1 Hansen SW. Autonomic neuropathy after treatment with cisplatin, vinblastine, and bleomycin for germ cell cancer. *Br Med J* 1990;**300**:511-2. (24 February.)
2 Cantwell BMJ, Mannix KA, Roberts JT, Ghani SE, Harris AL. Thromboembolic events during combination chemotherapy for germ cell malignancy. *Lancet* 1988;ii:1086-7.
3 Bruera E, Chadwick S, Fox R, Hanson J, MacDonald N. Study of cardiovascular autonomic insufficiency in advanced cancer patients. *Cancer Treat Rep* 1986;**70**:1383-7.
4 Samuels BL, Vogelzang NJ, Kennedy BJ. Severe vascular toxicity associated with vinblastine, bleomycin, and cisplatin chemotherapy. *Cancer Chemother Pharmacol* 1987;**19**:253-6.
5 Garstin WH, Cooper GG, Hood JM. Arterial thrombosis after treatment with bleomycin and cisplatin. *Br Med J* 1990;**300**: 1018. (21 April.)
6 Stefenelli T, Kuzmits R, Ulrich W, Glogar D. Acute vascular toxicity after combination chemotherapy with cisplatin, vinblastine and bleomycin for testicular cancer. *Eur Heart J* 1988;**9**:552-6.

Read clinical classification

SIR,—Dr J Chisholm's welcome for the purchase by the Department of Health of the Read clinical classification[1] provides a refreshing contrast to the dogmatic cynicism of a recent editorial in the *Lancet*.[2] The department's bold strategic move places this country ahead of the rest of the world in computing clinical data.

The government's intention is clear—to disseminate computing techniques as widely as possible throughout health care. Momentous matters hang upon this decision, not least questions of cost. The rubric "clinical classification" fails, however, to address computer analysis of the complete medical record including symptoms.[3]

Computers have a vital role to play in clinical medicine but the Read system has three fundamentals which augur ill. Firstly, neither the Read classification nor the ninth revision of the International Classification of Diseases (ICD 9) on which it relies is based on the frequency with which clinical events actually occur in medical practice. Thus back pain and cough are a million times more prevalent than, say, cholera and should therefore be correspondingly easier to enter.

Secondly, neither the Read classification nor ICD 9 was initially designed for use in front of patients, which is where most clinicians spend their working lives. Again, chest pain should be 20 times easier to record than myocardial infarction because it occurs more often among the living, and not at all among the dead.[4]

Both these factors impede the use of such codes in a clinical setting. Busy clinicians rightly begrudge computer systems that are too slow or cumbersome to use—doctors will tend to default, thereby threatening the validity of the data recorded.

Finally, the Read classification is a single faceted or uniaxial code, as the working party noted.[5] This makes analysing the data difficult. For example, if chest pain has only a single entry, it is impossible to refer to the terms pain and chest separately. This poses acute, even insuperable, difficulties in retrieval. Retrieval has always been the computer's Achilles' heel, rendering real time retrieval of clinical data especially challenging.

It is technically possible to use a five faceted code with 30 starting points and six levels of detail (based on the frequency with which patients presented symptoms during a busy decade in general practice[6]) to include a full range of clinical items, and to enter the entire medical record faster than writing longhand. This can be done without typing, indeed without using a keyboard—only a "mouse." Twenty four years' experience of medical computing, however, leaves me with no illusions as to the reception such an extravagant statement will probably evoke.

Instead, let me try another, tighter prediction. The coding of clinical data is vital for the healthy practice of medicine. Within the next decade, therefore, all clinical data will be recorded by a computer code which takes account of the factors I have mentioned. The time scale for this will be lengthened considerably if medical cynicism continues unabated—and could be sharply foreshortened if the truly astonishing benefits of clinical computing became known more widely.

R A JOHNSON

Oldham OL4 4EW

1 Chisholm J. The Read clinical classification. *Br Med J* 1990;**300**: 1092. (28 April.)
2 Anonymous. Medical informatics [Editorial]. *Lancet* 1990;**335**: 824-5.
3 Johnson RA. Computer analysis of the complete medical record including symptoms and treatment. *J R Coll Gen Pract* 1972;**22**:655-60.
4 Johnson RA. Quality assurance in health care. *Proceedings of Current Perspectives in Health Computing* 1990:108-14.
5 Vickery BC. *Faceted classification*. London: Aslib, 1960.
6 General Medical Services Committee, Royal College of General Practitioners Joint Computing Group. *The classification of general practice data: final report of the GMSC-RCGP joint computing group technical working party*. London: General Medical Services Committee, British Medical Association, 1988.
7 Johnson RA. Adverse reactions in ten years general practice, computer analysed. *J R Soc Med* 1986;**79**:145-8.

SIR,—We support strongly the need for standardised coding systems for clinical data.[1] There are dangers, however, in viewing the Read classification system as a panacea. We suspect that the system will not prove suitable for coding clinical data in all circumstances despite its seemingly limitless potential for expansion. This caution is prompted partly by the system's design as a tool for retrospective analysis and partly by the arbitrary nature of its alphanumeric coding scheme. Both points are particularly important when considering clinical data handled by modern laboratory information management systems.

In our pathology laboratory we deal mainly with clinical data before diagnosis. Our users provide us with data on clinical symptoms, signs, and differential diagnosis, which are extensively used in choosing tests and interpreting reported results. By coding such data and by using standard laboratory information systems the most appropriate tests may be chosen and reports of high quality may be delivered to clinicians.

We developed and now use routinely such systems with a mnemonic coding scheme for clinical details (R G Jones *et al*. Proceedings of seventh international conference on computing in clinical laboratories, Lugano, Switzerland, 1989). We considered the Read system of coding and rejected it as unsuitable for our purposes. Firstly, the coding was too precise and was unable to cope adequately with the uncertainties inherent in some diagnostic questions. This is not surprising as the classification was designed initially for retrospective coding and analysis.

Secondly, the data we receive are variable and sometimes idiosyncratic. Because we try to return clinical details to the user on the report form, both to put results in context and to encourage appropriate requesting, we wanted to avoid the normalisation of data that occurs with systems such as the Read classification.

Thirdly, our workload is such that coding with alphanumeric codes, even with the use of aids, would be too inefficient. Our clerks must maintain an input rate of 75-100 entries per hour per person, each entry comprising 10 fields with full demographic details of patients, dates and times of sample collection and receipt, as well as clinical data. Our mnemonic uses common medical abbreviations and four letter codes derived from the data used in the request and allows rapid coding of 95% of the details provided. Our non-medical clerical staff routinely code 70% of the requests received without recourse to search aids, thereby sustaining the necessary rates of data input. We have found in practice that codes can be used effectively to control the flow of work through the laboratory, increase efficiency, reduce unnecessary testing, and enhance the quality of diagnostic information.

We suggest that before adopting a clinical data coding system, particularly one so large and complex as the Read classification, the exact purpose of the planned task and the implications for staff should be fully considered. We believe that other coding systems will be adopted eventually as international standards but each will be designed in relation to the functions it is intended to support.

R G JONES
K B PAGE

Department of Chemical Pathology and Immunology,
University of Leeds,
Leeds LS2 9JT

1 Chisholm J. The Read clinical classification. *Br Med J* 1990;**300**: 1092. (28 April.)

The cyclotron saga

SIR,—Again a news report shows bias against neutron therapy[1]—or is the bias really against a £6m grant from the Treasury which certainly won't come into the NHS any other way?

Ms Jane Smith manages to write several lines on the Medical Research Council's decision to stop trials at Clatterbridge of neutron therapy in pelvic cancer without mentioning a trial on salivary gland tumours which was closed because the results for neutron therapy were so good that "it became very difficult to continue accrual to a randomised study containing photon treatment."[2] Ms Smith repeats the differences between results in the Hammersmith and Edinburgh trials in the 1970s and fails to note the considerable differences in dose and technique of neutron therapy and the stage of tumour treated, which make comparisons valueless.[1]

Apparently unaware of the authoritative letter from Dr William Powers and Dr Richard Maughan published in the *BMJ*, she repeats again an untrue statement about neutron funding in the United States.[4] Third party reimbursement by medical insurance companies of charges paid by patients is now routine in the United States. Ms Smith ignores this evidence, which was in a letter from the United States National Institutes of Health sent to her when she was preparing her article.

It would be difficult to conclude from the news report that patients are routinely treated with neutrons in Belgium, that a new high energy cyclotron is just undergoing final tests before being used to treat patients in Nice, and that there are cyclotrons working or being installed in Germany, India, Japan, South Africa, South Korea, and the United States.

Ms Smith introduces an unfounded connection between the release of the grant and the raising of funds. It is exasperating that the happy combination of public and private funding, NHS experience, and commercial management that will make neutron and proton treatment available in London in a major university hospital is not welcomed by those who readily accept that, for some patients with cancer, this is the treatment of choice. Just because your cancer is "rare" does not mean that you should not receive the best treatment.

Equally, just because neutron therapy is apparently unpopular in some circles that does not mean that it should not have a balanced news report. Factual omissions do not strengthen a case, nor do tasteless captions to accompanying photographs. Readers of the *BMJ* deserve better.

D J GROCOTT

Cyclotron Trust for Cancer Treatment,
Department of Radiotherapy and Oncology,
St Thomas's Hospital,
London SE1 7EH

1 Smith J. The cyclotron saga: the next chapter. *Br Med J* 1990;**300**:1155. (5 May.)
2 Griffin TW, Pajak TF, Laramore GE, *et al*. Neutron vs photon

irradiation of inoperable salivary gland tumors: results of an RTOG-MRC cooperative randomised study. *Int J Radiat Oncol Biol Phys* 1988;15:1085-90.
3 Catterall M. "Controlled" clinical trials in neutron therapy. *Int J Radiat Oncol Biol Phys* 1987;13:1961-5.
4 Powers WE, Maughan RC. The cyclotron saga continues. *Br Med J* 1990;300:192. (20 January.)

Drug Points

Red man syndrome associated with amphotericin B

Dr MICHAEL E ELLIS (Monsall Hospital, Manchester M10 8WR) and Mr WILLIAM THARPE (King Faisal Specialist Hospital and Research Centre, Riyadh 11211, Saudi Arabia) write: We report a case of red man syndrome associated with amphotericin B.

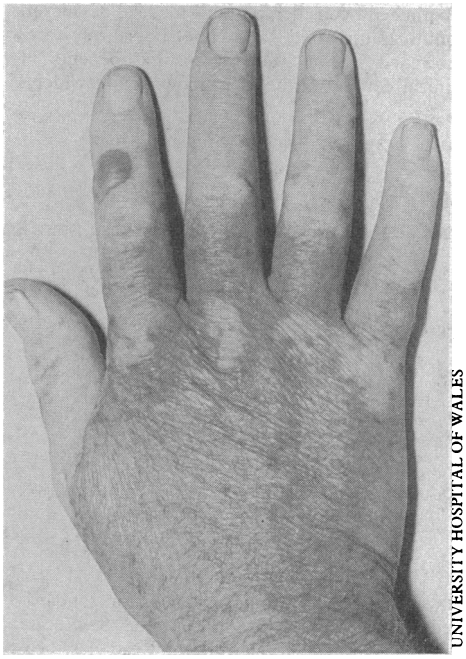
An 18 year old Saudi man was treated with daunorubicin and cytarabine for acute myeloid leukaemia. Ensuing febrile neutropenia ($0{\cdot}4\times10^9$/l) did not respond to intravenous piperacillin, gentamicin, metronidazole, and vancomycin so amphotericin B was added to cover the possibility of cryptic fungal infection. A test dose of 1 mg of amphotericin B was infused over two hours. Forty five minutes into the infusion an intense confluent blanching erythema appeared on the hands, soles, face, and neck and less so on the trunk. The hands became oedematous. A bounding sinus tachycardia (113 beats/min) developed with a blood pressure of 115/54 mm Hg. At the same time he was receiving intravenous vancomycin over one hour. Red man syndrome associated with vancomycin was diagnosed; amphotericin B and vancomycin were discontinued; intravenous diphenhydramine 25 mg with intravenous hydrocortisone 100 mg was administered; and the rash and swelling disappeared within four hours. On the next day vancomycin was withheld and a 1 mg test dose of amphotericin B repeated after premedication with diphenhydramine and hydrocortisone. The rash and swelling appeared as before. Once again the rash settled within two hours after the amphotericin B infusion was discontinued. Intravenous vancomycin was subsequently restarted with no incident, confirming that amphotericin B and not vancomycin had been responsible for the cutaneous reaction.

Common side effects of amphotericin B include fever, chills, and nephrotoxicity; a rash (maculopapular and truncal) has been reported only once,[1] and allergic reactions are rare.[2] This led to our wrongly blaming the vancomycin.[3] This report indicates that a similar reaction can occur with amphotericin B. The Committee on Safety of Medicines has had 20 reports of rash occurring in association with the use of amphotericin B over a recent 17 year period, but red man syndrome was not mentioned. Amphotericin B is the antimycotic of choice for systemic fungal infections, and its increasing use may yield further cases of red man syndrome.

1 Lorber B, Cutler C, Barry WE. Allergic rash due to amphotericin B. *Ann Intern Med* 1976;84:54.
2 Bennett JE. Chemotherapy of systemic mycoses. *N Engl J Med* 1974;290:30-1.
3 Garrelts JC, Peterie JD. Vancomycin and "red man's syndrome." *N Engl J Med* 1985;312:245.

Pseudoporphyria due to Dyazide in a patient with vitiligo

Dr RICHARD J MOTLEY (Department of Dermatology, University Hospital of Wales, Cardiff CF4 4XW) writes: A 65 year old man presented with a 12 month history of skin fragility and blistering confined to areas of longstanding vitiligo on the dorsum of the hands and fingers (figure). The condition started within one month of his starting Dyazide, one tablet a day, for hypertension, and resolved four months after its discontinuation. The patient was otherwise well and receiving no other medication. Immunofluorescence antibody studies of the skin were negative and investigations of his porphyrin metabolism were normal. Pseudoporphyria has not been previously reported with Dyazide, which is a combination of triamterene and hydrochlorothiazide, but a similar case was reported after naproxen treatment in a woman with vitiligo.[1] The distribution of these lesions suggests that sunlight may predispose to the development of this reaction. The patient now receives bendrofluazide (5 mg/day) and there has been no further evidence of skin fragility.



1 Burns DA. Naproxen pseudoporphyria in a patient with vitiligo. *Clin Exp Dermatol* 1987;12:296-7.

Lobular panniculitis associated with ciprofloxacin

Drs E RODRÍGUEZ, J A MARTÍNEZ, M TORRES, A NUBIOLA, and J BUGES (Hospital de L'Esperit Sant, 08923 Barcelona, Spain) write: Ciprofloxacin, a new fluoroquinolone antibacterial agent, has recently been implicated in causing an erythematous papular rash due to vasculitis.[1] We present a case of lobular panniculitis occurring after ciprofloxacin treatment.

A 67 year old woman with diffuse bronchiectasis, who had been treated for seven years with theophylline, prednisone, salbutamol, and beclomethasone, showed an increase in her usual cough and purulent expectoration. Sputum culture grew *Pseudomonas aeruginosa*, and oral ciprofloxacin 750 mg twice daily was prescribed. Four days later the patient had a rash on all her limbs. Physical examination showed a temperature of 38·5°C and many erythematous nodules in both legs, thighs, and forearms, which were painful on finger pressure. No other physical sign of systemic disease was found.

The red and white cell counts, hepatic and renal function, and values for plasma proteins, serum electrolytes, calcium, phosphate, creatine kinase, aldolase, amylase, antinuclear antibody, and complement were all normal or negative. Erythrocyte sedimentation rate was 80 mm in the first hour. The level of circulating immune complexes by Clq system inhibition was 20% (normal <15%). Skin biopsy showed a fragment of fat nodular tissue with fat necrosis and lymphocyte infiltrate with preservation of vascular and septal areas, all of which were typical of lobular panniculitis.[2] The fever and rash disappeared 10 days after ciprofloxacin was stopped.

Skin disturbances after ciprofloxacin administration occur in 0·7-2·2% of cases and have been described as nettle rash, pruritus, photosensitivity, and skin oedema.[3] We suggest that lobular panniculitis should be added to the list.

1 Choe U, Rothschild BN, Laitman L. Ciprofloxacin-induced vasculitis. *N Engl J Med* 1989;320:257-8.
2 Bondi EE, Latarus GS. Panniculits. In: Fitzpatrick TB, Eisen AS, Wolff K, Freedberg IM, Austen KF, eds. *Dermatology in general medicine*. New York: McGraw-Hill, 1987:1131-48.
3 Harkin H. Adverse effects of the fluoroquinolones. *Rev Infect Dis* 1988;10(suppl 1):S258-61.

Reversible hyperpigmentation associated with high dose hydroxyurea

DRS G MAJUMDAR, S E HEARD, and N G P SLATER (Department of Haematology, St Thomas's Hospital, London SE1 7EH) write: We recently treated two patients suffering from chronic granulocytic leukaemia in accelerated phase with high dose hydroxyurea, both of whom developed hyperpigmentation during treatment.

Case 1—A 61 year old man of African origin was treated for four years with intermittent busulphan during the chronic phase of the disease. In the accelerated phase he was initially treated with subcutaneous cytarabine 10 mg/m^2 daily for two weeks with no response. High dose hydroxyurea, 9 g/day for two days a week, was started on 23 May 1989. He showed partial response after a week and the dose was increased to 9 g/day for five days a week. Hyperpigmentation over the palmar creases and the forehead was noted on 16 June. Over the next two weeks the hyperpigmentation increased in both extent and depth and also affected the buccal mucosa. After six weeks' treatment he developed blastic transformation with thrombocytopenia and died of a cerebrovascular accident in August. Necropsy was not performed.

Case 2—A 47 year old man of African origin was diagnosed in the blastic phase and was initially treated with mitozantrone, cytarabine, and etoposide. He went into chronic phase after two such courses and was left without any cytotoxic or other drugs. Three months later he developed acclerated phase leukaemia. On 18 April 1989 he was started on hydroxyurea 9 g/day for two days a week, which was increased to four days a week after two weeks' treatment. Hyperpigmentation, most prominent over the forehead and palmar creases, was noted on 16 June, four weeks after the start of high dose hydroxyurea. He returned to chronic phase on 15 August, and the dose of hydroxyurea was reduced to 1·5 g/day given continuously. Over the next few weeks his hyperpigmentation regressed slowly and by 10 October, eight weeks after reduction of the dose, the level of pigmentation returned to normal.

Hydroxyurea has been reported to cause hyperpigmentation only after prolonged use in patients with psoriasis, concentrated in the affected areas.[1] In some patients hyperpigmentation was transient and disappeared even when hydroxyurea was continued. Lichen planus has been reported in patients with chronic myelogenous leukaemia after prolonged treatment with hydroxyurea.[2] We have not found any reports of reversible hyperpigmentation developing over a short period. Neither the Committee on Safety of Medicines nor the manufacturer has had any such report. The dose used in these two patients was higher than the usual dose of 1-3 g/day. Hyperpigmentation in our patients may have been related to the use of this high dose.

1 Dahl MGC, Comaish JS. Long-term effects of hydroxyurea in psoriasis. *Br Med J* 1972;iv:585-7.
2 Kennedy BJ, Smith LR, Goltz RW. Skin changes secondary to hydroxyurea therapy. *Arch Dermatol* 1975;111:183-7.