characteristics of the GBM to albumin was reported over a decade ago [4].

**Conclusion**

It would appear then, that both GBM and the renal parenchyma as a whole contain diverse charged components. Abnormalities of GBM anionic charge expression are more complex than at first conceived, reflecting often subtle alterations in membrane charged structures which may have a minimal or profound, direct or indirect influence on membrane permeability. The original concept of a charge-selective barrier maintained solely by the integrity of HS-PG networks in the GBM must now be inadequate.

**References**

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**Endothelin: what role in acute contrast nephropathy?**

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Acute renal failure following exposure to radiocontrast agents has been a well known clinical entity since the 1950's. Its pathogenesis is believed to include at least four aspects: (i) direct toxicity of the contrast agent to renal tubular epithelial cells, mostly of proximal tubular origin; (ii) intrarenal haemodynamic instability, including a brief period of vasodilatation (increased renal blood flow) followed by vasoconstriction (decreased renal blood flow); (iii) intratubular precipitation of Tamm–Horsfall protein possibly causing tubular obstruction; (iv) complement activation. Clinically much has been learned about important risk factors, but the role of Endothelin remains controversial.
factors for contrast nephropathy. In declining order of importance they are: full blown diabetic nephropathy (including renal insufficiency and proteinuria), renal insufficiency per se, dehydration, high-ionic, high-osmolar contrast agents and others. Therefore, in 1996 nephrologists—when faced with the necessity of an imaging procedure in a patient at risk—will probably replace the use of radiocontrast by an ultrasound procedure if they have a choice. If however radiocontrast cannot be avoided, this will generate a difficult situation because of a lack of efficient prophylactic interventions. To be sure nephrologists will do their best by giving the patient an infusion of 0.45% NaCl to produce a moderate degree of volume expansion; they will pretreat the patient pharmacologically (avoiding mannitol and furosemide) by the adenosin antagonist theophyllin (adenosin being an endogenous renal vasoconstrictor). But there is no established 'magic bullet' to prevent contrast nephropathy under most circumstances.

Some nephrologists would say that this is an academic discussion anyway. They would argue (i) that contrast nephropathy is usually a mild disturbance, necessitating dialysis only rarely; and (ii) that the risk factors are known and should be heeded. While this is correct it fails to address the clinical relevance of contrast nephropathy in 1996. It is now a daily clinical experience that radiocontrast has to be given despite the presence of important risk factors. An example is the patient with diabetic nephropathy suffering unstable angina pectoris: to survive he will need a coronary angiogram even if the nephrologist points out the risk to kidney function. It is this kind of a clinical dilemma which matters for decision-making. It will cause the physician uncertainty about the best approach to take, and temporary postponement of required procedures. The net result is longer hospitalization and increased cost to the health care system. This is the major reason for continuing the search for a more potent prophylactic approach to contrast nephropathy for patients at risk.

Finally, contrast nephropathy is important for the nephrologist in other ways: its risk is predictable, the timing of the individual study is known, and the total number of such procedures is large. In other words, contrast nephropathy may be the only clinical variety of acute renal failure in which prophylactic manoeuvres can be subjected to clinical testing. Given the enormous experimental effort over the last 20 years aiming at a prophylaxis of acute renal failure, clinical contrast nephropathy has something to offer to investigators.

It is in this context that attention has recently turned to endothelin and its inhibitors (e.g. Conference on Endothelin Inhibitors, San Diego, California, Feb. 5–7, 1996). Ever since its first description in 1988 endothelin-1—a potent endogenous vasoconstrictor—has been suspected as being an important contributor to ischaemic acute renal failure. In the years since 1988 impressive experimental evidence to support this view has been accumulated. Such has been obtained with or by: (i) using regional infusions of anti-endothelin-antibody into a branch of the renal artery 48 h after that same rat kidney had been subjected to clamping of its main renal artery for 25 min [1]; (ii) demonstration of increased renal endothelin gene expression and peptide-production triggered by 25–45 min of renal ischaemia in the rat [2]; (iii) reversal of post-ischaemic acute renal failure with a selective endothelin-A receptor antagonist given 24 h after ischaemia in the rat [3]. Additional support of a unique role of endothelin in ischemic acute renal failure has come from further observations, such as the following: the persistence of up to 7 days of ischaemia-induced endothelin gene transcription [2]; the finding that ischaemia and other kinds of injury to the kidney often increase endothelin-receptor-density as well as the receptor-affinity for endothelin [4]; the evidence of a positive feedback loop of endothelin generation in which endothelin once it is stimulated auto-induces its own production through the endothelin-B-type receptor [5]; the general notion that the vasoconstrictor-response of the renal vascular bed to endothelin is severalfold stronger than that of other vascular beds and the fact that endothelin mediated vasoconstriction is particularly longlasting.

While the data quoted above has been obtained in ischaemic acute renal failure, a number of recent observations have now extended the role of endothelin to include experimental contrast nephropathy [6–10]. In 1993 Epstein et al. [6] reported stimulation of endothelin by the non-ionic low osmolar radiocontrast agent ioversol. The observations were made in cultured bovine aortic endothelial cells. Comparable observations have been obtained by others using kidney cells, such as rat papillary collecting duct epithelial cells [10]. Epstein and co-workers went on to demonstrate in vivo using intact rats that an injection of the high-ionic high osmolar agent iothalamate triggered a sustained increase of the plasma endothelin concentration. It was associated with a short-lasting reduction of renal blood flow [11]. However when the same dose of iothalamate was injected into rats pretreated by salt depletion, indomethacin and uninephrectomy the contrast medium induced a 35% reduction of renal blood flow, which lasted longer than 60 min [11]. There was a simultaneous reduction of the glomerular filtration rate by 50%. The concentration of plasma endothelin, measured at 15 min after radiocontrast, correlated with the degree of necrosis of medullary thick ascending limbs. Further, there was also an inverse relationship of the endothelin concentration and the creatinine clearance [11]. The findings suggested that these changes might be interrelated. The same group then used the endothelin receptor antagonist CP 170 687 [7]. The antagonist prevented the 35% reduction of renal blood flow from iothalamate altogether. A comparable set of observations has also been reported by Oldroyd et al. [12]. They used the endothelin A receptor antagonist BQ 123 in isolated perfused kidney exposed to ioversol. Other animal models support these kinds of findings. Bird et al. [9] studied an interesting model in the rat which involved pretreatment of the
The Maillard reaction—from food chemistry to uraemia research

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The Maillard reaction in food

Cooking, baking or roasting of foods is essential for the formation of desirable flavour and colour (Figure 1). Among the numerous chemical reactions which occur during this heating process, the so-called Maillard reaction or ‘non-enzymic browning’ is of particular importance. This terms stand for a complex series of carbonyl–amine reactions, initially described by the French biochemist Louis-Camille Maillard in 1912, who was the first to report that aqueous solutions consisting of amino acids and reducing sugars turned progressively brown during heating [1]. For the next

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