were taken, and increased frequency of discharge in filaments of these preparations were observed following i.v. administration of taloximine. The electroneurograms were taken from multifilament preparations and could not be expressed in a quantitative manner. This supports the other data indicating that taloximine has a direct action on peripheral chemoreceptors.

appears that the dose that caused respiratory stimulation after reflexogenic area denervation was close to the convulsive dose.

It can be concluded that taloximine acts as a respiratory stimulant predominantly by its actions on the reflexogenic areas, but it also has central nervous actions amongst its pharmacological activities.

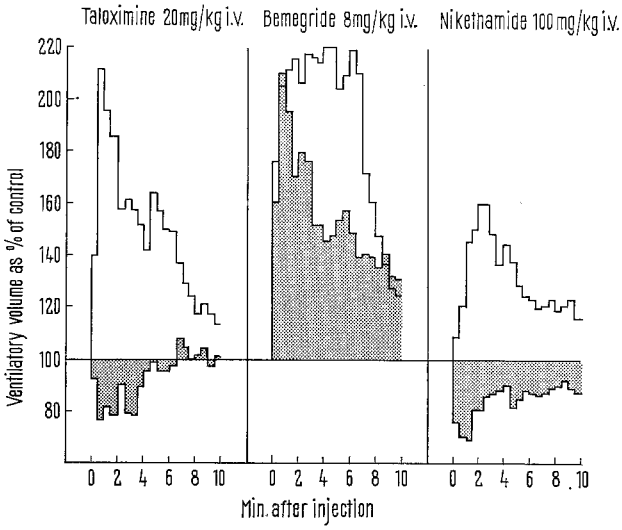

Fig. 3. Responses of 9 barbiturate anaesthetized cats to taloximine, bemegride and nikethamide given i.v. before denervation of the chemoreceptors (open histogram), and after denervation of the chemoreceptors (stippled histogram).

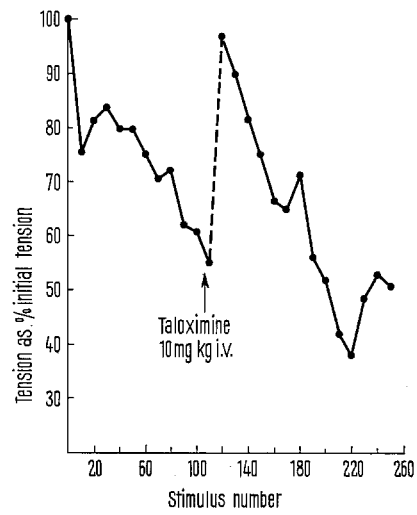

Fig. 4. Enhancement of the flexor withdrawal reflex in the decerebrate spincal cat preparation against a background of response decrement due to habituation following an i.v. dose of 10 mg/kg taloximine.

In view of the observations that large doses of taloximine stimulated respiration after denervation of the chemoreceptors it was decided to determine whether taloximine was effective in promoting some other parameter of central nervous system activity. The effect of taloximine on the flexor withdrawal reflexes was, therefore, examined in the decerebrate spinal cat preparation described by GRIFFIN and PEARSON[4]. In this preparation the isometric tension recorded from a slip of the biceps femoris muscle was measured in response to repeated application of uniform electrical stimuli to the ipsilateral hindpaw. Application of such stimuli results in a progressive decrement of the flexor response.

Enhancement of the flexor withdrawal reflex against a background of response decrement due to habituation was shown to occur with a dose of 10 mg/kg i.v. of taloximine (see Figure 4). Despite this enhancement of the flexor reflex at doses as low as 10 mg/kg i.v. taloximine was not shown to cause convulsions in the cat until doses in excess of 40 mg/kg were given. It therefore

Résumé. Une substance nouvelle, la taloximine, administrée par voie intraveineuse produit chez le chat à une dose de 20 mg/kg indemne une augmentation de l'effort respiratoire. On montre qu'à cette dose la taloximine accélère la fréquence des décharges enregistrées à partir de filaments multifibrillaires du nerf du corps carotidien.

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[4] J. P. GRIFFIN and J. A. PEARSON, Brain Res. *8*, 185 (1968).
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The Influence of β-Methasone on Antimicrobial Activity of Gentamicin

It is uniformly accepted that corticosteroids in high concentrations decrease metabolic functions. In certain low concentrations, however, they increase oxygen consumption of human and animal cells, as has been demonstrated in cell culture experiments; suspensions of microorganisms (bacteria and fungi in resting and proliferating phase) reveal an activated cell metabolism in the presence of corticosteroids in low concentrations, too [1–3]. For this reason, an inhibition of antimicrobial effects of antibacterial agents might occur when used

[1] W. RAAB and J. WINDISCH, Arch. klin. exp. Derm. *233*, 363 (1969).
[2] W. RAAB, Arch. klin. exp. Derm. *228*, 71 (1967).
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simultaneously with corticosteroids. Detailed studies of this problem seemed warranted.

Investigations on the combined effect of antibiotics and corticosteroids – especially in the case of water non-soluble corticosteroids – are rather difficult. The only method which has been successfully applied is the Warburg respiration technique. In previous studies, effects of several corticosteroids on antibacterial action of gentamicin already have been reported[4]. As gentamicin is used clinically combined with β-methasone, additional experiments to probe this question have been performed. For practical reasons, a new bacterial strain, *B. pyocyaneus*, has been included in the studies.

Experiments and results. (1) Bacterial strains. The investigations were performed on *Staph. albus* 802, *Staph. aureus* 6538p and *B. pyocyaneus*, isolated from a dermatological patient. Oxygen consumption of bacterial suspensions was measured with the Warburg technique under 2 types of conditions: resting bacteria (medium Ringer with glucose) and proliferating bacteria (medium bouillon). Decrease in oxygen consumption of resting bacteria will be referred to as bactericidal activity, decrease in oxygen consumption of proliferating bacteria as bacteriostatic activity. All experiments had to be performed with ethanol in final concentration of 3.3%, as the corticosteroid tested could only be introduced in ethanolic solution. (Details of the methods are reported in[4].)

(2) Effects of gentamicin. On *Staph. aureus* and *B. pyocyaneus*, gentamicin (Garamicin, Schering USA, GMC-5-M-4-1; potency 586 mcg/mg) exerts bactericidal activity in concentrations exceeding 300 mcg/ml (cf. Figure 1). On *Staph. albus*, such effect was not detectable in the concentration range tested (up to 1 mg/ml). On all 3 strains of bacteria, gentamicin revealed bacteriostatic activity in concentrations exceeding 0.5 µg/ml (cf. Figure 2).

(3) Effects of β-methasone. In concentrations of 33 µg/ml, β-methasone-17-valerate (Celestone, Schering USA, micronized, Code 991076, lot DOH-7-T-1) increases oxygen consumption of resting and proliferating bacteria (cf. Figures 1 and 2). Cell culture experiments (cf. [1]) permit the conclusion that this effect is due to an activation of cell metabolism.

(4) Combined effects. In the presence of β-methasone, neither bactericidal nor bacteriostatic activity of gentamicin was found decreased (Figures 1 and 2). On the contrary, a slight increase in antibacterial activity of gentamicin was encountered in all experiments due to the simultaneous presence of β-methasone. The mechanism for this effect is not yet clearly understood. Membrane active properties of corticosteroids causing increased or accelerated penetration of the antibiotic and/or direct metabolic effects of the corticosteroid have to be considered.

Conclusions. The presence of β-methasone-17-valerate does not impair bactericidal or bacteriostatic activity of gentamicin, despite the fact that the corticosteroid by itself activates oxygen consumption of resting and proliferating bacteria. For practical purposes, the conclusion may be drawn that preparations containing β-methasone and gentamicin may be used safely, without inhibition of antibacterial activity due the presence of the corticosteroid.

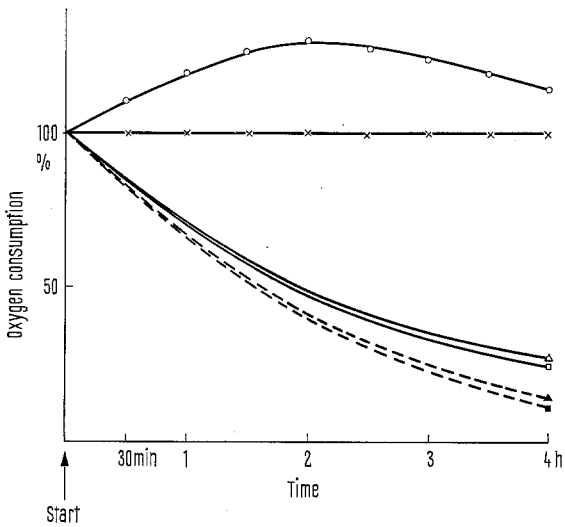

Fig. 2. *Staph. aureus* 6538p in proliferation. ×---×, control (bouillon, 3.3% ethanol); ○---○, β-methasone valerate 33 µg/ml; △---△, gentamicin 1 µg/ml; □---□, gentamicin 1 µg/ml + β-methasone val. 33 µg/ml; ▲---▲, gentamicin 2 µg/ml; ■---■, gentamicin 2 µg/ml + β-methasone val. 33 µg/ml.

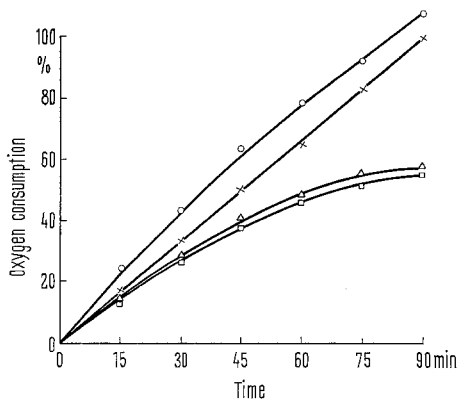

Fig. 1. Resting *Staph. aureus* 6538p. ×---×, control (Ringer, glucose, 3.3% ethanol); ○---○, β-methasone valerate 33 µg/ml; △---△, gentamicin 300 µg/ml; □---□, gentamicin 300 µg/ml + β-methasone val. 33 µg/ml.

Zusammenfassung. An 3 verschiedenen Bakterienstämmen (*Staph. albus, Staph. aureus* und *B. pyocyaneus*) konnte in Gegenwart von β-Methason eine nur geringfügige Verstärkung der antibakteriellen Wirkung von Gentamycin nachgewiesen werden, obzwar β-Methason allein in der geprüften Konzentration zu einer deutlichen Erhöhung des Sauerstoffverbrauches ruhender und proliferierender Bakterien führt. Die Versuche erfolgten unter Verwendung der Warburg-Technik.

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A-1090 Vienna (Austria), 16 January 1969.

[4] W. Raab and J. Windisch, Arch. klin. exp. Derm. *232*, 76 (1968).