

Fig. 1. The effect of fluorouracil (FU) and fluorodeoxyuridine (FdUR) on the frequency of recombination between the two mating type genes of *S. pombe* expressed in % of recombinant, homothallic colonies from ascospores of FU and FdUR treated crosses. FU and FdUR at the given concentration were added to the crossing medium.

● FU = fluorouracil; ○ FdUR = fluorodeoxyuridine.

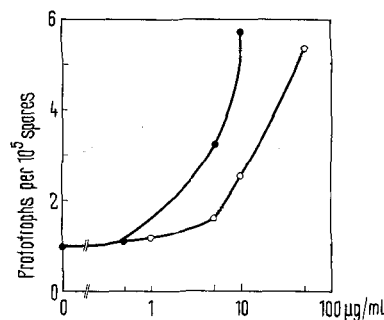


Fig. 2. The effect of FU and FdUR on the frequency of recombination between two allelic mutants *ad<sub>2</sub>-R-67* and *ad<sub>2</sub>-R-113* at the *Ad<sub>2</sub>* locus of *S. pombe*. FU and FdUR at the given concentration were added to the crossing medium. ● FU = fluorouracil; ○ FdUR = fluorodeoxyuridine.

ribotides and deoxyribotides respectively, inhibit the DNA synthesis in *S. pombe*. It seems therefore reasonable to assume that recombination in *S. pombe* occurs in the absence of DNA synthesis and the mechanism of recombination in this organism is of the breakage and rejoining and not of the copy choice type<sup>9</sup>.

A mechanism, similar to that observed in *B. subtilis*<sup>10</sup>, by which FU and FdUR induce single strand breaks in the DNA molecules, could also operate in *S. pombe*. Such breaks would facilitate genetic recombination. Alternatively one could speculate that FU and FdUR treatment of cells undergoing meiosis prolongs the period of chromosome pairing, thus increasing the probability of recombination.

**Zusammenfassung.** Die Rekombinationshäufigkeit, in inter- und intraallelen Kreuzungen bei *Schizosaccharomyces pombe*, wird durch Zugabe von Fluorouracil oder Fluorodeoxyuridin zum Kreuzungsmedium stark erhöht.

R. MEGNET

*Institut für Allgemeine Mikrobiologie, Universität Bern (Switzerland), December 20, 1965.*

<sup>9</sup> E. SIMON, *Science* 150, 760 (1965).

<sup>10</sup> H.-D. MENNINGMANN and W. SZYBALSKI, *Biochem. biophys. Res. Commun.* 9, 398 (1962).

## Lipid-Mobilizing and Hypoglycaemic Activity of Pituitary Homogenates from Alloxan-Diabetic Rats

The presence of substances with a lipid-mobilizing and hypoglycaemic activity in the pituitary has been known for 30 years<sup>1,2</sup>; nevertheless attempts to investigate these activities in the pituitary in relation to the physiological condition of the animal are still rare.

In the present work we investigated the lipid-mobilizing and hypoglycaemic effect of pituitary homogenates of intact and alloxan-diabetic rats. For the experiments male Wistar rats with an initial weight of  $197 \pm 10$  g were used. Diabetes was induced by administration of alloxan hydrochloride, 250 mg/kg, in two subcutaneous injections in the course of 4 h. The diabetic rats lost  $8.3 \pm 4.6\%$  of their weight within 8 weeks, their blood-sugar level varied from 275–563 mg%. The control animals gained in the same period  $58.5 \pm 5.1\%$  of their body-weight. The pituitaries were removed immediately after decapitation and homogenized in a Potter-Elvehjem glass homogeniser in 0.02M sodium phosphate solution (pH 8.6). In the experiments, pooled specimens of pituitary homogenate from 5–6 rats were examined. The activity of the homogenate was tested on male mice (strain H); as an index of lipid-mobilizing activity changes in the liver fat content and free fatty acid blood level 6 h after the subcutaneous administration of pituitary homogenate was used. The

free fatty acids were estimated by TROUT's modification<sup>3</sup> of DOLE's method<sup>4</sup>, the fat content of the liver gravimetrically after extraction, as described by FOLCH<sup>5</sup>, the blood sugar level by a modification of Somogyi-Nelson's method<sup>6</sup>.

Figure 1 summarizes the results of two separate experiments from which it appears that the administration of 1–3 mg pituitary tissue of alloxan-diabetic rats to mice led to a significantly smaller fatty infiltration of the liver and a smaller rise of the free fatty acid level in blood in comparison with the corresponding weight of control pituitaries. Similar results were obtained also in the subsequent experiment with rat pituitaries, and in a preliminary experiment with pituitaries from normal and alloxan-diabetic rabbits. From Figure 2 it appears also that the hypoglycaemic activity, which usually runs parallel with the lipid-mobilizing activity, is markedly reduced in the homogenates from diabetic rats; while,

<sup>1</sup> C. H. BEST and J. CAMPBELL, *J. Physiol.* 86, 190 (1936).

<sup>2</sup> K. J. ANSELMINO, D. L. HAROLD, and F. HOFFMAN, *Klin. Wschr.* 12, 1245 (1933).

<sup>3</sup> D. L. TROUT, E. H. ESTES, and S. J. FRIEDBERG, *J. Lipid Res.* 1, 199 (1960).

<sup>4</sup> V. P. DOLE, *J. clin. Invest.* 35, 150 (1956).

<sup>5</sup> J. FOLCH, M. LEES, and G. H. SLOANE-STANCEY, *Fedn. Proc. Am. Soc. exp. Biol.* 13, 209, (1954).

<sup>6</sup> H. FRANK and E. KIRBERGER, *Biochem. Z.* 320, 359 (1950).

after administration of pituitary homogenate from normal animals, a statistically significant drop in the blood-sugar level was recorded ( $P < 0.01$ ), the changes after injection of homogenate from diabetic rats were slight or insignificant.

The above results thus provide evidence that animals with chronic diabetes, not treated with insulin, have a

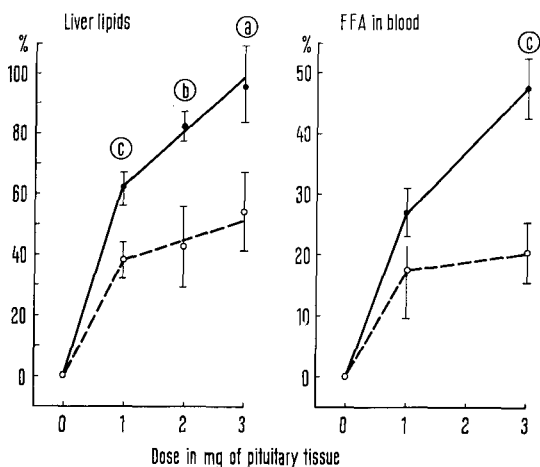


Fig. 1. Changes in the content of liver lipids and the free fatty acid level in the blood of mice after injection of pituitary homogenate from intact rats (●—●) and alloxan-diabetic rats (○---○). Expressed in % of value obtained in controls to which the same amount of solvent was injected. Individual values are averages of groups comprising 5–14 animals  $\pm$  S.E. Symbols for statistical significance between compared group averages: <sup>a</sup> ( $P < 0.05$ ); <sup>b</sup> ( $P < 0.02$ ); <sup>c</sup> ( $P < 0.01$ ).

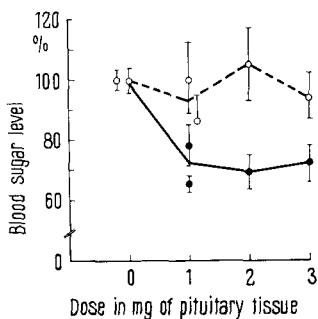


Fig. 2. Changes in blood sugar level of rats after injection of pituitary gland homogenate from intact rats (●—●) and alloxan-diabetic rats (○---○). Expressed in % of value obtained in controls to which same volume of solvent was injected. Individual values are averages of groups comprising 6–8 animals  $\pm$  S.E.

markedly reduced lipid-mobilizing and hypoglycaemic activity of the pituitaries. In alloxan-diabetic rats a reduced content of growth hormone was found in the pituitary and blood<sup>7,8</sup>, while the content of other pituitary hormones was unaltered<sup>7</sup>. The interpretation that for the observed decrease of lipid-mobilizing and hypoglycaemic activity the decreased amount of growth hormone in the pituitary is responsible, is however refuted by some of our unpublished experiments from which it appears that the decrease of growth hormone, e.g. during fasting<sup>9</sup>, need not be associated with a simultaneous decrease of the lipid-mobilizing activity of pituitary homogenates. It may be assumed that another factor or factors are involved which during fasting maintain the lipid-mobilizing activity of pituitaries, the decreased content of which in the pituitary of diabetic rats may participate in the observed changes. Perhaps lipid-mobilizing peptides described recently<sup>10–12</sup> are involved.

It is probable that the reduced lipid-mobilizing activity of homogenates of pituitaries from diabetic rats is rather the reflection of reduced formation of lipid-mobilizing substances than their increased turnover, as in other experiments we did not find an increased lipid-mobilizing activity in blood of alloxan-diabetic animals<sup>13</sup>. We may speculate whether or not it is a compensatory limitation of synthesis and secretion of pituitary lipid-mobilizing substances in alloxan-diabetic animals, which are more sensitive to lipid-mobilizing stimuli<sup>14</sup>.

*Zusammenfassung.* Die fettmobilisierende und hypoglykämische Aktivität in Hypophysenhomogenaten alloxandiabetischer Ratten ohne Insulinbehandlung ist nach achtwöchentlicher Diabetesdauer stark vermindert.

T. BRAUN and P. FÁBRY

*Physiological Department of the Institute of Human Nutrition, Prague-Krč (Czechoslovakia), November 8, 1965.*

<sup>7</sup> A. LAWRENCE, A. CONTOPOULOS, and M. SIMPSON, *Proc. Soc. exp. Biol. Med.* **99**, 35 (1958).

<sup>8</sup> R. L. HAZELWOOD and B. S. HAZELWOOD, *Am. J. Physiol.* **206**, 1137 (1964).

<sup>9</sup> R. C. FRIEDMAN and S. REICHLIN, *Endocrinology* **76**, 787 (1965).

<sup>10</sup> D. RUDMAN, R. L. HIRSCH, F. E. KENDALL, F. SEIDMAN, and S. J. BROWN, *Recent Prog. Horm. Res.* **18**, 89 (1962).

<sup>11</sup> E. B. ASTWOOD, R. J. BARRETT, and H. FRIESEN, *Proc. natn. Acad. Sci. U.S.A.* **47**, 1525 (1961).

<sup>12</sup> H. FRIESEN, R. J. BARRETT, and E. B. ASTWOOD, *Endocrinology* **70**, 579 (1962).

<sup>13</sup> T. BRAUN, Thesis, Czechoslov. Acad. Sci., Prague 1963.

<sup>14</sup> M. S. RABEN and C. H. HOLLENBERG, *J. clin. Invest.* **38**, 484 (1959).

### Mikrohistoautoradiographische Untersuchungen über die Verteilung von tritiummarkierten Phenothiazinen im Auge

Die Frage nach der Gewebs-Verteilung von Phenothiazinderivaten in den Strukturen des Auges wurde erstmals aktuell, als bei der klinischen Erprobung eines Versuchspräparates (NP 207 = 3-Chlor-10[2'-(N-methylpiperidyl-2'')-äthyl]-phenothiazin) Sehstörungen und abnorme

Netzhautpigmentierung festgestellt wurden<sup>1–6</sup>. Bevor noch die genauere Pathogenese dieser Schädigung aufgeklärt werden konnte, stellten wir in unseren Laboratorien fest, dass diverse substituierte Phenothiazine, inklusive Chlorpromazin, eine ausgeprägte Akkumulation im Bereich der melaninhaltigen Strukturen von Iris und Retina zeigten. Auf Grund mündlicher Mitteilung dieser erst später von RUTSCHMANN et al.<sup>7</sup> publizierten Ergebnisse konnte POTTS<sup>8–12</sup> unsere Beobachtung einer selektiven