previously. Usually *P vivax* is superimposed on *P falciparum* so that when the patient has apparently recovered *P vivax* malaria recurs.

This case of double infection with two relapses (recrudescences)⁵ of *P falciparum* malaria after chemotherapy with chloroquine and a relapse of *P vivax* malaria after the usual dosage of primaquine for radical cure confirms the increasing importance of the problem of drug resistant malaria imported from the tropics into Europe.

- 1 Rollo IM. Drugs used in the chemotherapy of malaria. In: Gilman AG, Goodman LS, Gilman A, eds. *The pharmacological basis of therapeutics*. 6th ed. New York: Macmillan, 1980:1038-69.
- 2 Bruce-Chwatt LJ. *Essential malariology*. 2nd ed. London: Heinemann, 1985: 224-5.
- 3 Alving AS, Johnson CF, Tarlov AR, Brewer GJ, Kellermeyer RW, Carson PE. Mitigation of the haemolytic effect of primaquine and enhancement of its action against exoerythrocytic forms of the Chesson strain of *Plasmodium vivax* by intermittent regimens of drug administration. *Bull WHO* 1960;22:621-31.
- 4 Peters W. Antimalarial drug resistance: an increasing problem. *Br Med Bull* 1982; 38:187-92.
- 5 Bruce-Chwatt LJ. Terminology of relapsing malaria: enigma variations. *Trans R Soc Trop Med Hyg* 1984;78:844-5.

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Increased serum pancreatic enzymes after treatment with methylprednisolone: possible evidence of subclinical pancreatitis

On the basis of anecdotal clinical evidence and the results of giving steroids to experimental animals it has been claimed that steroids may be associated with acute pancreatic injury. This report provides evidence that the serum concentrations of the three pancreatic enzymes (trypsin, lipase, and amylase) may increase after administration of large intravenous doses of methylprednisolone.

Patients, methods, and results

Ten patients with progressive endocrine exophthalmos (euthyroid and with normal renal function) were included in this study. Seven had previously been thyrotoxic and been treated with carbimazole or radioactive iodine. Two were currently receiving carbimazole 10 mg daily. One was hypothyroid and receiving a replacement dose of thyroxine 0.1 mg daily. Two had not had any thyroid dysfunction. All were treated with 1 g methylprednisolone in 500 ml saline intravenously over two hours on three consecutive days.

Blood samples were collected before the administration of methylprednisolone and daily after treatment for several days. In four patients blood samples were also collected at half hour intervals for three hours after the first methylprednisolone infusion. Serum immunoreactive trypsin concentration was measured by radioimmunoassay using a kit (Hoechst) as described previously.¹ Total and pancreatic amylase and pancreatic lipase concentrations were measured by kits.^{2,3}

In all 10 patients serum immunoreactive trypsin concentrations increased considerably (by 35-109%) after administration of methylprednisolone (table). This was paralleled by similar increases in pancreatic amylase and lipase concentrations. Salivary amylase activity in the serum did not alter. Immunoreactive trypsin concentration peaked on days 5-8 after the infusion, the peak occurring on day 5 in five patients. Peaks in pancreatic amylase and lipase concentrations also occurred on days 5-8. The increase in pancreatic enzymes was still observed on day 10, though the concentrations then were considerably lower than the peak values. There was a highly significant correlation between immunoreactive trypsin and pancreatic lipase; immunoreactive trypsin and amylase; and pancreatic lipase and amylase ($r=1.74$; $p=0.002$). No immediate effect of methylprednisolone on pancreatic enzymes was observed.

None of the patients developed clinical features of pancreatitis or parotitis.

Comment

In all cases but one the increase in pancreatic enzyme concentrations occurred more than two days after infusion and the peak occurred on days 5-8. The absence of an immediate increase after

Effect of intravenous methylprednisolone on serum pancreatic enzyme concentrations

Case No	Time of measurement	Immunoreactive trypsin (µg/l)	Lipase (U/l)	Amylase (U/l)		
				Total	Pancreatic	Salivary
1	Basal	412	253	102	96	6
	Peak (day 5)	857	298	192	174	18
	Day 10	627	229	150	132	18
2	Basal	344	72	168	78	90
	Peak (day 8)	699	200	300	156	144
	Day 10	499	180	200	160	140
3	Basal	323	147	138	102	36
	Peak (day 8)	730	286	252	222	30
	Day 10	499	249	240	216	24
4	Basal	217	89	90	66	24
	Peak (day 3)	930	350	330	306	24
	Day 10	360	141	162	120	42
5	Basal	223	81	282	126	156
	Peak (day 5)	342	99	228	168	60
	Day 10	214	74	222	144	78
6	Basal	239	82	65		
	Peak (day 5)	436	288	50		
	Day 10	420	235	55		
7	Basal	340				
	Peak (day 7)	510				
	Day 10	410				
8	Basal	320				
	Peak (day 5)	580				
	Day 10	425				
9	Basal	275				
	Peak (day 6)	600				
	Day 10	433				
10	Basal	410				
	Peak (day 5)	810				
	Day 10	700				
Normal ranges		140-400	50-200	40-150	30-160	

methylprednisolone and the delay before peak pancreatic enzyme concentrations were reached suggest that this effect was due to the cumulative effects of the steroid and not merely an alteration in the secretory pattern of these enzymes.

Increased serum pancreatic enzyme concentrations have previously been found in association with acute damage of the pancreas, as in acute pancreatitis, and with chronic pancreatic damage, as in cystic fibrosis³ and β thalassaemia with iron overload; and in elderly asymptomatic subjects.⁴ As serum concentrations of immunoreactive trypsin and other pancreatic enzymes do not increase greatly after a meal or the injection of pancreozymin (in contrast with the changes in intraduodenal pancreatic enzyme concentrations), their delayed and persistent increase after methylprednisolone probably reflects an injury of the pancreatic acinar cell or the acinar basement membrane, or both. This increase in immunoreactive trypsin concentration after methylprednisolone contrasts with the inhibition of exocrine pancreatic secretion into the duodenum after much smaller doses of hydrocortisone and adrenocorticotrophic hormone.⁵

We conclude that an increase in serum pancreatic enzyme concentration after a large dose of steroids may indicate subclinical damage of the pancreatic acinar cell. Persistence of such a stimulus, or its presence in combination with another pancreatic toxin like ethanol or with biliary disease, may predispose to clinical pancreatitis. Our data do not clarify the pathogenesis of pancreatitis induced by steroids, but they show a consistent injurious effect of large doses of these drugs on the exocrine pancreas.

- 1 Dandona P, Elias E, Beckett AG. Serum trypsin in diabetes mellitus. *Br Med J* 1978;ii:1125.
- 2 Foo Y, Rosalki SB, Ramdial L, Mikhailidis DP, Dandona P. Low pancreatic amylase in diabetes mellitus. *J Clin Pathol* 1980;33:1102-5.
- 3 Junglee D, Katrak A, Penketh A, Hodson M, Batten JC, Dandona P. Serum pancreatic lipase in cystic fibrosis. *Br Med J* 1983;286:1693-5.
- 4 Mohiuddin J, Katrak A, Junglee D, Green M, Dandona P. Serum pancreatic enzymes in the elderly. *Ann Clin Biochem* 1984;21:102-4.
- 5 Dreiling DA, Janowitz HD, Rolbin H. Effect of ACTH and adrenocortical steroids on external pancreatic secretion in man. *N Engl J Med* 1958;258:603-5.

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