A factor likely to be important in the progression to haemorrhagic pancreatitis although not considered by Keynes, is the vascular response to obstruction. In animals with an intact pancreatic vasculature, when interstitial ('oedematous pancreatitis') is experimentally produced, there is an associated increased perfusion. When the vasculature is experimentally impaired in the presence of ductal obstruction and oedema, however, haemorrhagic pancreatitis occurs. Decreased perfusion is also observed in conjunction with oedema and vascular injury, potentially serving to further promote haemorrhagic pancreatitis. In the absence of vascular impairment, haemorrhagic pancreatitis does not occur with ductal obstruction presumably because of adequate perfusion.

The variable pancreatic injury found at surgery and autopsy in acute gall stone pancreatitis is explicable in terms of the vascular response to obstruction and the duration of the obstruction, with haemorrhagic pancreatitis being exceptional, occurring only when pancreatic perfusion is inadequate to maintain oxygenation and nutritive support of acinar cells in the face of oedema.

Fortunately, in gall stone pancreatitis the transient nature of obstruction typically occurring from very small calculi coupled with an adequate vascular response may allow for what is usually a selflimited episode. More prolonged obstruction, however, particularly in elderly patients who are at greatest risk for an inadequate vascular response may be a predisposing factor for an adverse outcome, but one which can be reversed with timely intervention to relieve the obstruction.

Obstruction, therefore, which in exceptional circumstances leads to ischaemic necrosis, rather than reflux of cytotoxic producing bacteria, is a more likely mechanism for the widespread acinar cell necrosis recognised at autopsy in haemorrhagic pancreatitis. It is tempting to speculate that if the ischaemic necrosis were massive enough, trypsinogen might be present in necrotic acinar lobules in excess of inhibitors, at a pH and calcium concentration favouring autoactivation. Alternatively, in the presence of the severe acute inflammatory response which occurs with parenchymal necrosis, trypsin activation could occur from leucocyte derived cathepsin. Either mechanism may further serve to activate elastase, phospholipase A, and the bradykinin system, further serving to impair pancreatic perfusion and cause additional parenchymal necrosis as well as to promote the systemic absorption of activated enzymes which both in animal models and man is associated with the multisystem failure seen before death from haemorrhagic pancreatitis.
Correspondence

References


Pathogenesis of haemorrhagic pancreatic necrosis (HPN)

str. — Far from exploding the myth of pancreatic autodigestion as the cause of HPN, Keynes’ progress report (Gut 1988; 29: 1143–25) serves to perpetuate it — merely shifting the point of pancreatic enzyme activation to the duodenum and invoking reflux of the activation product lyssolecithin and/or bacterial toxins (from infected bile) as the mediators of cellular necrosis in gall-stone related disease. The convoluted arguments lack conviction, even in that limited setting, for two main reasons. First, the chronic transpancreatic passage of natural lyssolecithin generating ingredients is innocuous: yet, enforced ductal retention of an artificial brew rapidly causes HPN as does prior manipulation of the ductal permeability barrier. Second, germ free animals do not escape the vicissitudes of the closed duodenal loop. These anomalies (referenced in the review), along with Opie’s classical observations in a human victim, suggest that it is the trapping of bile in the pancreatic duct, whether infected or not, rather than its to and