hyperbilirubinaemia. In those patients with Gilbert's syndrome, in whom an enzyme defect had been demonstrated, a reduction in the level of plasma bilirubin and an improvement in the handling of ^{14}C-bilirubin was always observed. In a patient with congenital haemolytic anaemia and normal enzyme activity (and handling of ^{14}C-bilirubin) phenobarbitone therapy did not significantly alter either the plasma bilirubin level or the ^{14}C-bilirubin disappearance curve.

These observations indicate that a reduction in the level of unconjugated bilirubin in the plasma following phenobarbitone administration is suggestive evidence of a defect in bilirubin conjugation.

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Assessing reports of therapeutic trials

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The quality and reliability of clinical trials vary greatly, and before therapy is based on their results it is important to assess such trials critically, taking into account their design, methods and execution. We have developed a check list for examining reports of therapeutic trials systematically and for assessing their validity. The check list is intended to apply to any report of a prospective investigation of a therapeutic effect in patients. It is not suitable for the assessment of reports of pharmacological studies in man unless the drug was administered with therapeutic intent and the therapeutic effect was assessed. The check list is also unsuitable for reports of retrospective studies, and for case reports.

The check list first examines what information the report contains about the subjects studied, the drugs used, and the experimental design. The questions in this part of the list (sections 1 to 5) can all be answered by consulting the report of the trial. They are followed by questions which aim more directly at an assessment of the quality of the trial (sections 6 and 7); a subjective element is necessarily involved in answering these questions. The answers to all the questions in the check list can then be considered in relation to one another when it comes to assessing the trial as a whole.

With the help of this check list both of us have independently examined all the reports of therapeutic trials to be found in the issues of four British journals published between January 1 and June 30 in 1966 and 1969. The assessments made by the two observers largely agreed, though they sometimes differed on points in sections 2 to 4. These differences in opinion most often arose from ambiguities in the description. In the two weekly journals, 83% of the 82 reports published and in the monthly journals, 46% of the 59 reports published were acceptable or probably acceptable ($\chi^2=21{\cdot}6$, 1 d.f., $P<0{\cdot}01$). Furthermore the weeklies showed greater improvement in this respect between 1966 and 1969 than the monthlies.

The check list may be of help in the preparation of therapeutic trials and of reports describing them, in editorial offices, and in the assessment of claims made for drugs and other therapeutic measures. Copies may be obtained by writing to A. H.

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Drug-induced inhibition of tumour cell dissemination

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A characteristic feature of cancer and one of its major problems is dissemination of malignant cells from the primary growth. Attempts to discover drugs specifically to inhibit this dissemination have not, however, received much attention; perhaps because of inadequate experimental models. Recent work (Hellmann & Burrage, 1969) has shown not only that the Lewis lung carcinoma (3LL) may be a useful test system for tumour cell dissemination, but that there may be drugs which can control the appearance of metastases without overt influence on the development of the primary growth.

The 3LL carcinoma has now been used to study the effects of a number of bis-diketopiperazines, a new class of cytostatic agents (Hellmann, Newton, Whitmore, Hanham & Bond, 1969; Creighton, Hellmann & Whitecross, 1969; Hellmann & Field, 1970) and more particularly the mechanism of metastasis inhibition by one of them, ICRF 159, (±)-1,2-bis(3,5-dioxopiperazin-1-yl) propane. Cyclophosphamide, a well known inhibitor of cell division, has been studied for comparison.

Inhibition of metastases by cyclophosphamide paralleled inhibition of the primary growth, but ICRF 159 inhibited pulmonary metastases at doses which gave only slight inhibition of the primary growth as judged by weight differences.

Daily microscopical examination for 14 days of blood concentrates and lung sections from untreated mice inoculated with 3LL showed that pulmonary metastases developed rapidly from the ninth day onwards, but malignant cells could only be detected in the blood from day 10 onwards. In the treated mice, however, no malignant cells were seen in the blood at any time and no pulmonary metastases developed.

Primary tumours from treated and untreated mice were then examined microscopically. In untreated mice the actively growing border of the tumour was permeated with innumerable thin-walled vascular spaces. In striking contrast in the treated mice the same part of the tumour contained well formed discrete blood