CORRESPONDENCE

Clostridium Difficile Infection— Guideline-Based Diagnosis and Treatment

by Dr. med. Christoph Lübbert, Dr. med. Endres John, Prof. Dr. med. Lutz von Müller
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4. Magill SS, Edwards JR, Bamberg W, et al.: Multistate point-prevalence survey of health care-associated infections. *N Engl J Med* 2014; 370: 1198–208.

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Conflict of interest statement
The author declares that no conflict of interest exists.

Epidemiology of Clostridium Difficile Infection

According to Lübbert et al., the incidence of Clostridium difficile infection (CDI) in Germany is 5 to 20 cases per 100 000 persons (1). It can be assumed that this figure is much too low. An ecological study based on routine data identified a total of 9874 cases hospitalized because of CDI, as well as further 26 341 cases with CDI as a concomitant disease in 2006 (2). Prior to this, a dramatic increase in case numbers was observed since 2003. In parallel to these developments, the number of in-patient cases with adverse drug events (ADEs) increased in Germany to at least 5%. A secondary analysis for 2006 identified CDI consistently for the United States, United Kingdom and Germany as the most common ADE in hospitals reliably coded in routine data (3).

According to the publicly reported data of the Institute for the Hospital Remuneration System (InEK), 20 173 cases were hospitalized to receive treatment for CDI in 2012. CDI was reported as a concomitant disease in 46 119 cases treated. These figures, just like those cited above, include only so-called “inliers” which account for 77% of all cases. Based on this and provided CDI occurs only once a year, the lowest estimate of its incidence in Germany is 82 cases per 100 000 persons. This figure is in line with the incidence reported in a recent review of US patient file data (4).

The limitations of additional documentation requirements are evidenced by the difference between the CDI data provided by established reporting systems and those derived from routine data. It would be wrong to expect that service providers will collect identical data for public purposes several times, especially not in better quality. Consequently, routine data should be used for surveillance at a broader scale.

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Duodenal Application Is the Method of Choice

We would like to thank the authors for their insightful review of Clostridium difficile infection (CDI) (1) and to add the following information to complement the section about stool transplantation: At the SRH Kurpfalz Hospital, 22 stool transplantations (allogenic intestinal recolonizations) have been performed to treat CDI to date. In all of these cases, donor feces was infused exclusively into the duodenum using an endoscope, in line with the method described by van Nood (2). The clinical response rate was comparable with published data; 16 of 17 patients were relapse-free during the 3-month follow-up period.

Due to the pooling of the data on gastric and duodenal administration, no inferiority of the antegrade versus the retrograde route of administration can be derived from Table 3. In contrast to the information provided in the table, the 18 patients of Aas et al. (3) received the fecal suspension by gastric delivery. Thus, in 3 of 6 studies (45 of 101 patients) gastric application of the fecal suspension was performed, involving the risk of aspiration pneumonia by fecal bacteria, besides the inactivation of the donor microbiota by gastric acid. Another significant difference in the methods used is the preceding bowel lavage which, among the studies with antegrade application, was only used in the study by van Nood which was also the only randomized controlled trial (2). Colonoscopic application is more taxing for the patient and associated with the risk of perforation of the inflamed colon. Provided the patients receive sedation with propofol, the acceptance is excellent. The passage of the donor microbiota through the small intestine does not represent an undesirable contamination but is rather seen as favorable, as it accelerates the reconstitution of the resident microbiota. Thus, we consider duodenal application after peroral bowel lavage as described by van Nood as the reference method until other data from randomized trials have become available. DOI: 10.3238/arztebl.2015.0345b

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In Reply:

In our article (1), the recommendations for and dosing of the drugs to treat *Clostridium difficile* infection are based on the current European guidelines (2). However, treatment with oral metronidazole requires some minor modification to reflect the special situation in Germany where the oral formulation of metronidazole contains only 400 mg. With no oral 500 mg formulation available, uncomplicated *Clostridium difficile* infection (CDI) should be treated with 400 mg four times a day (1600 mg daily) instead with the internationally recommended oral metronidazole dose of 500 mg three times a day (1500 mg daily).

Frequently, questions about vancomycin-tapering treatment for relapse are asked. The proposed regime is based on the few case series available (2, 3) and starts after the 2-week induction therapy with an oral vancomycin dose of 250 mg four times daily. The tapering period starts with an oral vancomycin dose of 250 mg twice a day over 7 days, followed by an oral dose of 250 mg once a day for further 7 days. Subsequently, the patient is treated with oral doses of 250 mg every 48 hours (altogether 4 doses), followed by oral doses of 250 mg every 72 hours (five doses).

Regarding the epidemiology of *C. difficile*—We appreciate Professor Stausberg's comment on the epidemiological significance of *C. difficile* in Germany which is still underestimated. The evaluation of routine data from the DRG system (Institute for the Hospital Remuneration System, INEK) and health insurances definitely help to estimate the incidence density rate (4). However, prompt detection of infection and outbreak events with the potential to respond can only be achieved when CDI becomes a notifiable disease based on mandatory reporting strategies; some European countries have already embraced and done this step.

Optimization of microbiota transfer—Microbiota transfer ("stool transplantation") for relapsing CDI is an attractive causal treatment. Our review showed that

both antegrade and retrograde application are feasible options for microbiota transfer; here the advantages and disadvantages of the two routes of application are to be considered based on personal experiences, as highlighted by Dr. Ehlermann. Consequently, the best route of application should be decided individually for each patient, taking into account the special experiences of the center and any risk factors the patient may have. It can be expected that in the next years microbiota transfers will be further simplified and optimized, and defined bacterial mixtures will be approved as oral medicines in the future. As a first step to simplify the application of donor microbiota, fecal samples will be packed and cryopreserved in capsules for easy oral administration (5). This approach has the potential to achieve a comparable treatment success without invasive interventions. DOI: 10.3238/arztbl.2015.0346

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Conflict of interest statement

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