microsomes[10]. The results reported here therefore indicate that tumour-bearing rats are somewhat more sensitive towards some drugs than normal rats. This fact must be taken into consideration in cancer chemotherapy.

In vitro metabolism of hexobarbital, strychnine and meprobamate by microsome-containing supernatant fraction obtained from normal and tumour-bearing rats

	Controls	Tumour-bearing rats	Variations %	*P*
Number of rats	8	8		
Hexobarbital metabolism (μg/g/h)	363 ± 10.9	179 ± 8.7	−53%	<0.001
Strychnine metabolism (μg/g/h)	240 ± 8.8	163 ± 7.2	−32%	<0.001
Meprobamate metabolism (μg/g/h)	52 ± 3.5	28 ± 2.7	−46%	<0.001
Body weight (g)	313 ± 6.9	307 ± 7.2		
Tumour weight (g)	—	25.2 ± 3.4		
Tumor weight / Body weight ×100	—	8.3 ± 0.61		

Enzyme activity expressed as metabolized drug after 1 h incubation with microsome-containing supernatant obtained from 1 g of rat liver.

Riassunto. Ratti portatori di carcinosarcoma di Walker, presentano una notevole diminuzione di attività di quel gruppo di enzimi microsomici epatici da cui dipende il metabolismo di una numerosa serie di farmaci. I nostri rilievi sono stati fatti prendendo in considerazione il metabolismo dell'esobarbital, della stricnina e del meprobamato.

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[10] A decreased activity of the gonads in male rats also produces a decrease in the activity of the enzymes responsible for metabolisms of hexobarbital and strychnine[8,11,12]. Therefore the possibility arises that some factors produced by the tumour cell may interfere with the male sex gland activity.

[11] B. B. BRODIE, J. Pharm. Pharmacol. *8*, 1 (1956).

[12] R. KATO, E. CHIESARA, and G. FRONTINO, Biochem. Pharmacol. *11*, 221 (1962).

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On the Possibility of Spontaneous Tuberculous Infection in the Course of Long-Term Trials in Mice

The possibility of transmission of tubercle bacilli from one mouse to another in a group of animals living in the same cage during long-term chemotherapeutic or immunologic trials is still poorly understood. It was shown by KIRCHHEIMER et al.[1] that isolation of virulent tubercle bacilli could be accomplished from the faeces of intravenously infected mice. Moreover, virulent tubercle bacilli have also been found in gastric contents of such mice. It may therefore be suggested that inter-animal transmission of tubercle bacilli is possible, since the environment in the cage must contain a great number of virulent mycobacteria. We had, by chance, the opportunity to investigate such a possibility in the course of a chemotherapeutic trial.

Twenty white mice of the H strain, allegedly femals, were infected intravenously with 0.25 mg of semi-dry weight of the H37Rv-M strain of *M. tuberculosis* and maintained in a glass cylinder. Therapy with perorally administered isoniazid (5 mg/kg of weight, added to Larsen diet) was started the day after infection. The animals were observed daily, and in dead mice the advancement of the disease was assessed by microscopy and, in some cases, by enumeration of viable tubercle bacilli recovered from lungs and spleens.

On the 40th day of duration of the experiment, one female mouse littered 5 young mice. These were identified by a mark and maintained in the original cylinder up to the end of the experiment (2nd generation). Approximately a month later another female mouse littered again 4 young mice which were treated in the same way as mentioned above (3rd generation). A month later another litter of 4 young mice was observed in still another mouse (4th generation), followed by the last litter of 3 young mice again in another mouse (5th generation). The young mice were proceeded in the exactly same way as these of the 2nd generation. The time interval for which the individual generations lived in close contact with the originally infected animals is registered in Table I.

Ten days after the last litter, all mice born in this cylinder were killed with ether. All animals were autopsied and their lungs and spleens were removed and weighed under sterile precautions. Average weight of both organs obtained from animals of individual generations is presented in Table II.

Tab. I. Duration of contact with the tuberculous environment

2nd generation	107 days
3rd generation	72 days
4th generation	45 days
5th generation	10 days

Tab. II

Average organ weights observed in animals of different generations

Generation	Lungs (mg)	Spleen (mg)
2nd	563.7	282.2
3rd	341.3	212.0
4th	169.4	128.7
5th	100.1	39.9

[1] F. W. KIRCHHEIMER, A. R. HESS, E. H. WILLISTON, and G. P. YOUMANS, Amer. Rev. Tuberc. *62*, 481 (1950).

Thereafter lungs or spleens of all mice of one generation were homogenized by grinding with sterile saline in a mortar, and after decontamination with hydrochloric acid followed by neutralisation with sodium hydroxide, the number of viable mycobacterial units was determined by means of the serial dilution test on Löwenstein-Jensen media in Petri dishes. The numbers of tubercle bacilli calculated per 1 g of a given organ are shown in Table III.

Tab. III. The number of viable mycobacterial units recovered from lungs or spleens and calculated per 1 mg of tissue

Generation	Lungs	Spleen
2nd	$>1.7 \times 10^6$	2.4×10^4
3rd	1.1×10^7	2.17×10^6
4th	0	0
5th	0	0

This study could be accomplished because of including by mistake a male mouse in the original group of animals. The original mice group was infected with a mycobacterial strain which is highly virulent for mice (median survival time of untreated animals infected intravenously with 1 mg of semi-dry weight of the H37Rv-M strain does not exceed 10 days).

It may be seen in Table II that average weight of both lungs and spleens removed from mice of the 2nd and 3rd generations exceeded that of later generations, which difference may be attributed, besides the age factor, undoubtedly to tuberculous involvement of these organs (see Table III).

The detection of tubercle bacilli in lungs and spleens of mice not artificially infected, but born and maintained in a tuberculous environment may be taken as indicative for the possibility of spontaneous infection. This could be acquired, of course, either during pregnancy or in the course of post-natal life, as the result of close contact with animals suffering from chronic generalized tuberculosis. The latter possibility is in good agreement with the observation that tubercle bacilli were recovered only from animals being in contact with the tuberculous environment for more than 2 months.

The practical importance of this observation lies in the proof of the possibility of tuberculous infection being acquired during longterm close contact with a tuberculous environment, in animals with a relatively high natural resistance against this disease. Such a possibility might complicate and confuse various experimental findings observed in chemotherapeutic or immunologic trials in mice.

Zusammenfassung. Virulente Tuberkelbakterien wurden in Lunge und Milz von Mäusen entdeckt, die von intravenös infizierten Müttern geboren wurden und die mehr als 2 Monate in engem Kontakt mit den tuberkulösen Eltern lebten.

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Tuberculosis Research Institute, Prague-Bulovka (Czechoslovakia), July 17, 1962.

Zur Pathogenese des Urämiesyndroms[1]. Über den Einfluss von Tyramin auf die Acetoinsynthese aus Brenztraubensäure in Rattenleberhomogenat[2]

Biogene Amine wie Tyramin, Dopamin, Tryptamin steigern die Acetoinsynthese aus Brenztraubensäure in Rattenleberhomogenat[3] (vergleiche Anmerkung Figur 1). Eine signifikante Veränderung der Acetoinbildung tritt nur bei gleichzeitiger Oxydation des zugesetzten Amins ein. Wird die oxydative Desaminierung der Amine durch einen Monoaminoxydasehemmer verhindert, so wird die Acetoinsynthese nicht gefördert[3]. Der Wirkungsmechanismus dieses Vorganges ist nicht abgeklärt.

Die vorliegende Arbeit stellt eine Erweiterung früherer Untersuchungen über die Wirkung von Tyramin auf die Acetoinsynthese aus Brenztraubensäure in Rattenleberhomogenat dar. Sie befasst sich mit der bisher nicht bestimmten Abhängigkeit des Tyramineffektes von Tyramin- und Brenztraubensäurekonzentration. Daneben wird der Einfluss von Abbauprodukten des Tyramins (Tyrosol, *p*-Hydroxyphenylessigsäure) auf die Acetoinsynthese studiert.

Ergebnisse. Beziehungen zwischen Acetoinsynthese, Pyruvatabbau und Tyraminkonzentration: *Acetoinsynthese.* Die Abhängigkeit der Acetoinsynthese aus Brenztraubensäure von der Tyraminkonzentration ist in Figur 1 dargestellt. Die Tyraminwirkungskurve ist durch ein Maximum und ein Minimum gekennzeichnet. Das scharf ausgeprägte Maximum lag in 6 Fällen bei $2{,}5 \times 10^{-3}$ m Tyramin, in 2 Fällen bei 5×10^{-3} m Tyramin, das Minimum in allen Fällen bei 10^{-2} m Tyramin. Im Maximum der Tyraminwirkungskurve betrug bei 6 Versuchen die Steigerung der Acetoinbildung zwischen 50% und 107%, im Minimum zwischen 16% und 54%. Bei 2 Leberhomogenaten betrug die Synthesesteigerung von Acetoin im Wirkungsmaximum bei $2{,}5 \times 10^{-3}$ m Tyramin nur 6% bzw. 16%. In diesen Fällen wurde bei 10^{-2} m Tyramin eine Hemmung der Acetoinsynthese von 8% und 12% festgestellt. Bei fünf von acht Homogenaten stieg zwischen 10^{-2} m und 4×10^{-2} m Tyramin die Wirkungskurve praktisch linear an und erreichte bei 4×10^{-2} m Tyramin Werte, die bis zu 100% über dem Kurvenmaximum bei $2{,}5 \times 10^{-3}$ m bzw. 5×10^{-3} m Tyramin lagen.

Pyruvatabbau. Die Wirkung von Tyramin auf den Brenztraubensäureabbau und die Acetoinsynthese verlief nicht parallel (Figur 1). Bis 10^{-2} m Tyramin stieg in allen Fällen der Brenztraubensäureumsatz an und erreichte im Maximum eine Steigerung zwischen 33% und 84%. Eine

[1] Mit Unterstützung des »Schweizerischen Nationalfonds« und der Firma F. Hoffmann-La Roche & Co. AG, Basel.

[2] 8. Mitteilung. 1. Mitt.: H. Thölen, F. Bigler und H. Staub, Path. Microbiol. (Basel) *24*, 262 (1961). – 2. Mitt.: F. Bigler, H. Thölen und H. Staub, Helv. physiol. Acta *19*, C 11 (1961). – 3. Mitt.: H. Thölen, F. Bigler und H. Staub, Exper. *17*, 359 (1961). – 4. Mitt.: F. Bigler, H. Thölen und H. Staub, Schweiz. med. Wschr. *91*, 1259 (1961). – 5. Mitt.: H. Thölen, F. Bigler, A. Heusler, W. Stauffacher und H. Staub, Exper. *18*, 454 (1962). – 6. Mitt.: F. Bigler, H. Thölen und H. Staub, Schweiz. med. Wschr. *92*, 746 (1962). – 7. Mitt.: F. Bigler, H. Thölen und H. Staub, in Vorbereitung.

[3] F. Bigler, H. Thölen und H. Staub, Helv. physiol. Acta *19*, C 11 (1961).