the results of Carneri et al.[5], a fact which was attributed to the pharmacokinetical peculiarities of the drugs in mice and rats. The authors reported that the active fraction of metronidazole in mouse urine was more than twice that of nimorazole, whereas in rats and man the opposite is true. They thus considered that the mouse was not particularly suitable for assessing the therapeutic properties of nimorazole in human infections. This supposition to some extent contradicts the present as well as previous results[6], since the compounds show similar activity to metronidazole in rats as well as in mice, if they are infected intravaginally. The degree of systemic efficacy of nimorazole in the experimental animal does not correlate exactly with the activity in the urine.

Tinidazole was the most effective drug in both models and showed a clear superiority in the new one. These results correlate closely with the dosage of tinidazole used in practice, which are lower than those of the other drugs[7] recommended for a 7-day-course treatment of trichomoniasis. These findings underline the suitability of the intravaginal test systems.

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Effects of 5-bromodeoxyuridine and 2-aminopurine on antheridium differentiation in Anemia phyllitidis L.

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Summary. Both 5-BUdR and 2-Ap cause AG/TC transitions during DNA replication or transcription. However their effects on differentiation of antheridia in the fern Anemia phyllitidis differ totally. Since 5-BdU causes pattern simplification, 2-Ap leads to suppression of correlative cell interactions. This results indicate different targets for this mutagenic compounds in Anemia-DNA.

Gibberellins substitute for the native antheridiogens of the fern Anemia phyllitidis[1,2]. Addition of these phytohormones to culture media causes the premature differentiation of male sexual organs (antheridia)[3]. Although the hormonal induction of cell differentiation is not blocked by inhibitors of protein and nucleic acid synthesis, 5-bromodeoxyuridine (BUdR) has a striking influence on the manifestation of the antheridial pattern[4]. Identical effects are obtained with 5-iododeoxyuridine and 5-bromodeoxycytidine. Addition of these analogues to the culture medium (2×10^{-5} M–5×10^{-4} M) gives rise to the formation of simplified sexual organs. With high inhibitor concentrations, or after long times of application, the antheridia finally resemble vegetative chloronemata (Figure 1 a, b). As in various animal cells[5], the inhibition of cell differentiation precedes the inhibiting effect on rate of cell division.

The presence of BUdR in total DNA of prothallia of Anemia phyllitidis fed with ^{14}C-labelled BUdR was proved by Koop[6]. Since these effects of BUdR on anther-

1 My thanks are due to Miss C. Stiele for technical assistance and Dr P. Macnicol for checking the English version of the manuscript. Supported by the Deutsche Forschungsgemeinschaft.
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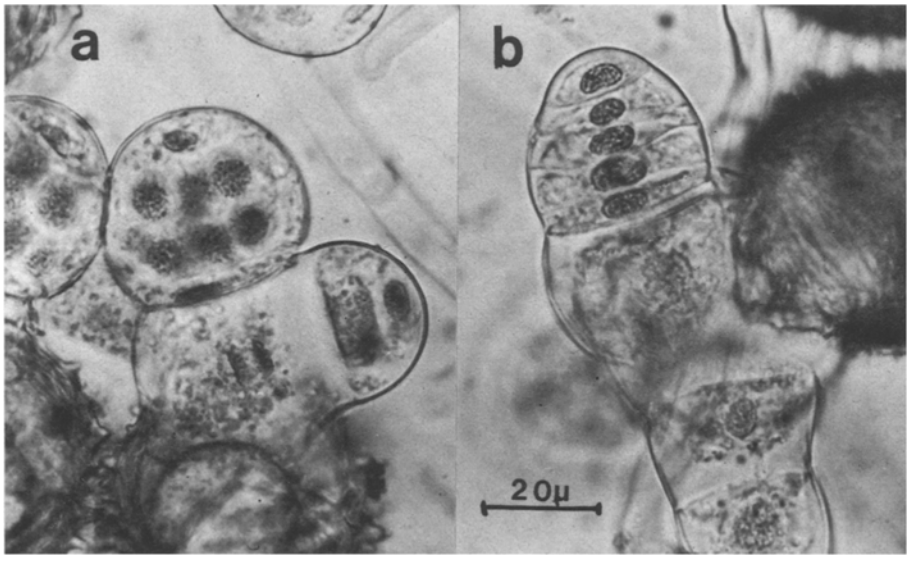

Fig. 1. Effect of BUdR on antheridium differentiation of light grown prothallia of Anemia phyllitidis. a) Control; 10^{-5} g/ml Gibb A_3; b) 2×10^{-5} M BUdR; 10^{-5} g/ml Gibb A_3. 10 d; 20 °C; continuous light ($1{,}2 \times 10^3$ erg cm^{-2} sec^{-1}).

Effect of 2-AP-addition to the cultur medium of light grown prothallia of Anemia phyllitidis

Conc. 2-AP	Mean cell number
0	13.0 ± 0.5
10^{-3} m	3.1 ± 0.2
7.5×10^{-4} m	5.5 ± 0.2
5×10^{-4} m	6.8 ± 0.2
2.5×10^{-4} m	8.5 ± 0.4
10^{-4} m	10.3 ± 0.5
5×10^{-5} m	12.2 ± 0.5

t = 10d; 20 °C; continuous light (1.2×10^3 erg cm^{-2} sec^{-1}).

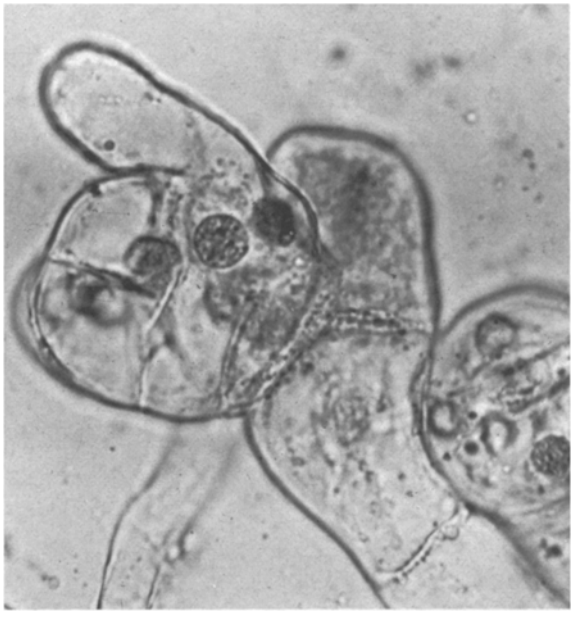

Fig. 2. BUdR on antheridium differentiation in continuous darkness. Reduced antheridium pattern. Beginning regeneration from the ring cell. (2×10^{-5} M BUdR, 10^{-5} g/ml Gibb A_3). 10 d; 20 °C.

idial differentiation can equally well be demonstrated in dark-grown gametophytes (figure 2), an increase in radiation sensitivity – well known with BUdR – must be excluded as cause for the suppression of the differentiation pattern. It is therefore probable that the observed morphogenetic effect is the consequence of an alteration in protein structure due to BUdR-induced base transitions during replication or transcription.

Since the purine analogue 2-aminopurine (2-AP) causes comparable AT/GC transitions[7], it seemed worthwhile to compare the effects of this mutagenic compound with those induced by BUdR. Teratological antheridial differentiation in gibberellin-treated (10^{-5} g/ml) prothallia is abundant after application of 2-AP in concentrations between 2.5×10^{-4} M and 10^{-3} M. Although BUdR has only a weak effect on cell division[5], the morphogenetic effect of 2-AP is accompanied by a significant lowering of division rate (table 1).

Although both analogues cause AT/GC transitions, the morphogenetic effects following 2-AT treatment differ totally from those induced by BUdR. While the latter are characterized by an increasing simplification of the antheridial pattern accompanied by early loss of the ability to produce fertile spermatozoa, treatment with 2-AP leads predominantly to suppression of the correlative cell interactions which are responsible for correct antheridial development (figure 3 a, b). Pattern-typical blocks of cell division in the stalk cell, the ring cell or the bell cell are abolished after 2-AP treatment. The normally strict synchronisation of cell division in spermatogenous tissue is disturbed, leading to differing developmental stages of the spermatozoa. Since the de-blocked stalk or ring cells give rise to initiation of new gametangia very complicated patterns arise, predominantly characterised by a loss of correlative regulation.

Although it is difficult even in haploid fern gametophytes to get exact experimental data on the loci of transitions caused by analogues, the presented results indicate different and analogue-specific DNA sections as targets for the effects of halogen-substituted pyrimidine deoxyribosides (BUdR, IUdR, BCdR) and 2-AP, respectively.

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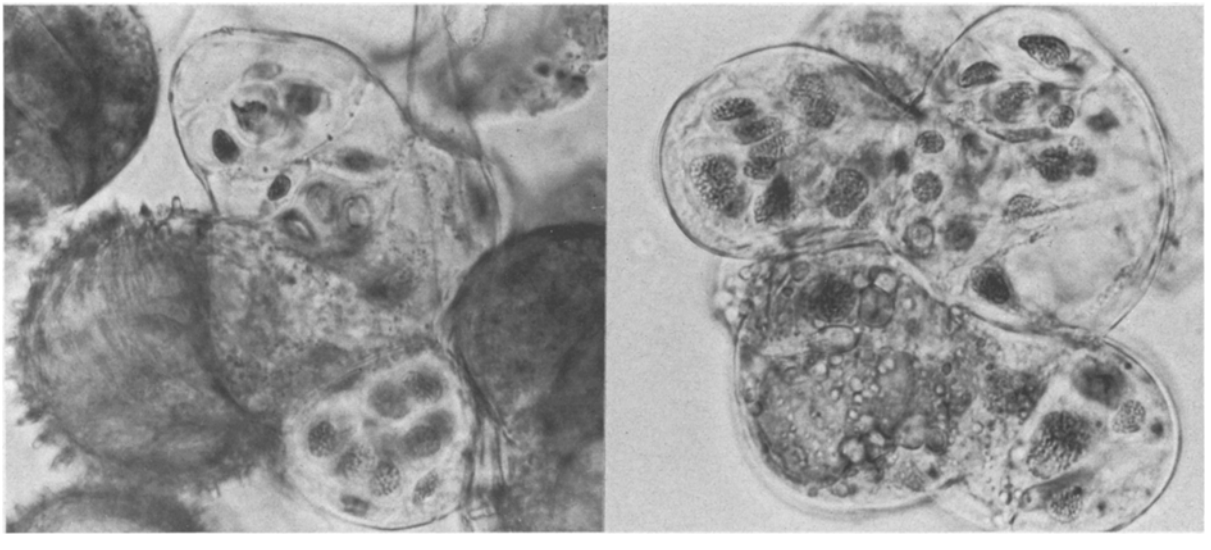

Fig. 3. Effect of 2-AP on antheridium-differentiation of light grown prothallia of Anemia phyllitidis. 7.5×10^{-4} M 2-AP; 10^{-5} g/ml Gibb A_3. 10 d; 20 °C; continuous light ($1{,}2 \times 10^3$ erg $cm^{-2}sec^{-1}$).