effects from the treatment with this compound were observed either in cell suspension or organ culture[15,16].

Zusammenfassung. Der Einfluss vom Kalbsthymus Histon (CTH) und seines diazotierten Derivatives (DCTH) auf Vitalität und Zelldifferenzierung verschiedener Gewebe des Hühnerembryos wurde geprüft. Die LD_{50} für CTH wurde bei 25 µg/ml der Zellsuspensionen festgestellt. Es wurden keine bedeutenden Änderungen in der Differenzierung der embryonalen Gewebe in Kulturen bei sublethalen Konzentrationen gefunden.

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Variation in Intestinal Serotonin Levels, and the Effect of Reserpine in Sprague-Dawley Rats from Different Sources

Approximately 60% of the total body serotonin in rats is present in the gastrointestinal mucose[1]. Consequently, this tissue has been used frequently to study the effects of various drugs on serotonin metabolism. In earlier communications it has been reported that fasting[2] and prior exposure of the rat to anesthetic agents[3] adversely affect bowel serotonin. Of greater importance is that both sex and strain differences of statistical significance exist in bowel serotonin levels in rats of Sprague-Dawley origin from different suppliers[4]. Because of this latter finding it would seem important to identify the strain of the experimental animal, and also the laboratory of origin. It seems reasonable to assume that the failure to reproduce published experiments may depend in part (even when extreme care is observed to follow reported techniques) on strain differences in drug metabolism or response. In vivo experiments are subject to the intrusion of many variables, such as diet, alterations in room temperature or housing, seasonal or circadian influences etc. While investigating the effect of reserpine on bowel serotonin metabolism one shipment of rats was found to respond poorly to the depleting effect of this amine. Because no satisfactory explanation could be found to account for this finding, the source of the animals was investigated. The standing order of rats shipped every 2 weeks, routinely came from the Charles River laboratories' breeding shed I. However, on this occasion rats had been shipped from breeding shed IV. Both of these sheds contain colonies of randomly-bred rats of Sprague-Dawley origin[5], but maintained separately and autonomously. It is generally realized that animals of a second species may respond differently to drugs or experimental procedures. However, of equal importance is the fact that animals of the same species, and from the same supplier, may exhibit variations in drug response. The purpose of this communication is to emphasize the fact that animals of the same species may differ greatly, and that this difference may introduce an important source of biological error.

Male Sprague-Dawley rats weighing between 200–300 g from the Charles River breeding sheds I and IV were used. Animals were kept in colony cages and fed commercial Purina rat chow with a tryptophan content of 0.22%. To avoid any possible circadian influences on serotonin levels (to date only reported for rat brain[6]), rats were always killed between 0800 and 1000 on the day of assay. Rats were decapitated by a small animal decapitator (Harvard Apparatus Co. Inc., Dover, Mass.), without prior exposure to anesthesia. Five to eight $^1/_2$ inch segments of jejunum commencing 6 inches distal to the pyloric sphincter were taken from each rat. Details of our method of mucosa muscle separation and spectrophotofluorometric analysis have been reported previously[4]. Reserpine (5 mg/kg) was injected i.p. in one dose. Rats killed at 0 time received i.p. saline.

Results were compared statistically using the t test and are indicated in the Table. There is a statistically significant difference between the values at 0 time in rats from the 2 separate strains ($p < 0.025$). Although a depletion of jejunal serotonin develops following reserpine, reaching a maximum at 4 h in both groups, the fall is greater and more prolonged in those rats from shed I. The maximum fall in serotonin concentration is 54% for the rats from shed I, and 19% for the rats from shed IV. The reason(s) for this discrepancy between the untreated and the reserpine pretreated rats is not clear, and certainly calls for further study. The literature contains conflicting reports of the effect of reserpine on bowel serotonin levels. In the rat, ERSPAMER has shown that minimal serotonin depletion occurs following reserpine[7], while MORAN and WESTERHOLM[8] report no effect on serotonin levels following reserpine. SANYAL and WEST[9] on the other hand report depletion of rat intestinal serotonin by pretreatment with reserpine; however, these authors give no actual values. This divergence of opinion may in part be

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Serotonin levels in $\mu g/g$ mucosa $\pm$ 1 standard error, and as a % of control values in rat jejunal mucosa before and after reserpine (5.0 mg/kg i.p.) in 2 strains of rats

Time in h post-injection	Rat source Shed I[a]	%	Shed IV[a]	%	p value
0	7.51 ± 0.28 (17)[b]	100	6.80 ± 0.19 (26)	100	< 0.025
0.5	8.37 ± 0.23 (15)	111[c]	6.44 ± 0.35 (5)	95	< 0.001
2	4.74 ± 0.24 (13)	63	5.79 ± 0.17 (14)	85	< 0.005
3	3.88 ± 0.09 (23)	52	5.95 ± 0.25 (10)	88	< 0.001
4	3.48 ± 0.11 (17)	46	5.53 ± 0.17 (26)	81	< 0.001
16	5.01 ± 0.16 (8)	67	6.81 ± 0.27 (12)	100	< 0.001

[a] Indicates the breeding shed of origin at Charles River laboratories. Each shed being of separate Sprague-Dawley origin and autonomous. [b] Indicates the number of rats. [c] Results expressed as a % of the values at 0 time.

explained by such factors as indicated in this short communication.

It is unlikely that a more rapid metabolism of reserpine in the animals from shed IV was responsible for the differences noted, as the development of and persistence of systemic signs of reserpine treatment were similar in the 2 groups[10].

Zusammenfassung. Es wurde ein statistisch gesicherter unterschiedlicher Serotoningehalt im Darmtraktus zweier unabhängig gezüchteter Rattengruppen von Sprague-Dawley Abstammung und ihre unterschiedliche Ansprechbarkeit auf die Serotonin entleerende Wirkung des Reserpins gefunden.

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Zur Spezifität des durch Bradykinin, Kallidin und Met-Kallidin ausgelösten Blutdruckreflexes an der Katze

Bei intraarterieller Gabe von Bradykinin in die isolierte Hinterpfote der Katze kommt es zu einer Vasokonstriktion im peripheren Gefässgebiet[1]. Die quantitativen Verhältnisse für Bradykinin und Kallidin wurden von uns bereits dargestellt[2]. Über die pharmakologische Beeinflussung der Gefässverengung durch Sympathikolytika vom α- und β-Typ, Kokain, Guanethidin und Reserpin haben wir kürzlich berichtet[3]. Danach ist zu vermuten, dass Bradykinin ohne Vermittlung von Katecholaminen direkt am Gefäss angreift. Darüber hinaus lösen Kinine im Körper des Tieres einen Blutdruckreflex und eine Atemstimulation von kurzer Dauer aus (LIM et al.[4–6], HASHIMOTO et al.[7], WIEGERSHAUSEN und REINCKE[2]).

Mit dieser Mitteilung beabsichtigen wir eine Erweiterung unserer Befunde insofern, dass wir mit der von uns bereits geschilderten Methode[2] an Katzen auch Reaktionen der Nickhaut erfassten und ein weiteres Kinin, das Met-Kallidin[8], in unsere Untersuchungen einbezogen. In dieser Versuchsreihe stand vor allem die pharmakologische Beeinflussung des reflektorischen Geschehens am Ganztier im Vordergrund, da auch andere Substanzen, wie zum Beispiel das Acetylcholin, ähnliche Reaktionen auslösen können.

Met-Kallidin (10–20 μg/Tier) intraarteriell in die isolierte Extremität gegeben, führt qualitativ zu den gleichen Reaktionen, wie wir sie bereits mit den anderen Kininen beobachten konnten. Darüber hinaus wird im Zusammenhang mit der durch die Kinine ausgelösten Stimulation des sympathischen Systems die Nickhaut regelmässig kontrahiert. Es ist sehr wahrscheinlich, dass die afferente Erregung über sensible Strukturen des N. ischiadicus geleitet wird[4]. Die Abschwächung bzw. das Verschwinden der Reflexe im Verlauf des Versuchs lässt sich weniger durch eine Tachyphylaxie erklären, als vielmehr durch eine zunehmende Abnahme des Leitungsvermögens des Nerven infolge der sich ausbreitenden nervalen Anoxie bei längerer Versuchsdauer.

Bei molarem Vergleich einiger bekannter Substanzen, die einen Blutdruckreflex auslösen können, erweisen sich Kinine als hoch spezifisch (Tabelle). Histamin, das ebenfalls peripher vasokonstriktorisch wirkt, ist in einer Dosierung bis zu 400 μg nicht in der Lage, an der Katze einen Blutdruckreflex zu induzieren, im Gegensatz zu den

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