An outbreak of piracy in the literature

A rash of what appears to be piracy has turned up in the scientific literature. At least three cases are known in which either authors or editors of journals have drawn attention to the appearance elsewhere of articles which are substantially identical with articles that they have published. A common theme in these events is the appearance of the name of Dr E.A.K. Alsabti as one of the authors of the pirated articles. One illustration of the phenomenon is the appearance last year in the *Japanese Journal of Medical Science and Biology* of an article "Effect of platinum compounds on murine lymphocyte mitogenesis" which inspection shows to be a close copy of an article by Dr D. Wierda and Dr T.L. Pazdernick also published last year in the *European Journal of Cancer*. Among the three authors of the article in the Japanese journal is E.A.K. Alsabti, whose address is given as the Royal Scientific Society, Amman, Jordan.

Platinum compounds in cancer

The objectives of the research reported by Wierda and Pazdernick, and in the paper by Alsabti *et al.*, are given as the investigation of the effects of various platinum compounds of the spleen lymphocytes known as T and B cells. The issue is of practical importance because platinum compounds, like other anti-tumour drugs, kill not merely tumour cells but also the circulating lymphocytes of the immune system.

Interest in platinum compounds dates back more than a decade, when the compound DDP (*cis*-dichlorodiamine platinum) was shown by Rosenberg *et al.* (*Nature*, **222**, 385; 1969) to be effective against tumours in mice. Daniel Wierda says that his own interest in the field dates back to 1975, when his then supervisor, Dr Pazdernick, at the Department of Pharmacology of the University of Kansas, suggested a library search for evidence on which to base a search for analogues of DDP whose effects on the immune system would be less marked than those of the original compound.

In the research described in the two papers now published, mice have been used to demonstrate that the analogues of DDP are more toxic to T than to B cells. From this emerges the suggestion that platinum compounds might be used in conjunction with drugs which are more toxic to B cells than to T cells. Therapeutic regimes using DDP have been introduced in the past few years, and both papers come to the conclusion that clinical trials with the analogues now studied should be carried out.

Attempts in the past few days to trace Dr Alsabti and his fellow authors have been unsuccessful. The Scientific Attaché at the Jordanian Embassy in London said on the telephone on Monday this week that he had heard of Dr Alsabti, but that he knew nothing of his present whereabouts, believing him to be in Jordan.

The attaché also said that Dr Alsabti had no present affiliation with the Royal Scientific Society in Jordan. "Some years ago", Dr Alsabti had been allowed to use the address of the Royal Scientific Society, but this arrangement had since been terminated. He had no knowledge of the two other authors.

One feature of the paper in the Japanese journal is that readers are invited to send requests for reprints to an address in Brighton, "c/o Mrs W. Aljaff, Flat No. 5, 8 Norfolk Terrace, Brighton BN1 3AD, England". No name resembling Aljaff appears in the current Brighton telephone directory. A caller at 8 Norfolk Terrace earlier this week discovered that the occupant of Flat No. 5 spoke with a pronounced English accent and that he did not know of either Aljaff or Alsabti.

The two versions of the paper differ from each other in minor but perhaps significant details. The title of the paper in the Japanese journal is given as "Effect of platinum compounds on murine lymphocyte mitogenesis". The two American authors acknowledge the help of their technical assistant, while the three Jordanian authors say that "This work was supported by His Royal Highness Crown Prince Hassan of Jordan".

The references quoted at the end of Jordanian version do not however include the reference to earlier work of Pazdernick, one of the two American authors whose joint paper with Dr Wierda in the *European Journal of Cancer* had referred to a paper by Pazdernick first published in 1978.

The dates at which the two manuscripts were processed by the respective journals are very similar. Dr H. J. Tagnon, editor of the *European Journal of Cancer*, has confirmed in writing that the American paper was received in the Brussels office on 10 October 1978 and accepted for publication on 5 January 1979. The version published in the Japanese journal carries a note "Received November 20, 1978", implying that the manuscript had been received in Tokyo before a final decision on the American paper had been made in Brussels.

The editor of the Japanese journal during the period concerned, Dr Hideo Fukumi, said in Tokyo on Monday this week that he had now retired from that post and did not know who had succeeded him. He said that he could remember nothing of the circumstances attending the publication of the paper by Alsabti *et al.*

The processing of the corresponding American paper in Brussels appears to have followed a more or less normal course. It was sent to two referees in the United states, one of whom replied (returning the manuscript and the prints of the diagrams eventually published with the article). After some delay, it turned out that the second referee had died, and that copy of the manuscript has not since been recovered.

Dr Wierda says that he is sure in his own mind that no unauthorized person would have been able to obtain a copy of his material in advance of publication, but Dr Tagnon is equally firm in his assurances that there could have been no unauthorized leakage from his office.

Whatever the circumstances, this appears not to be the first occasion on which Dr Alsabti has had the misfortune to be involved with issues of copyright to written materials.

In April this year, Professor E Frederick Wheelock of the Jefferson Medical College in Philadelphia wrote to *The Lancet* to complain that a section of a grant proposal which he had written for the US Public Health Service (and which was sub-

Two conclusions — Alsabti et al. *superimposed*

In conclusion, we have observed that the platinum complexes tested were more toxic to splenic T lymphocyte function than splenic B lymphocyte function. Collectively, the results of these experiments demonstrated that the type of immunosuppression produced by the platinum compounds is markedly different from the type of inhibition caused by such commony used immunosuppressants as cyclophosphamide (Turk and Poulter, 1972; Gale et al., 1975). Because of this unique suppression, we believe that further clinical testing of these compounds as potential antitumor agents is warranted.

In conclusion, we have observed that the platinum complexes tested were more toxic to splenic T-lymphocyte function than splenic B-lymphocyte function. We have also demonstrated that DBCH and DBCP were con- one marrow nuc- sults) and spleen DP and DBP, yet inhibited T- and lectively, the re- emonstrated that ion produced by he platinum compounds is markedly different from the type of inhibition caused by such commonly used immunosuppressants as cyclophosphamide [22, 23] or X-irradiation [20]. Because of this unique suppression, we believe further clinical testing of these compounds as potential antitumor agents is warranted.

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sequently funded) had appeared in a review article entitled "Tumour Dormancy" by A. E. K. Alsabti (*Journal of Cancer Research and Clinical Oncology*, **95**, 209; 1979) which had also appeared in the Czech journal *Neoplasma* (26, 351; 1979).

Professor Wheelock said earlier this week that he was hoping to persuade each of the journals to publish a correction. He said that Dr Alsabti had worked in his laboratory for a period of five months but that he had asked him to leave after a disagreement about the authenticity of some experimental data.

Another case in which Dr Alsabti's authorship is questioned is his article "Diagnosis of serum lipids in hepatoma", published in *Oncology* (36, 11 1979). This so resembles an article by Yoshida *et al.* in the *Japanese Journal of Clinical Oncology* (7, 15; 1977) that the editor of the journal has written to *Oncology* saying "I was shocked by the appearance of Dr Alsabti's article which seems a copy of that by Yoshida *et al.* . . .". A copy of this letter has been seen by Dr J. Moglivit of the Anderson Medical Center in Houston, Texas, who was for seven months the immediate supervisor of Dr Alsabti during his spell as a volunteer (unpaid) technician there at the end of 1978.

Dr A. Clarke, president of the Medical Center, said on the telephone earlier this week that Alsabti had come to work in Texas on the recommendation of a Jordanian friend of the hospital but that in the end he was dismissed as a volunteer because of reports reaching the hospital of his exaggerated claims about the work that he had been doing.

One of the referees to whom the paper by Wierda *et al.* was sent by the *European Journal of Cancer* was Dr J. A. Gottlieb of the Anderson Center at Houston. Dr Alsabti was at the center towards the end of 1978. Dr Gottlieb had died some time before.

Index Medicus records that Dr Alsabti published 13 articles in the scientific literature during 1979 and ten in the first five months of this year.

Drug regulations Signs change

Washington

The drug industry has won a measure of support from the General Accounting Office in its complaint that the bureaucracy takes too long to license new products. In a report published last week (6 May), and based largely on comparisons with licensing practice in other industrialised countries, the GAO says that American practice is "lengthy" and that this circumstance "delays the benefits important drugs can provide to the public".

The fact that a new drug application takes on the average 20 months between the submission of test data and the receipt of licensing approval has been a hot potato in Washington for almost ten years. Without making any explicit judgement on the time needed to ensure that the scientific data is adequately reviewed, the GAO report does echo what many pharmaceutical companies have been saying for the past decade.

Excessive regulation, they claim, has not only escalated the costs of bringing a new drug to the market — now estimated at an average of $62 million — but has led to a growing proportion of their research being conducted outside the United States in countries with easier licensing regulations.

The Food and Drug Administration accepts that its licensing process is lengthy and has taken steps to accelerate the scientific review process. Two years ago, for example, it committed itself to reducing the time taken to license important new drugs by 25 per cent a year over three successive years, and claims to be on target. But the charges continue that the FDA is not doing enough. And last week congressmen keen further to speed the process quoted the GAO's conclusion that, based on a comparison of the time taken to license fourteen important drugs in six countries, the United States was slower than most in all but one case. According to the GAO, whereas it took on average five months to have a new drug approved in Great Britain and sixteen in Canada, the average time in the United States was 23 months, exceeded only by Sweden's 28 months. FDA counters with its own statistics. Analysis shows, it says, that "the few important drugs that genuinely advance medical care . . . tend to be approved today at reasonably similar times (generally within a few months) in most developed countries".

In response to the charge that its review procedures are too stringent, the agency replies that "of all new molecular entities [drugs whose active ingredient has not previously been marketed in the US] introduced into world medicine in the past decade, no country has approved more than 50 per cent of the total".

Behind the numbers game lie deeper arguments that illustrate how the time taken to approve new drugs is determined as much by the way that the United States has chosen to regulate the drug industry — with a heavy emphasis on administrative record and documented evaluation — as on the adequacy of particular regulations. Pointing to European countries, for example, where independent advisory committees can provide a buffer between a regulatory agency and the industry, the GAO suggests similar expert committees might be used more to review and approve new drugs in the United States.

The FDA disagrees. It says that the open nature of regulatory decision-making in the United States, the right of individuals to sue the government over regulatory actions and the powerful role of congressional oversight each make it difficult to go beyond the thirteen advisory committees now in place.

Another issue is that of post-marketing surveillance. The GAO report points out that in countries such as Great Britain with a national health care system, close contact between doctors and the health services encourages feedback and limits the potential dangers of premature licensing. The FDA, however, has very limited authority to take action on a drug once it has been released, and thus tends to be more cautious before giving licensing approval. There are also suggestions that physicians and hospitals may be dissuaded by the fear of increased medical liability from reporting their experiences.

Tighter provisions for post-marketing surveillance, including in particular the requirement that manufacturers should oblige doctors to notify them of any adverse side-effects, are a central feature of

Two figures — Wierda et al. *bottom left*

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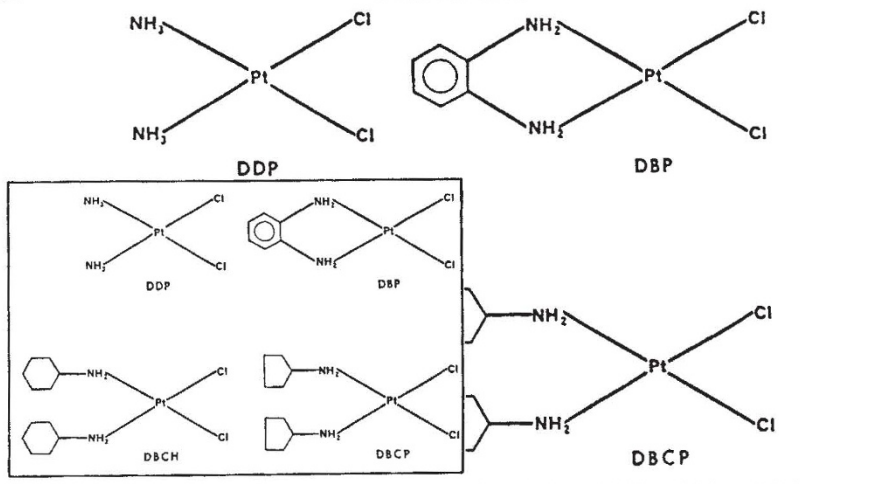

Fig. 1. Chemical structures of *cis*-dichlorodiammine platium (DDP), dichloro 1,2 benzenediamine N,N′ platinum (DBP), *cis*-dichlorobis(cyclohexylamine) platinum (DBCH), and *cis*-dichlorobis(cyclopentylamine) platinum (DBCP).

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