As for Fenoterol, introduced as an bronchodilator in asthma, the activity described was observed for the first time. However, the inhibitory action of Fenoterol is not surprising since it is known that various reagin-mediated reactions (see introduction) are inhibited as well by some other β-adrenergic stimulants, i.e. in vitro in human basophiles[8] in human[9–11], and primate[12] lung, and in vivo in man[13] (Prausnitz-Küstner test) and rats[14] (PCA). Thus β-adrenergic stimulants should not only be considered as agents producing symptomatic relief of bronchospasm in asthma[13]; they are potent protective agents against anaphylactic reactions and their action can be demonstrated employing the method described here.

Zusammenfassung. Eine Methode zum Studium der reaginvermittelten Mastzelldegranulation im Mesenterium der Ratte, bei der der Grad der unspezifischen Degranulation sehr niedrig ist, wird beschrieben. Die spezifische (reaginvermittelte) Reaktion ist hemmbar durch die drei Pharmaka Fenoterol, Salbutamol und Natrium-cromoglycat, deren antiasthmatische Wirkung bekannt ist.

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Immunization of Mice Against Transplantable Tumor

In 1965 GOLD and FREEDMAN[1,2] described a carcinoembryonic antigen (CEA) of adenocarcinoma of the human digestive system and of human fetal digestive organs during early periods of gestation. Since then the CEA has been shown to be a glycoprotein intimately associated with the tumor cell membrane[3,4]. The definition of tumor cell antigens as specific products of the tumor cell is, however, still subject to some question since cell surface antigens of certain virus induced tumors are products under virus control[5]. The cell surface antigens which are found are part of the cell membrane and the immune responses which they have been shown to elicit are similar to an allograft reaction. Thus it is recognized that cell mediated immune responses may play a part in tumor rejection. Little is known about how CEA promotes an antibody response in a tumor bearing animal.

It has been recognized for some time that the peculiar properties of tumor cells are dependent to a large extent on the properties of the cell membrane[6–8]. The surface properties are in turn dependent on the membrane composition which includes both proteins and phospholipids. Alteration of the composition of the cell membrane would be expected to alter the metabolite properties of the cell. This has been shown to occur following treatment of cells with Tween 80[9]. Despite the marked alterations in metabolic properties of the cells, and their change in permeability after the use of Tween 80 the cells remain viable and show similar patterns of growth in host mice to that found with untreated cells[10].

The earlier results obtained with the use of Tween 80 prompted an investigation of whether this agent might act as a possible unmasking agent for cell surface antigens in these cells. Such an unmasking of tumor specific antigens, which as indicated are firmly attached to the membrane, should elicit a stronger antibody reaction and allow the host to reject the tumor by a normal antibody antigen reaction.

Cells of the highly malignant Ehrlich-Lettré hyperdiploid strain were used in these experiments and stock tumor was maintained by serial transplant of 0.2 ml of ascites fluid i.p. into host mice. For the immunization experiments ascites fluid was drained from the tumor bearing mice, and the fluid with contained cells was irradiated with a dose of 5000 rad, a dosage required to kill the cells. The fluid was centrifuged at 1000 *g* for 10 min and the packed cells were mixed with 0.25 *M* sucrose containing 1% Tween 80 and allowed to stand for 15 min at room temperature. This procedure has been shown previously to result in marked permeability changes with consequent metabolic alterations in these cells[9]. The suspension was centrifuged at 1000 *g* for 10 min and the packed cells were suspended in 0.9% NaCl, such that 1 ml contained 0.5 ml packed cells. 1 ml of this suspension was injected i.p. into the experimental mice. At the same time, 0.1 ml of complete Freund's adjuvant was injected i.m. Subsequent injections of irradiated and Tween 80 treated cells of the same concentration were made at 1 week and 2 week intervals after the initial insult.

After the third insult the experimental mice developed a marked enlargement and fluid was aspirated under light ether anesthesia 1 week after the third injection of the killed and Tween 80 treated cells. Examination of this fluid showed a marked infiltration of lymphocytes and neutrophils. Many lymphocytes were present attached to

Mortality of mice

	No.	Death (No./day)
Control	10	1/12, 1/13, 2/14, 1/15, 2/16, 3/17
Experimental	10	1/20

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disintegrating ascites cells which were seen to be under all stages of destruction.

Two weeks following the aspiration of fluid, and 3 weeks following the last insult of irradiated and Tween 80 treated cells, the experimental mice and a control group were injected i.p. with 0.2 ml of a cell suspension of normal ascites cells which were treated with Tween 80 as above but without irradiation. This treatment has been shown previously to make no difference in the normal growth of this tumor in host mice[10]. The control group and the experimental group were allowed to remain for observation. Food and water were available ad libitum to each group.

In 2 separate experiments, employing 5 mice in a preliminary study and a larger group of 10 mice in control and experimental series the control mice all died as a result of tumor development in the usual period of about 2 weeks (Table). The surviving experimental mice remain tumor free in the first experiment after 4 months. In the second experiment 1 mouse died of unknown causes with 9 mice remaining normal in all aspects 2 months after the injection of viable Ehrlich ascites tumor cells.

It is apparent that the immunization procedure involving the use of Tween 80 treatment of cells killed by irradiation must unmask cell surface antigens and permit specific antibody formation leading to rejection of the tumor. It has been shown that Tween 80 removes phospholipids from the cell membrane with a resultant change in cell permeability[9]. It seems likely that such a treatment, at the same time, exposes the cell surface glycoprotein antigens. It remains to be determined if the mouse serum contains specific antibodies directed against the exposed cell surface antigens of the Ehrlich ascites cells. A preliminary study with the use of fluorescein labelled serum globulin of the experimental mice has shown that it does bind specifically to Tween 80 treated cells. This aspect of the problem is under further investigation.

Zusammenfassung. Nach i.p. Injektionen von mit Tween 80 behandelten Ehrlich-Lettré Ascites Krebszellen immunisierten Mäusen ergab sich bei diesen eine Widerstandsfähigkeit gegenüber Transplantaten von lebensfähigen Tumorzellen, woraus geschlossen wird, dass diese Behandlung die spezifischen Antigene der Zelloberfläche freisetzt.

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Inhibition of Thyroid Function Following the Administration of Metopiron (SU-4885)

Pharmacological effects of metopiron (SU- 4885, Ciba) are generally believed to produce a specific inhibition of 11-β-hydroxylation of steroids by the adrenal cortex followed by a compensatory increase of pituitary ACTH secretion[1]. An investigation into the effect of prolonged treatment with metopiron (SU-4885) on the hypothalamo-hypophysial neurosecretory system has led to the observation that this drug can produce more subtle effects on spermatogenesis[2,3].

In view of this finding, we decided to investigate the effect of this compound on pituitary thyrotrophic function. The effect of the goitrogenic action of metopiron (SU- 4885) was investigated in bat (*Rhinopoma* and *Taphozous*) and desert rat (gerbil). The criteria used in this investigation were 1. Thyroid weight and its microscopic structure. 2. Collection of radioactive iodine by the thyroid gland. 3. Protein-bound radioiodine (Pb I^{131}) conversion rate.

Materials and methods. Rhinopoma kinneari (Wroughton); *Taphozous perforatus*. In *Rhinopoma* and *Taphozous*, the testis is at its peak from late January till the end of April in the arid zone region of Rajasthan, India (KUMAR)[4].

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Effect of metopiron (SU-4885) on the thyroid radioiodine uptake

Group No.	Treatment		No. of days	Total dose (mg)	Body weight	Average thyroid wt. (mg)[b]	Thyroid weight (mg/100 g body wt.)	I^{131} uptake[a] (c/min/thyroid)	Normal (%)	CR (%)	Statistical comparison
	Rhinopoma										
1	None	(10)	–	–	23 ± 1	1.74 ± 0.1	6.3 ± 2.1	615972	100	–	$P < 0.01$ compared
2	Metopiron	(10)	6	15	26 ± 2	2.23 ± 0.1	8.6 ± 0.4	917654	149	–	with group 1
	Taphozous										
3	None	(10)	–	–	39 ± 2	4.40 ± 2.0	11.1 ± 2.7	753000	100	66	$P < 0.001$ compared
4	Metopiron	(10)	8	40	45 ± 1	9.40 ± 2.8	20.9 ± 1.6	1105000	147	30	with group 3
	Gerbil										
5	None	(10)	–	–	71 ± 5	3.30 ± 0.4	4.6 ± 0.4	183410	100	60	$P < 0.01$ compared
6	Metopiron	(10)	10	100	82 ± 6	6.40 ± 0.2	7.8 ± 0.4	272688	149	36	with group 5

Figures in parentheses indicate the number of animals examined. [a] 5 and 10 μCi carrier free I^{131} was injected in bat and gerbil respectively [b] ± Standard error.