yawning after intramuscular administration to rhesus monkeys[4] yet there is no evidence that this hallucinogen has marked effects on the cholinergic system in this species.

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URBÁ-HOLMGREN AND HOLMGREN REPLY—In Cowan's experiments with 'exmorphine addict' baboons, although physostigmine 0.05 mg per kg s.c. *per se* did not evoke yawning, this dose strongly potentiated naloxone-induced yawning. Perhaps a higher dose of physostigmine (0.10 mg per kg) would have elicited yawning directly even in monkeys, as it does in rats[1] and in infant guinea pigs, kittens and dog pups (unpublished observations). In infant rabbits we have had to use a still higher dose (0.15–0.20 mg per kg).

We certainly agree with Cowan that other factors are also important in yawning. The stretching and yawning syndrome induced by ACTH and MSH (quoted in ref. 1) is a well-known example. In recent experiments with (3,4 dihydroxyphenylamino)-2-imidazoline (DPI, Böhringer) we have observed that this drug, which according to Cools *et al.*[2] has a specific and potent agonistic activity at dopamine inhibitory receptors, in doses of 5 mg per kg intraperitoneally, elicits moderate, but statistically significant yawning in infant rats (from 9 to 15 d in age). It would be rash at this stage, to hypothesise that drugs shown to elicit the yawning act necessarily through a final common path including a cholinergic link.

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Lysogeny by f2 phage?

ZGAGA[1] claims to have produced "the first demonstration that bacteria can also contain the genetic information for the production of an RNA phage", and raises the question whether RNA phages can lysogenise their host in certain conditions. Her criteria are the "spontaneous release of phage particles" and the "immunity" of the host to superinfection.

Davern[2], and Hoffmann-Berling and Mazé[3] reported that *Escherichia coli* infected with RNA phage (can$_1$ or fr, respectively) when incubated at 32°C rather than 37 °C seemed to grow normally while producing phage at a low level. The suggestion that single infected cells excreted phage without lysing[3] has been challenged[4]. Davern further noted that even at 37 °C phage-infected cultures showed variable degrees of lysis and the surviving cells seemed to multiply normally while producing phage indefinitely in successive cycles of subculture. Such cells, when used as host bacteria in a plating assay, did not permit formation of plaques. The latter observations have been repeated several times in our laboratory when indicator bacteria have been accidentally contaminated with phage.

The state in which bacterial cultures produce phage without lysing and are resistant to superinfection has been called 'carrier state'[2] or 'viral persistance'[5] without implying any mechanism. Resistance to lysis occurs in certain physiological states of *E. coli*[6] and resistance to superinfection (interference) has been described as a normal consequence of RNA phage infection[7]. The phenomena described by Zgaga are reminiscent of the earlier observations and raise the question whether guanidine is required to establish cultures of bacteria "containing genetic information for f2 biosynthesis".

The term 'lysogeny' implies that the viral genome is present in the host in a non-infectious form, in particular that it is integrated into the host genome[8]; until evidence for such criteria is adduced in the case of RNA phages it would be preferable to retain the original designation of 'carrier state'.

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ZGAGA REPLIES—Weissmann's objection is based on the observations of Davern[1] and of Hoffmann-Berling and Mazé[2], that *E. coli* infected with some RNA phages apparently grow normally at lower temperatures while producing phage at a low level. Loeb and Zinder[3] showed that at 37 °C f2 phage lyse the bacteria they infect. Lerner and Zinder[4] showed, by the study of release of bacteriophage f2 from single infected cells, that at 30 °C as well as at 37 °C phage are released by cell lysis, and not by excretion from intact cells. Therefore, the definition of 'carrier state' mentioned by Weissmann ("the state in which bacterial cultures produce phage without lysing and are resistant to superinfection") obviously cannot be attributed to phage f2.

Originally, 'carrier state'[5] denotes "bacterial cultures that are persistently contaminated with phage, but from which uninfected cells could be recovered readily". Thus, the maintenance of this state depends on the presence of free phage and sensitive bacteria. To eliminate any possibility of reinfection during bacterial growth, female (*con.* f2) cells, which are genotypically resistant to f2 phage, were constructed. It turned out that F$^-$ (*con.* f2) bacteria produce phage spontaneously. In addition, 'carrier state' is not stable. Therefore phage-free, sensitive clones can usually be isolated by growth in the presence of phage antiserum, or by serial subcultures of single colonies[6]. On the contrary, the principal feature of 'lysogeny' is its stability. Hayes said[6]: "In practice, the existence of lysogeny should be judged by rather rigorous criteria of its stability, since interaction of some virulent phage with their hosts may superficially simulate the condition" ('carrier state'). (*Con.* f2) state, once established, has been stable for 2 yr. It is stable in male as well as in female cells and quite unaffected by serial subculture of single colonies or by antiserum treatment.

The functional state and the location of genetic information for phage production in (*con.* f2) bacteria are still under investigation. But, I do not agree with Weissmann's notion that the term 'lysogeny' in particular implies, that the viral genome is integrated into the host genome. For example, in lysogens carrying phage P1, the prophage does not occupy a characteristic site, if any, in the bacterial chromosome[7], but there is strong evidence to suggest that it is a nonchromosomal element[8], and a part of the bacterial membrane replicatory system[9–11].

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