoneal necrosectomy with adequate drainage of the remaining tissue should be the goal of every therapy. As in other septic disease, a prolonged antibiotic therapy after a period of 7 days following the control of the infectious focus is not nec-

essary. Some studies investigate the sole use of antibiotic therapy in necrotizing pancreatitis. From the authors' point of view it is unlikely that these studies will result in non-inferior or superior results compared to a combination of surgery and antibiotic therapy. Necrotic tissues have a poor vascular supply; thus, the local bioavailability of the antibiotics will be very low.

Question 4: How do you treat an intra-abdominal abscess? Interventionally (sonography, computed tomography (CT)), surgically, or with antibiotics?

Eckmann: The old latin rule 'ubi pus, ibi evacua' ('wherever you find pus, evacuate it') is still applicable today. Any abscess means that the immune system of the patient was able to build up a wall between the area of infection and the rest of the body. This makes it difficult for antibiotics to penetrate into the abscess. Therefore, CT-controlled drainage of an intra-abdominal abscess is always preferred. It has been shown to be successful in up to 90% of all cases. We initiate antibiotic therapy only if the infection has caused septic complications (severe sepsis, septic shock) or if resistant species are involved.

Keck: The therapy of choice is an interventional drainage of the abscess either guided by sonography or CT. If the drainage is unsuccessful, an open surgical procedure is necessary, as the source of infection, here an abscess, has to be eliminated. An indication for antibiotic therapy in patients with an intra-abdominal abscess is not needful and will not be successful in the majority of cases.

Rodloff: The therapy of an intra-abdominal abscess lies in the hands of the interventionists. Abscesses may not be penetrated by antimicrobial agents.

Thus, drainage and lavage is necessary. In the process of clearing, it may be helpful to start with systemic antimicrobials. This may also prevent hematogenous spreading.

Schlörcke/Hoffmann: Complete and adequate source control is pivotal for the patients' outcome. Interventional techniques are associated with good results in patients with distinct fluid collections with respective density values. Prior to any intervention it is mandatory to have an interdisciplinary discussion of the radiologic images and clinical parameters of the patient. Because of the significantly reduced access trauma with reduced morbidity and mortality, interventional techniques are also the primary option in patients on the ICU or with several risk factors in whom a surgical therapy is often only the second-best option. An operation is often necessary in patients with fluid collections that are indistinct, constituted of several cells, or not accessible for interventional measures due to their localization. Extended

necrosis, patients with images and clinical signs indicative of hollow viscous perforation, and peritonitis must be treated with an operation. Antibiotic therapy to achieve source control is not justified without the usage of interventional or surgical therapy.

Question 5: What are the criteria for antifungal treatment in necrotizing pancreatitis?

Eckmann: To date, there is no reason to start antifungal prophylaxis in non-immunocompromised patients. In cases of colonization with *Candida* spp. on multiple sites in addition to substantial risk factors (recent repetitive abdominal surgery, ICU stay >7 days, total parenteral nutrition), a pre-emptive initiation in critically ill, hemodynamically unstable patients appears to be useful. Patients on the ICU with isolation of fungi from pancreatic necroses have to be treated, preferably with echinocandins.

Keck: No study offers an advantage of antifungal prophylaxis and empiric or pre-emptive antifungal therapy in patients with necrotizing pancreatitis. The risk of fungoid infection in acute necrotizing pancreatitis is high due to prolonged antibiotic therapy.

If *Candida* spp. is microbiologically or histologically proven, antifungal therapy should be initiated. Azoles or echinocandins should be administered according to the different species of *Candida*.

Rodloff: Whenever fine-needle aspiration results in culture positivity for *Candida* species, antifungal therapy should be immediately delivered.

Alternatively, positive results in antigen testing could guide therapy. Molecular techniques are so far not validated for *Candida* infections in the abdomen.

Polymerase chain reaction (PCR) results might be false-positive.

Schlörcke/Hoffmann: Pancreatic necroses constitute an ideal environment for the growth of fungi. The superinfection of pancreatic necroses with fungi is associated with a worsening of the prognosis of the individual patient. Antifungal therapy must always be initiated with any positive intra- or retroperitoneal microbiology specimen. This is independent from the quantity of fungi detected in the specimens. If *Candida albicans* is proven, fluconazole is the drug of choice. In patients with resistant *Candida* species against fluconazole for antimycotic treatment, echinocandins are recommended. Patients with necrotizing pancreatitis are critically ill. For reasons of broader spectrum and cause of the lower toxicity, echinocandins might be the first-line therapy.

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