tioned in $5 \cdot 10^{-4} M$, $5 \cdot 10^{-5} M$ and $5 \cdot 10^{-6} M$ concentrations.

As we can see from the graph, these drugs inhibit the adrenalin induced platelet aggregation completely in the $5 \cdot 10^{-4} M$ concentration. In the $5 \cdot 10^{-5} M$ concentration this inhibition is still statistically significant, but there is practically no effect in the $5 \cdot 10^{-6} M$ concentration. There are no statistically significant differences between the respective drugs, yet nortriptyline and norimipramine seem to be the most potent. Their higher effectiveness is in keeping with the fact that nortriptyline and norimipramine are the most potent inhibitors of adrenalin uptake as well[9,11].

As can be seen from our results, the investigated drugs in the concentration of $5 \cdot 10^{-5} M$ reduce the action of adrenalin to $^1/_{10}$ of its real concentration (Figure 2, middle part).

The fact that the drugs used inhibit the adrenalin induced platelet aggregation proves that adrenalin acts in keeping with O'BRIEN's theory[6]: it penetrates the cells and liberates ATP from platelets, ATP converts into ADP which is the proper aggregation factor.

Zusammenfassung. Anti-Depressiva vom Imipramin-Typ, die die Aufnahme der biogenen Amine blockieren, hemmen auch gleichzeitig die durch Adrenalin bewirkte Thrombozyten-Aggregation. Dieser Befund unterstützt die Theorie des Mechanismus der Thrombozyten-Aggregation durch Adrenalin: Adrenalin dringt in die Zellen ein und setzt ATP aus den Thrombozyten frei, das sofort in ADP – den eigentlichen Aggregationsfaktor – umgewandelt wird.

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Balance Studies on Free and Bound Pantothenic Acid in Humans after Administration of Calcium Pantothenate or Coenzyme A

Introduction. Infusions containing coenzyme A, α-lipoic acid and diphosphopyridine nucleotide have been administered intravenously to patients with hepatic coma. During therapy the state of consciousness was improved and a decrease of blood pyruvic acid and the fraction acetoin and 2,3-butylene glycol towards normal values could often be observed[1,2]. It is assumed that these effects might be at least partly due to coenzyme A[3], which is involved in the oxidative breakdown of pyruvate (synthesis of acetyl coenzyme A) and acts as an acyl carrier in metabolism (e.g. in vivo formation of acetylcholine).

Nothing is known about the fate of coenzyme A after intravenous infusion (oxidation, breakdown, penetration into cells, excretion). In the present study, blood and urinary concentrations of free and of bound pantothenate (= coenzyme A) have been determined before, during, and after administration of coenzyme A. Similar balance studies have been made after infusion of calcium pantothenate.

Methods. (a) Laboratory investigations: In blood and urine, free pantothenic acid and coenzyme A (= bound pantothenate) were determined microbiologically with *Lactobacillus plantarum* (ATCC 17-5 8014) according to the method of SKEGGS and WRIGHT[4], coenzyme A after previous degradation to pantothenic acid with alkaline phosphatase and pigeon liver peptidase as proposed by LIPMANN[5].

(b) Infusions: Coenzyme A or calcium pantothenate was administered intravenously to convalescent patients with normal glomerular filtration rates. The infusions contained 250 μM coenzyme A (Farmochimica Cutolo-Calosi, Naples, Italy) or 250 μM D-pantothenic acid in the form of the calcium salt (F. Hoffmann-La Roche Inc., Basel, Switzerland) dissolved in isotonic glucose or saline (240 ml) and were given at a rate of 1 ml/min for 4 h. The coenzyme A content of each preparation was determined microbiologically. The coenzyme A was further characterized with the phospho-transacetylase-test and the hydroxyacyl-coenzyme-A-dehydrogenase-test[6].

(c) Collection of blood and urine samples: Before, during, and after administration of coenzyme A or calcium pantothenate, the blood level and the daily urinary excretion of coenzyme A and pantothenic acid were checked. Venous blood samples were drawn immediately before and 2, 4, $8^1/_2$ and 24 h (1 case), 2, 4 and 24 h (1 case), 24 h (1 case) or 24 and 72 h (3 cases) after the beginning of the infusion.

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Results. The blood levels of free and bound pantothenic acid after infusion of coenzyme A or calcium pantothenate: (a) During the intravenous administration of coenzyme A, blood levels of free and bound pantothenic acid increased. 20 h after the end of the infusion, the blood concentrations of free and bound pantothenate were still found to be elevated (Figure). (b) During the infusion of calcium pantothenate, the free pantothenic acid in blood rose, whereas the bound pantothenic acid remained unchanged or was within the range of experimental error.

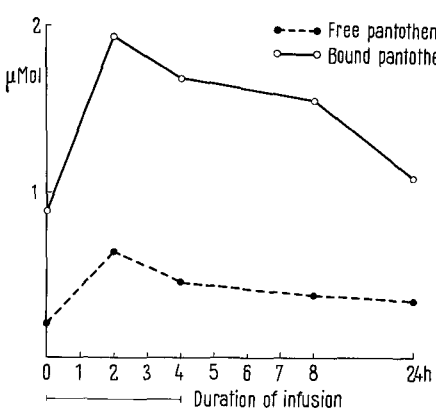
The urinary excretion of pantothenic acid during and after infusion of coenzyme A or calcium pantothenate: (a) The daily urinary excretion of free pantothenic acid was elevated after the administration of coenzyme A and normal again 2 days after the beginning of the infusion. In 3 cases, the extra pantothenate excretion corresponded to 22–24%, and in 1 case to 52% of the infused amount of coenzyme A. No bound pantothenic acid could be detected in urine. (b) For 2 days an extra daily urinary excretion of pantothenic acid was observed after the infusion of calcium pantothenate. It corresponded to 16% and 29% of the calcium pantothenate administered.

Discussion. In humans with normal glomerular filtration rates, an extra urinary excretion of free pantothenic acid is observed after intravenous administration of coenzyme A. This fact and the elevated free blood pantothenate during and after the infusion point to a breakdown of the injected coenzyme A in the organism. On the other hand, the blood level of bound pantothenate is raised after administration of coenzyme A and was found to be still elevated 20 h later.

It is not known whether the enzymatic degradation of coenzyme A to pantothenate by phosphatases and peptidases takes place in the circulating blood in the extravascular extracellular compartment or within the cells.

In 3 out of 4 balance studies with coenzyme A, 20–30% of the dose infused was excreted as pantothenate with the urine. The fate of the remainder is not known. It is assumed that the main part of the coenzyme A infused is adsorbed on the cell surface or is taken up by the cells either as coenzyme A or as one of its breakdown products (dephospho-coenzyme A, phosphopantethein, pantethein, pantothenic acid).

The urinary excretion of infused calcium pantothenate corresponded to 15–30%. This is similar to the results obtained after infusion of coenzyme A and is in good agreement with the observations of SCHMIDT[7,8].



Free and bound (coenzyme A) pantothenic acid in blood before, during, and after intravenous infusion of coenzyme A, α-lipoic acid, diphosphopyridine nucleotide and cocarboxylase. M. S., 1949 ♂; normal glomerular filtration rate.

Zusammenfassung. Bei Versuchspersonen mit normaler glomerulärer Filtration und normaler Leberfunktion wurde nach intravenöser Infusion von Calcium-D-Pantothenat oder Coenzym A die Bilanz der freien und der gebundenen Pantothensäure (Coenzym A) ermittelt. Es konnte gezeigt werden, dass infundiertes Coenzym A teilweise zu freier Pantothensäure abgebaut wird. Ungefähr 70% des infundierten Coenzym A konnten weder im Urin (als Pantothenat) noch im Blut wiedergefunden werden.

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Effect of Choline Salicylates and Some Other Analogues of Salicylic Acid on the Replication of EMC Virus in vitro

It has recently been reported that certain simple aromatic phosphonic and carboxylic acids have antiviral activity[1–3]. This communication presents further evidence for the effect of some derivatives of salicylic acid on the replication of encephalomyocarditis (EMC) virus in the secondary mouse embryo tissue culture. Therefore, some aspects of the relationship between the chemical structure of the drugs and their virus inhibitory action are discussed.

The methods used for the assay of antiviral activity of drugs were the same as described hitherto[1–3].

In the Table virus inhibitory action of eleven drugs has been summarized and compared. It can be seen that the antiviral effect of these drugs is connected with the characteristic structure of salicylate. The substitution of oxygen by larger but also bivalent sulphur in the *ortho*-phenolic group enhanced the antiviral activity of the compound (III). On the other hand, the substitution of

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