15 Dosage of Antibiotics in Impaired Renal Function

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Principles:

Individual variation: Even when following the dosage tables, some patients can always show divergent serum concentrations, since metabolism, excretion, albumin binding, etc. can vary markedly on an individual basis. Particularly substances with a narrow therapeutic range (e.g. aminoglycosides) must be closely monitored.

Children: The dosage tables are constructed for adults with steady-state impairment of renal function. Therefore, they are generally not valid for children.

Elderly patients: In old age the glomerular filtration rate decreases, and with it the excretion of many antibiotics. The dosages given for adults are valid up to the age of around 65 years. All dosages can be reduced by 10% in patients over 65, by 20% in those over 75, and by 30% in those over 85. More exact dosages can be derived by calculating the glomerular filtration rate (creatinine clearance).

Estimation of creatinine clearance (CrCl): A 24-h urine sample for calculation of creatinine clearance is rarely available and is usually not necessary for dose adaptation of antibiotics. In patients over 60 years of age or with creatinine >1 mg/dl or with body weight (BW) under 60 kg, however, it is indispensable to estimate the CrCl by means of the stable serum creatinine level (mg/dl) according to Cockcroft and Gault:

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\text{Creatinine clearance} = \frac{140 - \text{age}}{\text{serum creatinine}} \times \frac{\text{BW}}{72} \times 0.85 \text{ for women}
\]

Note:
1. The estimation of creatinine clearance is mandatory for the determination of maintaining dose of antibiotics. Calculation of dosage derived from serum creatinine is inappropriate since height, weight and gender influence the creatinine value. At a serum creatinine level of 1 mg/dl a 20-year-old man has a CrCl of 120 ml/min, but a 90-year-old man has a CrCl of 50 ml/min! A cachectic 90-year-old man weighing only 36 kg has a CrCl of only 25 ml/min! In a woman of the same age and weight the muscle mass is 15% lower, so the CrCl is 25×0.85=21.35 ml/min.

2. Alternatively the MDRD equation is used by many laboratories for creatinine clearance calculation. This equation, however, should only be used in cases where the CrCl value is below 50 ml/min. It should not be used for CrCl values within the normal range because this would lead to CrCl underestimation and therefore underdosage of the antibiotic. Many laboratory reports include “CrCl (MDRD: 4-variable Modification of Diet in Renal Disease)”. These CrCl values can also be used at a CrCl <50 ml/min.

Note:
The most frequent overdosages are those where serum creatinine is “almost normal” and the CrCl is falsely estimated as “normal=100 ml/min”.

Note:
Only stable serum creatinine values should be used. Even in anuria (CrCl=0 ml/min) serum creatinine rises by only 1–1.5 mg/dl per day. Although the CrCl is obviously zero, the creatinine level (albeit rising) may be as little as 2 mg/dl!

Rules for dose adaptation in renal insufficiency:
- **Renal and/or hepatic elimination:** The maintenance dose must be reduced for antibiotics that are eliminated largely renally rather than mostly via the liver.
- **Initial dose unchanged:** The size of the first dose of a medicinal drug depends on its distribution volume (e.g. 2 mg/kg