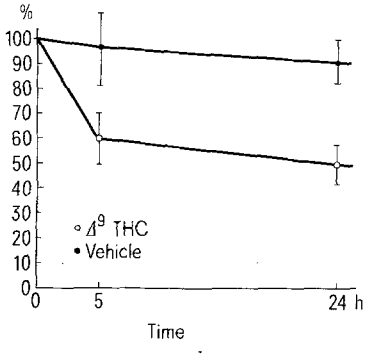
alpha-tocopherol after 5 h, and the reduction to about 50% of the initial value after 24 h.

No in vitro interactions of alpha-tocopherol with Δ^9-THC were observed in presence of 1,1-diphenyl-2-picrylhydrazyl (DPPH·) according to the method of Boguth[9], at IR-spectrophotometry and by elution of the mixture of the 2 compounds on Sephadex LH-20 columns.

In experimental animals, however, the pertinent data of the literature and of our previous studies and the results of the present research seem to demonstrate that the normal intake of vitamin E with food is not sufficient to prevent losses following administration of Δ^9-THC. Studies on the effects of alpha-tocopherol given in excess to animals chronically treated with Δ^9-THC are in progress[10]. In humans no such lesions or biochemical related alterations have been reported, but an inconstantly reduction of testosterone levels and cases of gynaecomastia[11], which might possibly be consistent with a relative alpha-tocopherol-deficiency. We have no data at present to explain the interaction of alpha-tocopherol with Δ^9-THC. However, it has been stated that alpha-tocopherol, by interference with arachidonic acid, has a stabilizing action on the cellular membrane[12], while Δ^9-THC has an opposite action, as demonstrated by the alteration of membrane enzymes[13]. It is possible that alpha-tocopherol is firmly bound in plasma to Δ^9-THC or to Δ^9-THC-lipoprotein complex, or involved in the metabolism of Δ^9-THC.



See in abscissa the time (h) after treatment; in ordinate the percent of the initial values of serum alpha-tocopherol.

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Effects of lithium chloride on peripheral acetylcholine release and brain acetylcholine levels in the guinea-pig

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Summary. Lithium chloride administered acutely or chronically to guinea-pigs had no effect on brain level of acetylcholine or on peripheral release of acetylcholine from longitudinal muscle of the ileum. The results suggest differences between in vitro and in vivo action of lithium.

Acute in vitro application of lithium chloride (LiCl) has been shown to enhance the resting release of acetylcholine (ACh) while decreasing evoked release at neuromuscular junction[4,5], in ganglia[6], from brain cortical slices[7,8], and at smooth muscle neuroeffector junction[8,9].

When injected chronically, in vivo, LiCl has been shown to decrease the level of ACh in the medulla-oblongata area of rat brain, while producing no changes in any other brain area[10]. On the other hand, evoked release of ACh from cortical slices taken from rats treated chronically with LiCl was not different when compared with slices taken from controls[11].

It would appear that there are some differences between acute in vitro and chronic in vivo effects of LiCl. Since the clinical use of LiCl requires chronic in vivo application, it would be of interest to simultaneously study LiCl for both peripheral and central effect on ACh in the same animal. The guinea-pig provides the means for doing this. The purpose of the present work was to investigate the effect of acute and chronic LiCl in vivo on ACh release at the neuroeffector junction in guinea-pig ileum myenteric-plexus preparation and on levels of ACh in whole brain from the same animal.

Material and methods. Male albino guinea-pigs (250–300 g) were injected once daily with either 2.5 mEq/kg of LiCl or an equal volume of 0.9% saline (NaCl). Animals were sacrificed either 2 h following a single injection (acute treatment) or 2 h after the final injection of a series of between 5 and 10 injections (chronic treatment). Animals were sacrified by decapitation and blood samples were immediately taken for serum analysis of LiCl.

The ilea from these animals were removed, the longitudinal muscle stripped off and set up for electrical stimulation as previously described[12]. Acetylcholine output at rest and following electrical stimulation (0.4 msec, 0.3 Hz, supramaximal voltage) was measured using a bioassay technique[13]. All collection periods were 30 min, and unknown samples were matched against standard curves derived from assaying known quantities of ACh. Standards were run each day of the experiment. Pretreatment of the assay tissue with 3×10^{-7} M atropine sulfate completely eliminated the responses to the ACh standards and the unknown samples, confirming that contraction of the assay tissue to the unknown samples was the result of the presence of ACh.

The brains of these animals minus cerebellum were

removed, weighed, and ACh extracted by a formic acid-acetone method[14], with the exception that the final volume was adjusted to 3 ml with distilled water. These concentrated samples containing ACh were diluted with buffer and bioassayed for ACh activity as described above.

Results and discussion. Effect of LiCl on ACh release from the longitudinal muscle is shown in table 1. There were no differences in spontaneous or evoked release of ACh between acute and chronic treatments for either the NaCl group or the LiCl group. Therefore, data for acute and chronic treatments were pooled for each group and the data presented in table 1 analyzed via Student's t-test. Values for either spontaneous or evoked release of ACh were not different for LiCl treated animals compared to NaCl treated animals.

The data of table 2, analyzed by a Student's t-test, show no significant differences in brain levels of ACh between the treatment groups. Once again there were no differences between acute and chronic treatments; therefore, the data of table 2 are the result of pooling across injection schedules. Flame photometric analysis of serum samples showed LiCl levels to be within the clinical range (0.5–1.5 mEq/l)[15].

Table 1. Spontaneous and evoked release* of acetylcholine from longitudinal muscle-myenteric plexus of guinea-pig ileum*

	NaCl	LiCl
Spontaneous	0.0317 ±0.01 n=4	0.0569 ±0.0137 n=10
Evoked**	0.0682 ±0.0287 n=4	0.1261 ±0.0316 n=10

* All values are expressed as μg/min/g tissue ± SEM. ** 0.4 msec duration; 0.3 Hz frequency; supramaximal voltage, 30 min.

Table 2. Whole brain* level** of acetylcholine

NaCl	LiCl
2.317 ±0.226 n=6	2.283 ±0.156 n=12

* Except cerebellum. ** All values are expressed as μg/g tissue ± SEM.

The results of the present study indicate that acute or chronic LiCl treatments in vivo have no effect on the spontaneous or evoked release of ACh at neuroeffector junction or on whole brain levels of ACh.

Although we have found that whole brain shows no effects of LiCl treatment in terms of level of ACh, this does not eliminate the fact that changes in specific brain areas may be taking place. This was noted by Ronai and Vizi[10], who showed a significant fall in ACh content of medulla oblongata-pons-mesencephalic area in rats treated with lithium.

In summary, we conclude that in vivo administration of LiCl has no effect on release of ACh from nerve terminals in myenteric plexus or on whole brain levels of ACh compared to NaCl treated animals.

These data suggest that LiCl therapeutic effect is not the result of a presynaptic interaction on cholinergic sites to alter release of the transmitter. This, of course, does not eliminate other mechanisms of interaction such as post-synaptic changes[16] or block of synthesis of ACh by LiCl[8]. Further evidence concerning these latter possibilities could provide meaningful insight into LiCl therapeutic effects.

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Acetylsalicylic acid-induced morphological changes in the ductus arteriosus of the chick embryo[1]

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Summary. The effect of acetylsalicyclic acid upon the ducti arteriosi of the embryonic chick was studied. A spectrum of gross malformations and histological findings associated with premature closure of the right ductus arteriosus is presented.

It has recently been demonstrated that the ductus arteriosus (DA) can be chemically manipulated in patients with congenital heart disease[2,3]. Prostaglandins, in addition to indomethacin and acetylsalicylic acid (ASA) (inhibitors of prostaglandin synthesis), have been employed both experimentally[4] and clinically[5] due to the physiological and morphological changes which these agents induce in the DA. It has been suggested that one of several pharmacological mechanisms of indomethacin[6,7] and ASA[8], namely inhibition of endogenous prostaglandin synthesis and subsequent increased catecholamine release[9], may relate to changes in vasomotor tone and ultimately closure of the DA. Although many studies have demonstrated closure of the DA with ASA and/or indomethacin, detailed morphological changes in the DA have not been documented.

The purpose of this report is to delineate changes in a) the DA proximal and distal to the right pulmonary artery (RPA) and b) in the pulmonary artery itself, and in this manner to suggest a morphological mechanism involved in premature closure of the DA.

Chick embryos (exclusively developmental stage 26)[10] were used in this study. In the avian embryo, the ventral-dorsal extension of the 6th aortic arch is known as the ductus arteriosus[11]. The right DA is a right-sided secondary flow