organotypic cultures of mouse dorsal root ganglia induce disrupture of microtubules, formation of abnormal tubular structures (200–250 nm in diameter instead of the usual 20–25 nm), and accumulation of bundles of neurofilaments in some perikarya[10]. This hypothesis should be verified with an EM study.

It is known that hippocampal cells are connected with several other brain regions, including the hypothalamus[11]. It is therefore tempting to correlate the symptoms noted (darkening of the skin, loss of appetite, slowing down of the movements, inability to recuperate after hibernation), with a hypothalamic dysfunction secondary to a damage of hippocampo-hypothalamic interconnected neurons. However, zinc ions are essential for several biologically active enzymes, some of which are involved in the mechanisms of neuro-hormonal regulation. Further studies are needed to clarify the pathogenic modes of action of excess zinc in the surrounding medium, which acts as a serious pollutant factor on our animals. More specifically, one might wonder whether zinc poisoning might not impair precisely the physiological mechanisms which normally require a limited amount of this ion.

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Mianserin reduces plasma levels of β-endorphin immunoreactivity in depressed patients

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Summary. Eight depressed patients were treated for 25 days with the antidepressant drug mianserin (3×20 mg/day). β-Endorphin immunoreactivity, measured in blood samples withdrawn before and after the treatment, appeared to be significantly reduced by mianserin. Since endogenous opioids can play a role in the etiology of depression, the observed effects of mianserin could be of relevance for its anti-depressant activity.

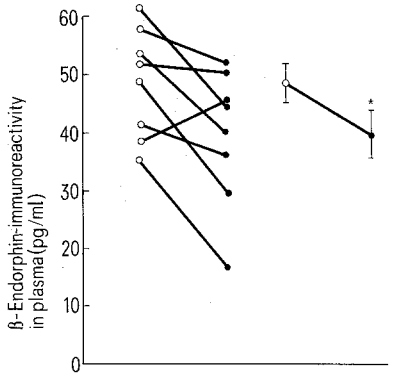
Mianserin HCl (2,3,4,10,14b-hexahydro-2-methyl-dibenzopyrazino-azepine monohydrochloride) is a clinically efficacious anti-depressant[2]. Its profile of action includes presynaptic α-adrenoreceptor blocking activity and anti-histamine properties, but not central anti-cholinergic activity[3].

Elevated concentrations of opioid material have been observed in the cerebrospinal fluid of depressed patients[4]. Treatment of such patients with lithium reduced these levels. Treatment with the opiate antagonist naloxone (Narcan®) also reduced levels of opioid material in the cerebrospinal fluid of depressed patients, though not to a clinically observable extent[5]. Although the relation between the opioid activity found in cerebrospinal fluid and brain endorphins is largely unknown, these observations have been correlated with functional disturbances in the central endorphin systems[6].

We were therefore interested in investigating the effect of mianserin on the plasma levels of β-endorphin immunoreactivity in depressed patients.

All patients (4 males and 4 females, 25–46 years old, mostly with unipolar depression) were hospitalized during the trial. The selection criterium was a minimal 2 months drug-free period before hospitalization. Mianserin (Lantanon®, Organon B.V., Oss, The Netherlands) was given orally in a daily dose of 3×20 mg, for 25 days. Blood samples were withdrawn before and after the treatment. Endorphins were extracted from plasma using Vycor-glass[7]. Assay of β-endorphin immunoreactivity in the extracts was performed using a radioimmunological method[8]. The antiserum used showed 60% cross-reactivity with β-LPH (mole/mole basis).

Results are depicted in the figure. Plasma levels of β-endorphin immunoreactivity appeared to be decreased after mianserin treatment in all patients except one (left side of the fig.). The statistical analysis of the results



Effect of mianserin on plasma β-endorphin immunoreactivity of depressed patients. Left side: effect on single patients. Right side: means (± SE) of all samples. ○, before the treatment; ●, after the treatment. * $p < 0.05$ (repeated t-test).

indicated a significant difference between the means ($p < 0.05$, repeated t-test, right side of the fig.). A substantial improvement in symptoms, as measured by a modified comprehensive psychopathological rating scale[9] (CPRS), was observed after mianserin treatment. Interestingly, no improvement was noted in the patient who did not show a decrease in β-endorphin immunoreactivity.

Present findings suggest that mianserin may interact with β-endorphin release from the pituitary and/or its peripheral metabolism. This peptide itself has been tested in depressed patients, but its anti-depressant effectiveness remains questionable[10].

Indirect evidence that mianserin may act as an antagonist of β-endorphin has recently been provided[11]. In fact, treatment with mianserin prevents the hypotensive effect of peripheral administration of β-endorphin in rats, possibly by an interaction with serotoninergic transmission.

In view of the possible role of opioids in the etiology of depression, the effect of mianserin on the endorphin system described here could be of relevance for its anti-depressant activity. Interestingly, a reduction in plasma β-endorphin levels has also been observed in depressed patients after desimipramine treatment[12].

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Inhibition by carbaryl of DNA, RNA and protein synthesis in cultured rat lung cells[1,2]

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Summary. The carbamate pesticide carbaryl rapidly inhibited DNA, RNA and protein synthesis in L-2 cells from rat lung. The inhibiton was partly reversible and was not accompanied by inhibiton of transport of tritiated precursors into intracellular pools or destruction of the integrity of the cell membrane.

The pesticide carbaryl (1-naphthyl-N-methylcarbamate) (C.A.S. 000063252) is used on nearly 100 food, forage and other crops[3]. Because of extensive use of carbaryl in agriculture and for domestic insect control, large numbers of people may be exposed to the pesticide by inhalation. In additon, smokers may inhale small quantities of carbaryl residues in cigarette smoke (less than 1 µg/cigarette[4]). We tested the effects of carbaryl on macromolecule synthesis in lung cells as part of a project aimed at evaluating the biological effects of carbaryl by short-term in vivo and in vitro bioassays.

Materials and methods. Carbaryl was extracted with acetone from the commercial formulation Sevin, recrystallized from hexane-acetone solution, and dissolved in dimethyl sulfoxide (DMSO). L-2 cells, a cell line of Type II pneumonocytes from rat lung[5], were used in these studies. L-2 cells retain differentiated functions in vitro, continuing to synthesize lecithin, produce multi-lamellar osmiophilic bodies[6], and make high levels of certain inducible enzymes[7]. L-2 cells were grown in F12K medium[8] (Grand Island Biological Co.) supplemented with 10% fetal bovine serum, penicillin, and streptomycin and were incubated at 37 °C in 5% CO_2 in air.

In toxicity studies, cells were harvested by trypsinization 24 h after addition of carbaryl or DMSO (solvent control) and numbers of viable cells were determined by the trypan blue dye exclusion method[9]. The effects of carbaryl on DNA, RNA and protein synthesis were examined by comparing the incorporation of tritiated precursors, ^{3}H-methyl-thymidine, 5,6,-^{3}H-uridine and L-(3,4,5-^{3}H(N))-leucine (New England Nuclear, NEN), into trichloroacetic acid (TCA)-insoluble material in control and treated cultures at various intervals after addition of treatments. At the end of the labeling period, the cells were rinsed with cold phosphate buffered saline (PBS) containing the corresponding unlabeled precursor, scraped off the plates, and

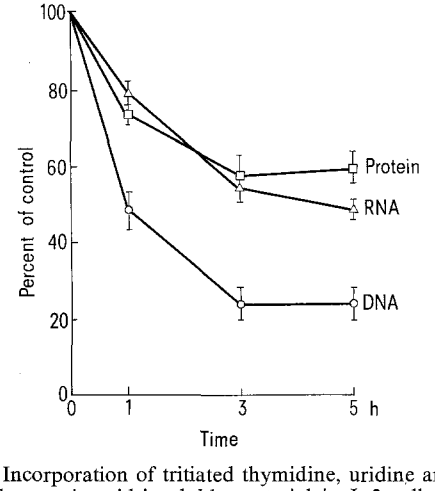

Figure 1. Incorporation of tritiated thymidine, uridine and leucine into trichloroacetic acid-insoluble material in L-2 cells after 1, 3 and 5 h of exposure to 8×10^{-5} M (16 ppm) carbaryl. Cultures in triplicate were pulse-labeled with 1 µCi of ^{3}H-thymidine (56.4 Ci/mM), 1 µCi of ^{3}H-uridine (41.3 Ci/mM) or 2 µCi of ^{3}H-leucine (147.0 Ci/mM) per ml of medium for 20 min at each time point.