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Report on the 1st International Symposium on Antibiotic Tissue Concentration

Sils-Maria, Switzerland, January 7–10, 1976

The 1st International Symposium on Antibiotic Tissue Concentration brought together some 40 investigators actively interested in the determination and significance of antibiotics in various tissues, especially in the kidney and prostate, from all over Europe and the United States to present research data, exchange information, and discuss problems on this subject. All papers and the discussion from this symposium will be published in a special supplement to the journal Infection.

The conference opened with the presentation by M. Barza (Boston, Mass., USA) on the concentration of 13 antibiotics in the liver, kidney, bile, and urine of dogs. In his canine model, Barza cannulated the femoral artery and vein as well as the portal, hepatic, and renal veins. After the injection of each antibiotic, he measured and compared the concentration in serum, urine, and bile with the tissue concentration of liver and kidney simultaneously under normal and various pathological conditions.

C. Simon (Kiel, West Germany) discussed the concentration of antibiotics in serum, saliva, tears, and wound fluid. Simon's model was in human volunteers in whom he created a blister after application of a cantharidin cream upon the skin. Subsequently he measured the concentration of antibiotics in the fluid obtained from this blister and compared it with levels found in the serum. This wound fluid has a protein concentration similar to that of serum and does not represent true interstitial fluid.

One of the highlights of the meeting was the discussion by G. D. Chisholm (London, England) on the concentration of antibacterial agents in lymph. The author cannulated the lymphatic channels of the kidney in dogs and, after injection of an antibiotic, measured the concentration in the renal lymph and compared it with the level found in the plasma and in lymph from the thoracic duct. He concluded that because the concentration found in the renal lymph was similar to that found in the serum there could not be a significant diffusion of antibiotic from the high concentration in the urine into the renal interstitium.

H.-U. Eickenberg (Louisville, Ky., USA) described a canine model for obtaining and measuring antibiotic concentrations in renal interstitial fluid. Polypropylene capsules implanted into renal tissue came into equilibrium with the interstitial fluid and were found to contain renal interstitial fluid. In time-concentration studies, various antibiotics were found to be in a much lower concentration in renal interstitial fluid than in the urine but always exceeding that in the serum.

D. Adams (Munich, West Germany) compared the concentration and kinetics of various cephalosporins in human tissue. This was followed by Eickenberg's presentation on antibiotic concentration in prostatic interstitial fluid. Comparing the concentration of various antibiotics in the prostate with the levels found in serum Eickenberg found that the antibiotic level in the prostatic interstitial fluid was always lower than in the serum.

F. Kolb compared the concentration of antibiotics found in wound fluid with the serum levels. These studies were made in patients who underwent operations and in whom the fluid was obtained via a tube draining the operative site.

Daschner (Munich, West Germany) then reported on the antibiotic amikacin (BBK8) in children. He studied 21 children who underwent elective operations and from whom he collected fat and muscle tissue after injection of BBK8 Daschner then assayed the tissue for this antibiotic and demonstrated a lower level in muscle and fat than in serum at all times.

S. Wysock (Heidelberg, West Germany) investigated the tissue concentration of several

antibiotics in 61 patients. The tissues studied were skin, subcutaneous tissue, skeletal muscle and cartilage, heart muscle, and heart valves. He found a surprisingly high concentration of antibiotics in poorly vascularized tissue.

G. Linzenmeier (Essen, West Germany) studied the serum levels of two different cephalosporins in 20 patients on cardiac bypass machines and compared these findings with serum levels in 20 normal patients. This very straightforward test demonstrated a similar concentration for both antibiotics despite a difference in protein binding.

In a second paper, Chisholm characterised the fluid obtained from subcutaneous ,"tissue cages": he emphasised that all of his studies have led to the conclusion that this fluid represents true interstitial tissue fluid and that the antibiotic concentrations in this fluid are representative of those in the interstitium of the soft tissue. He then demonstrated that the significant difference in distribution of penicillins into the "tissue cages" was directly related to their protein binding.

W.A. Craig (Madison, Wisc., USA) emphasized the effects of disease states on serum protein binding of antimicrobial agents. After studying protein binding in human serum in vitro, he concluded that an inhibitor may exist in uraemic patients. Tightly bound to albumin, this inhibitor could be free fatty acid, however, free fatty acid may not cause the basic inhibitory defect but may only accentuate it.

In a classic presentation, K. Naber (Straubing, West Germany) discussed the renal lymph concentration of cephalosporins in relation to protein binding and renal metabolism and distribution. Using a canine model, he studied the levels of various cephalosporins after intravenous infusion in the renal lymph, which he believes is representative of renal interstitial fluid.

Barza further discussed the effect of protein binding on antibiotic distribution and of continuous versus intermittent infusions. He presented two models by which he measured antibiotic concentration representative of that found in interstitial fluid. The fluid was obtained either by a disc dipped into subcutaneous tissue or an autologous blood clot buried in subcutaneous tissue.

The presentation by J.A. Raeburn (Edinburgh, Scotland) on antibiotic concentrations in inflammatory and interstitial fluids described a human model for collecting wound fluid. Following skin abrasion the exudate was absorbed on sterile discs. In addition to measuring the antibiotic concentration in this wound fluid, Raeburn studied various parameters of immune response at the humoral and cellular level to assess the host response against bacterial invasion. In patients with leukaemia, he found lower than normal concentrations of antibiotics; this is the same group of patients found to have a decreased host defense mechanism.

The discussion by P. Madsen (Madison, Wisc., USA) of factors influencing the concentrations of chemotherapeutic agents and antibiotics in prostatic tissue and fluid in dogs and in man was based primarily on the well-established canine model of measuring antibiotic concentration in prostatic secretion which he compared with total tissue concentration. He also presented his findings in a patient with high urinary diversion who provided a large amount of prostatic secretion uncontaminated by urine, which was assayed for antibiotic concentration.

In a paper on antimicrobial tissue binding, Craig pointed out that drugs are not only bound to protein but also to haemoglobin, cell membranes, and even intracellular substances, and that this must be considered when measuring the activity of antibiotics.

The final presentation was by H. Mattie (Leiden, Netherlands) who, when discussing the in vivo significance of antibiotics in the tissues, emphasised the quantification of kinetics of bacterial growth in studying concentrations. He pointed out that the antibiotic concentration should be measured where the bacterial infection takes place.

Marget (Munich, West Germany) summarized the symposium and placed some of the data in perspective. The general consensus was that the new data presented and ideas exchanged at this 1st International Symposium on Antibiotic Tissue Concentration had proved helpful as a basis for future investigation and that the newly developed models for studying tissue pharmacokinetics would lead to more precise and effective clinical use.

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