Beta-lactam antibiotics

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Constantin Cojocel passed away in 2007.
This chapter was updated by the editors.
The editors wish to dedicate this chapter to his memory.

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Introduction

The large family of β-lactams comprises penicillins, cephalosporins, cephamycins, monobactams, carbacephem and carbapenems and are so named since they all containing the β-lactam moiety.

Penicillin was the first β-lactam antibiotic and was discovered in 1928 by Sir Alexander Fleming at St. Mary's Hospital, London [1]. The β-lactam chemical structure for penicillin was first proposed by Abraham and Chain in 1943 and finally established in 1945 by X-ray crystallographic analysis. In the same year, Giuseppe Brotzu, a Sardinian professor of bacteriology, isolated Cephalosporium acremonium from the sea near a sewage outfall at Cagliari, which produced antibiotic material with a broad spectrum of activity. It was almost eight years later in 1953 when Newton and Abraham, while studying the production of antibiotics by Brotzu’s Cephalosporium, that they discovered a penicillin-like substance providing resistance to hydrolysis by penicillinases which was named cephalosporin C.

By 1959, Rolinson and coworkers completed the isolation of the penicillin nucleus, 6-aminopenicillanic acid, (Figure 1) in quantity. At about the same time the β-lactam-dihydrothiazine structure for the cephalosporin C was proposed [2] and confirmed subsequently by X-ray crystallographic analysis. In 1962, Morin and coworkers established a chemical method for the production of 7-aminocephalosporanic acid (Figure 1) from cephalosporin C in quantity. These developments opened the way to the preparation of a large number of semi-synthetic cephalosporins with hopes of being used as therapeutic agents. Cephalothin was prepared in 1962 and was the first semi-synthetic cephalosporin to find extensive clinical use in the 1960s. Cephalothin was followed by cephaloridine, in which the acetoxy group at C-3' of cephalothin was replaced by a pyridinium group (Figure 2). These cephalosporins were followed by four generation of cephalosporins that are now categorized based on their spectrum of activity.