REFERENCES

BERTLER, A., CARLSSON, A. & ROSENGREN, E. (1958). *Acta physiol. scand.*, **44**, 273–292.
DEARNALEY, D. P. & GEFFEN, L. B. (1966). *Proc. Roy. Soc. B*, **166**, 303–315.
IVERSEN, L. L. (1965). *Br. J. Pharmac. Chemother.*, **25**, 18–33.
LAVERTY, R. & SHARMAN, D. F. (1965). *Ibid.*, **24**, 538–548.
THOENEN, H., HÜRLIMANN, A. & HAEFELY, W. (1963). *Helv. physiol. pharmac. Acta*, **21**, 17–26.
VENDSALU, A. (1960). *Acta physiol. scand.*, **49**, *suppl.* 173, 23–32.

Removal of plasma metyrapone in rats submitted to previous pharmacological treatment

Metyrapone [SU 4885; Metopirone; 2-methyl-1,2-di(3-pyridyl)propan-1-one] a relatively specific 11-β-hydroxylase inhibitor, is currently used for testing the pituitary ACTH reserve (Liddle, Estep & others, 1959). Several authors have reported that the metyrapone test is not reliable in patients under therapy with other drugs like for instance phenobarbitone and diphenylhydantoin (Krieger, 1962; Rinne, 1966, 1967; Werk, Thrasher & others, 1967). Metyrapone is metabolized by the liver to form a reduced compound [SU 5236; 2-methyl-1,2-di(3-pyridyl)propanol] (Kraulis, Traikov & others, 1968), a process which is blocked *in vivo* by the administration of an inhibitor of liver microsomal enzymes such as SKF 525 A (S. Szeberenyi, unpublished). It may be possible therefore that the level and the disappearance of metyrapone from plasma are affected by treatment with various drugs known to influence the activity of liver microsomal enzymes. This note summarizes preliminary data obtained by measuring the half-life of metyrapone in plasma of rats pretreated with several drugs known to increase the rate of metabolism (induction) of foreign compounds. Female Sprague–Dawley rats (140 g) were treated with various drugs twice a day (9.00 a.m. and 9.00 p.m.) for 5 days as reported in Table 1. 36 h after the last treatment, metyrapone hydrochloride was injected intraperitoneally at the dose of 66 mg/kg. 5, 15 and 30 min after metyrapone administration, animals were killed and metyrapone was determined in plasma according to the method of Szeberenyi, Szalay & Tacconi (1968). At least 12 animals per drug were used.

Table 1. *Half-life* ($t\frac{1}{2}$) *of metyrapone in plasma of rats pretreated with several drugs*

Drug	mg/kg (twice daily for 5 days)	$t\frac{1}{2}$ (min) of metyrapone in plasma
Saline	(0·5 ml)	17 ± 0·6
Niketamide	100 orally	14
Phenylbutazone	62·5 i.p.	13·5
Diazepam	50 i.p.	13
Meprobamate	100 i.p.	12
Diphenylhydantoin	37·5 i.p.	12
Pentaerythritol tetranitrate	25 i.p.	11
Hydrocortisone	40 s.c.	10·5
Phenobarbitone	37·5 i.p.	9

From Table 1 it is evident that all drugs tested are able to shorten the half-life of metyrapone. The effect was maximum for phenobarbitone and then in decreasing order for hydrocortisone, pentaerythritol tetranitrate, diphenylhydantoin, meprobamate, diazepam, diphenylbutazone and nikethamide. All these drugs are known to induce microsomal enzymes (Conney, 1967).

Although it is impossible to extrapolate these data to humans, it may be that previous therapeutic treatment could affect the metabolism of metyrapone and therefore influence the functional significance of this test.

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Istituto di Ricerche Farmacologiche "Mario Negri",
Via Eritrea, 62,
20157 *Milan, Italy.*

SZ. SZEBERENYI*
K. SZ. SZALAY†
S. GARATTINI

December 18, 1968

* Present address: The Chemical Works of G. Richter, Ltd., Csezkesz- u 63, Budapest X, Hungary.

† Present address: Institute of Experimental Medicine, Hungarian Academy of Sciences, Department of Pathophysiology, Budapest, Hungary.

REFERENCES

CONNEY, A. H. (1967). *Pharmac. Rev.*, **19**, 317–366.

KRAULIS, I., TRAIKOV, H., LI, M. P., LANTOS, C. P. & BIRMINGHAM, M. K. (1968). *Canad. J. Biochem.*, **46**, 463–469.

KRIEGER, D. T. (1962). *J. clin. Endocr.*, **22**, 490–493.

LIDDLE, G. W., ESTEP, H. L., KENDALL, J. W., JR., WILLIAMS, W. C., JR. & TOWNS, A. W. (1959). *Ibid.*, **19**, 875–894.

RINNE, U. K. (1966). *Confinia neurol.*, **27**, 431–440.

RINNE, U. K. (1967). *Medna Pharmac. exp.*, **17**, 409–416.

SZEBERENYI, SZ., SZALAY, K. SZ. & TACCONI, M. T. (1969). *J. Chromatog.*, In the press.

WERK, E. E., JR., THRASHER, K., CHOI, Y. & SHOLITON, L. J. (1967). *J. clin. Endrocr.*, **27**, 1358–1360.

Corticosteroid modification of guinea-pig anaphylaxis

It is well established that a wide variety of experimental allergic reactions may be modified by prior administration of cortisone or related compounds (Rose, 1954, 1959). One notable exception is the anaphylactic reaction in the guinea-pig, for which a mass of contradictory evidence has been published.

The most inconsistent evidence has resulted from experiments on anaphylaxis induced by intravenous administration of antigen; the severity of the reaction being evaluated by subjective scoring, or mortality methods. A protective influence of corticosteroids was observed by Hajos (1926), Wolfram & Zwemer (1935), Simonsen (1950), Humphrey (1951), Zelenka, Zitka & Jirasek (1957) and Jaques (1961). Using similar methods no significant protective effects were observed in experiments described by Stoerck (1950), Dworetsky, Code & others (1950), Friedlander & Friedlander (1950), Malkiel (1951), Dews & Code (1951), Arbesman, Neter & Bertram (1951), Landau, Nelson & Gay (1951), Germuth, Ottinger & Oyama (1952), Criep, Weigler & Meyer (1952), Marcus, Carlquist & others (1952), Bertola (1958) and Csaba & Kassay (1966). Literature concerning the protective effects of corticotrophin against guinea-pig anaphylaxis may similarly be divided into two conflicting groups.