

## References

- BRUNO, J.J., TAYLOR, L.A. & DROLLER, M.J. (1974). Effects of prostaglandin  $E_2$  on human platelet adenyl cyclase and aggregation. *Nature*, **251**, 721-723.
- FENICHEL, R.L., STOKES, D.D. & ALBURN, H.E. (1975). Prostaglandins as haemostatic agents. *Nature*, **253**, 537-538.
- GORDON, J.L. & DRUMMOND, A.H. (1974). A simple fluorimetric microassay for adenine compounds in platelets and plasma and its application to studies on the platelet release reaction. *Biochem. J.*, **138**, 165-169.
- GORDON, J.L. & MacINTYRE, D.E. (1974). Inhibition

- of collagen induced platelet aggregation by aspirin. *Br. J. Pharmac.*, **50**, 469P.
- MURER, E.H. (1972). Factors influencing the initiation and extrusion phase of the platelet release reaction. *Biochem. biophys. Acta*, **261**, 435-443.
- SMITH, J.B., SILVER, M.J., INGERMAN, C.M. & KOCSIS, J.J. (1974). Prostaglandin  $D_2$  inhibits the aggregation of human platelets. *Thromb. Res.*, **5**, 291-299.
- VIGDAHL, R.L., MARQUIS, N.R. & TAVORMINA, P.A. (1969). Platelet Aggregation: Adenyl cyclase, prostaglandin  $E_1$  and calcium. *Biochem. Biophys. Res. Commun.*, **37**, 409-415.
- WILLIS, A.L. (1974). Isolation of a chemical trigger for thrombosis. *Prostaglandins*, **5**, 1-25.

## Enlargement of the caecum in the rat

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Enlargement of the rat caecum has been found to occur following the repeated administration of a wide range of materials which are ingested by man. These include certain antibiotics e.g. neomycin, erythrosine (Butterworth, Gaunt, Grasso & Gangolli, 1975) and modified starches (de Groot, Til, Feron, Dreef-van der Meullen & Willems, 1974). A notable feature of the above studies was that the histological appearance of the caecal tissue was reported as normal. Thus when sub-acute and chronic toxicity studies have been performed on these materials, it has been found to be difficult to determine the biological significance of this enlargement. Experiments have been performed to determine some of the factors associated with the caecal enlargement produced by erythrosine.

Groups of 10 male, 4-week old, Wistar rats were fed a diet containing 0 or 2% erythrosine (2,4,5,7-tetraiodofluorescein) for 17 weeks. At post-mortem examination the weights of the caeca, both 'full' and empty, of these animals were  $9.37 \pm 1.33$  g (mean and 95% interval estimate) and  $1.31 \pm 0.22$  g respectively, compared with  $4.25 \pm 0.70$  g and  $0.90 \pm 0.13$  g for the control animals. The total amount of faecal material passed by the animals fed erythrosine was 137% of the control value ( $P < 0.01$ ), although there was no comparable increase in the food or water consumptions. Examination of the caecal contents revealed statistically significant changes ( $P < 0.05$ ) in the microflora of the treated animals when compared with the controls. The total number of

coliforms was increased to  $8.21 \pm 0.22$  g<sup>-1</sup> expressed as log<sub>10</sub> (controls =  $6.04 \pm 0.48$ ). Similarly the strict anaerobes were increased to  $10.07 \pm 0.38$  (control =  $9.44 \pm 0.17$ ) and *Streptococcus faecalis* to  $5.95 \pm 0.17$  (control =  $5.21 \pm 0.47$ ), while the lactobacilli were reduced to  $4.28 \pm 1.44$  (control =  $8.10 \pm 0.27$ ). The staphylococcal count was reduced in the treated rats to  $2.24 \pm 1.30$  (control =  $3.68 \pm 0.29$ ), but the decrease was not statistically significant. No differences were observed in the protein, lipid, or water content when expressed per unit weight of the caecal tissue. However the DNA content was increased from  $871 \pm 93$  to  $1275 \pm 333$  mg 100 g<sup>-1</sup> dry weight of tissue ( $P < 0.05$ ).

It is postulated that erythrosine, in altering the bacterial flora of the caecum, reduced the breakdown of certain dietary constituents, which then were excreted in increased amounts. Although it cannot be assumed that the underlying mechanisms of caecal enlargement induced by different agents are the same, it is suggested that, in the case of erythrosine, the increase in bacteria and undigested material placed an extra load on the caecum leading to a 'work' or functional hypertrophy and possibly hyperplasia. Work is in progress to investigate this hypothesis.

## References

- BUTTERWORTH, K.R., GAUNT, I.F., GRASSO, P. & GANGOLLI, S.D. (1975). Acute (mouse and rat) and short-term (rat) toxicity studies of erythrosine BS. *Fd Cosmet. Toxicol.* (in press).
- DE GROOT, A.P., TIL, H.P., FERON, V.J., DREEF-VAN DER MEULLEN, HARRIET, C. & WILLEMS, MARIAN I. (1974). Two-year feeding and multi-generation studies in rats on five chemically modified starches. *Fd Cosmet. Toxicol.*, **12**, 651-663.