tee is the creation of large mental hospitals having a primarily custodial function, which has been shown to be no answer and should be discouraged. A hopeful sign is that the emphasis in this report, though not eschewing treatment, has moved towards prevention—in which ultimately there must lie much greater profit.

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Prolactin, pregnancy, and lactation

There are two distinct phases of lactation; milk secretion, the synthesis of milk within the mammary alveolar cells and its excretion into the alveolar lumen; and milk ejection, the transfer of the secreted milk into the larger ducts and sinuses, where it is obtainable by suckling.[1] The first phase is dependent on the anterior pituitary hormone prolactin and the second on oxytocin released from the posterior pituitary. Prolactin is normally under inhibitory control from the hypothalamus, and recent evidence suggests that the prolactin inhibitory factor is not a polypeptide similar to the hypothalamic-releasing hormones but is dopamine itself.[2] Recently, interest in this first phase of milk secretion has been stimulated by the development of a specific radioimmunoassay for prolactin[3 4] and the introduction of bromocriptine,[5] a dopaminergic drug which inhibits prolactin secretion.

Prolactin has been shown to enhance the production of specific enzymes concerned in the synthesis of milk protein[6] and lactose,[7] and it may also affect the production of nucleic acids.[8] In pregnancy the prolactin level becomes raised by the eighth week of gestation and rises steadily to term. If the woman does not breast feed it returns to normal within two to three weeks of delivery.[9] This rise in prolactin, which is of pituitary origin, is paralleled by an increase in placental production of a similar hormone, human placental lactogen (HPL). Both hormones are lactogenic; nevertheless, little or no lactation occurs before parturition, because increased levels of ovarian and placental steroids block their peripheral actions—as was first suggested by the classic experiments of Lyons[10] and Nandi[11] in hypophysectomised rats and mice. They showed that lobuloalveolar proliferation could be induced by a combination of oestrogen, progesterone, prolactin, growth hormone, and adrenal corticoids and that milk secretion could then be initiated by continuing the injections of prolactin and corticoids while stopping those of the ovarian hormones and growth hormone. Further indirect evidence was obtained by Brun *et al*,[12] who found that in patients in the postpartum period prolactin levels fell immediately after administration of bromocriptine and that this decrease was associated with lack of milk formation. Patients treated with a standard oestrogen preparation also did not lactate, though serum prolactin levels remained raised.

The relation between the raised prolactin levels and puerperal amenorrhoea is still disputed. Evidence exists for a direct action of prolactin on the ovaries, for high levels inhibit progesterone synthesis in vitro.[13] An action on the hypothalamus or pituitary has also been suggested, since puerperal women have low basal FSH levels, which rise as prolactin falls during treatment with bromocriptine.[14]

When bromocriptine is generally available it will be useful in the suppression of lactation,[15] for oestrogen therapy is associated with a 12% failure rate[16] and a risk of thromboembolism,[17] while diuretics are ineffective when given alone.[16]

Human prolactin secretion may be stimulated by thyrotrophin-releasing hormone (TRH)[18] and several drugs including the phenothiazines, rauwolfia alkaloids, imipramine, haloperidol, methyldopa, metoclopramide, and high doses of oestrogens. TRH is probably not important in the physiological regulation[19] of prolactin secretion but a rise in endogenous prolactin secretion in postpartum women using this hormone is associated with an increase in milk production and milk fat composition.[20] However, there appears to be little therapeutic use for such drugs in the stimulation of prolactin production.

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Facile mutagenesis by hair dye constituents

Several highly sensitive techniques based on the use of microorganisms have been developed for detecting mutagenic activity. The hall-mark of such systems is that the changes that occur do so with great facility. Those who use such tests claim that, since known carcinogens give positive results, any other substance of unknown carcinogenic potential which does so should also be suspected of carcinogenicity or even regarded as carcinogenic until proved otherwise.

At the cellular level, it is likely that any mutation-like change that leads to cancer is rare. A priori, therefore, it is most doubtful whether a mutational change which is very easily brought about can be an appropriate model for testing for carcinogenic potential. In any case the main purpose of safety tests on environmental chemicals should not be the relatively academic one of detecting carcinogenic potential but the more practical one of pin-pointing agents which constitute real hazards. It is already clear that a number of substances such as caffeine and formaldehyde, which show definite mutagenic activity in bacterial systems, present no detectable carcinogenic hazard for man.

Regulatory authorities in general agree that the role of mutagenicity tests in the assessment of carcinogenicity is limited to two main aspects. Firstly the screening of many compounds cheaply to see which should be subjected to much more costly long-term tests for carcinogenicity in animals or to a full battery of mutagenicity tests such as recommended by the Canadian authorities.[1]

The recent flurry of interest in the possibility that some hair-dye constituents constitute a cancer risk is based on positive results obtained in bacterial mutagenicity test systems. At a meeting of the National Academy of Sciences in March 1975 Bruce Ames[2] reported that 150 out of 169 hair dye formulations which depend for their action on the oxidation of various aromatic diamines by hydrogen peroxide are active in producing mutations of the so-called frame-shift type in a strain of *Salmonella typhimurium* highly sensitive to the production of this type of mutation. Base-pair substitution mutations were not produced in the same strain, and no frame-shift mutations were produced by any of the agents in a number of other frame-shift-sensitive strains of the same organism. Some of the agents tested were active only after mixture of the diamine with hydrogen peroxide. The agent found by Ames to have the most activity was 2,4-diaminoanisole, which is closely related to 2,4-diaminotoluene, which in turn is known to cause tumours when fed to rats.[3]

A more recent report by workers in Britain has blown on the embers of the fire started by Ames and his colleagues. Searle *et al*[4] have found, in an experiment that was incomplete at the time their paper was published, a slightly increased incidence of virus-associated tumours of the lymphoid system in two strains of mice in response to the repeated application to the skin of two proprietary hair-dye preparations. The mechanisms underlying the increase in incidence have not been investigated by the workers concerned. Since non-specific factors, such as changes in hormonal and nutritional status, can appreciably influence the age-standardised risk of lymphoid neoplasia in mice,[5] it would be unjustifiable to assume that changes reported were a direct result of mutations produced by the test materials. A feature of chemically-induced as distinct from virus-induced cancers is that they are heterogeneous with regard to antigenic structure. It would be interesting to see whether the lymphoid neoplasms seen in mice exposed to hair-dye constituents are distinguishable from each other or from the common virus-induced lymphomas of mice.

Searle and his colleagues[4] concluded that their findings indicated a need for a comprehensive toxicological evaluation of hair colourant constituents, in particular of nitrophenylenediamines, which have previously been little investigated. This is certainly the case—not so much because of the positive results reported by Ames and Searle and their colleagues, but mainly because it is prudent to establish the safety of commonly used chemicals, particularly those absorbed into the bodies of men and women who use them,[6] and particularly if the chemicals concerned are structurally related to known carcinogens. Not surprisingly this policy had in fact already been acted upon before Ames and his colleagues held their press conference. In 1973 Kinkel and Holzmann[7] reported that *p*-toluenediamine, resorcinol, and *m*-diaminoanisole gave rise to no toxic effects when applied repeatedly to the skin of rats over a period of two years, and more recently negative results in tests for chronic toxicity, teratogenicity, and effects on reproduction in various species have been reported[8] for a number of hair-dye constituents including some nitrophenylenediamines. The accumulation of such evidence from properly designed long-term studies on animals together, if possible, with epidemiological data from human studies should provide the main basis for deciding whether commonly used chemicals are likely to constitute cancer hazards for humans. Scares based on wild extrapolations from ultra-short-term studies in artificially susceptible laboratory systems serve to confuse issues rather than to elucidate them.

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Looking at the skin

Before the last war few self-respecting dermatologists would examine a patient without having a magnifying glass fixed, more or less expertly, in one eye; some would even use binocular glasses. Now there is a tendency to look first for the presence or absence of antinuclear factor, the IgE level, and the results of immunofluorescent investigation before glancing at the patient to see whether his lesions correspond to these findings. Rightly the days of arguments about diagnosis based on hair-splitting differences in morphological features have largely disappeared and been replaced by a more dynamic and fruitful approach, but there is a danger that something of value may be lost. A recent article[1] on the importance of being visually literate maintained this and discussed the mechanism of observation and reasons for deficiencies in it—though a quotation from Ruskin, "to see clearly is poetry, prophecy and religion—all in one," was perhaps a little extreme.

In our approach to a patient it is essential to decide exactly what is our objective. Are we basic research workers seeking clues to the cause of some common or obscure skin condition and inclined sometimes to be somewhat scornful of those who are simply trying to make a correct diagnosis and treat a sick patient? Most of us would not claim to be in this class, and very few of our students will ever reach such dizzy heights. Most will go into general practice and will have to diagnose and treat skin diseases with little help from a laboratory. Some will become consultants, but general physicians and even surgeons would benefit from an elementary though sound knowledge of skin conditions. Students must be taught to "see" a skin properly, and this can be done only if they are shown how by their teachers, who must set a proper example by their own careful observation. How many times have students said that they have never seen a seborrhoeic wart even though they have spent a year or more examining chests and hearts in patients who have been covered with them? Many patients nowadays suffer from scabies for months because their doctors have never learnt to examine a skin properly and have routinely prescribed a steroid ointment, the "cure" for all undiagnosed dermatological ills.

A sound training in skin morphology is a most valuable part of medical education, not only for the facts learnt but also in instilling correct methods of observation. The appearance of a lesion should not only be noted but should be described verbally. A student often has the greatest difficulty in describing