There are two main reasons that this is not always so in practice. The first is that the skull also has considerable effects on the geometry of the ultrasound beam, varying from a simple shortening of the focal distance (due to refraction and refocusing) to complete disintegration of the sample volume caused by irregularities of the inner bony surface ("split beam"). The first of these may possibly be compensated for by increasing the acoustic output of the instrument, but this will have no beneficial effect in the second case. The second reason is that attenuation in the cancellous bone of the diploe, where this is present, is between 10 and 30 times as great,¹ and which has an even more destructive effect on the beam geometry. Osteoporotic changes in postmenopausal females cause a similar effect,² and neither can be rectified by increasing ultrasonic intensity.

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References

Response
It is thought that the transcranial Doppler examination is useful for monitoring real-time changes of blood flow signals and screening for cerebrovascular diseases. Therefore, in our recent study,¹ we checked a success rate for recording Doppler signals from the middle cerebral artery (MCA) in Japanese subjects, and by increasing emitted power we attempted to overcome the problem of obtaining no signals in elderly females.

For the adjustment of the emitted intensity, by learning Halsey’s method² from a specialist at Medacroncos who was in communication with Prof Halsey, we modulated only the amount of the electrical power to the transducer crystal to obtain the desired emitted power. As described in his reply to the Eden letter,² the term "power of N mW/cm²"² used throughout our article should be understood to mean "that power that would result in an estimated in situ intensity of N mW/cm²." As pointed out by Dr Eden, we mistakenly calculated the product of time and intensity; for safe recording, the exposure time at an emitted intensity that results in an in situ intensity of 400 mW/cm² should be limited to 71 seconds. In the majority of the subjects examined at higher emitted power, we finished the examination within 60 seconds, and fortunately any subjected to longer exposure time (from 70 to 120 seconds) did not complain of side effects.

From our results, increasing the emitted intensity undoubtedly improved the successful recording rate to some degree; however, as described in Dr Eden’s letter, there are still some problems to overcome for successful recording of MCA flow signals in elderly female patients. I agree that the problem of the recording failure would not be solved by increasing only the ultrasonic intensity. I think that increasing the sensitivity of the transducer³ as well as the emitted intensity would be necessary to improve the successful recording rate. I hope that a safe and accurate MCA detective instrument for elderly female subjects would be developed in the near future.

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References

Hyperglycemia in the Acute Phase of Stroke and Stress Response
We read with interest the article published in the August issue of Stroke by van Kooten et al.¹ We have carried out similar work, the results of which have been published recently.² van Kooten et al studied the relationship between blood glucose and the stress response in the acute phase of stroke. Plasma catecholamine levels were used as the sole measure of stress response. The authors found that there was significant hyperglycemia in acute stroke and that both hyperglycemia and plasma catecholamines were related to the severity of the acute illness but were not related to each other. The absence of a relationship between catecholamines and blood glucose was interpreted as evidence that hyperglycemia is unrelated to stress response. This may not be true. Our work suggests that there is a significant relationship between plasma glucose levels in the acute phase of stroke and the stress response at that time.

We recruited 68 patients with acute stroke who had fasting blood samples taken within 24 hours of stroke onset. Fasting levels of plasma glucose, serum cortisol, plasma insulin, noradrenaline, glucagon, and hemoglobin A1c were determined. Those with known diabetes mellitus or taking drugs likely to cause hyperglycemia were excluded, as were those with coexisting acute illness that could have caused a spurious stress response. Blood sampling was carried out at a fixed time of day, using a standardized procedure. Outcome was assessed as 3-month mortality.

Fasting plasma glucose was higher in those who died (P=.04). Noradrenaline was elevated in this group, but the difference did not reach statistical significance. Using multivariate analysis, with plasma glucose as the dependent variable, we found that serum cortisol (r=.494, P <.001), plasma insulin (r=.475, P <.001), and hemoglobin A1c (r=.40, P <.001) were significantly and independently related to plasma glucose. Noradrenaline levels did not correlate with plasma glucose either on univariate or multivariate analysis.

The significant relationship between plasma glucose and serum cortisol suggests a direct relationship between glycemia and stress response. The positive correlation between insulin and plasma glucose suggests insulin resistance, another feature of stress response. The relationship between hemoglobin A1 and plasma glucose is not surprising, as preexisting levels of glycemia are related to current levels of blood glucose.
There was a significant relationship between plasma glucose and the volume of the intracerebral lesion volume as measured on computed tomographic scan \((r=469, P<.001)\), but a stronger relationship was observed between serum cortisol and lesion volume \((r=.542, P<.001)\). Neither hemoglobin A1 nor plasma noradrenaline levels were significantly correlated with lesion volume.

Fasting plasma glucose was measured in survivors over the course of the study. There was a significant decrease in the fasting glucose levels on the order of 1 mmol/L over the first 7 days after stroke onset. This is in keeping with the results of Melamed,2 who found that hyperglycemia after stroke returned to normal levels a mean of 3.5 days after stroke. Hyperglycemia after stroke fulfills the criteria for stress hyperglycemia, i.e., it is elevated in proportion to the severity of the illness, it is related to the mediators of the stress response, and it is a temporary phenomenon.

van Kooten and colleagues were not able to demonstrate this phenomenon because they measured only catecholamines. While catecholamines are related to injury, they are extremely sensitive to stress. Admission to a hospital is a stressful event, and this “background noise” may have obscured the relationship between glycemia and catecholamines. Even though we attempted to standardize the stress as much as possible, other factors known to alter plasma catecholamine levels,5 such as caffeine intake, sodium intake, cardiac output, and renal clearance of catecholamines, were not controlled in either study. The estimation of picogram quantities of adrenaline and noradrenaline is technologically difficult. The plasma half-life of these substances is quite short, and a proportion of the noradrenaline or the majority of the adrenaline intake, cardiac output, and renal clearance of catecholamines, may have decayed even before the first sample in the van Kooten study was taken, as the flow phase of the stress response is established after 24 hours.4

In short, we agree with the findings of van Kooten et al, but we cannot agree with their conclusion that hyperglycemia after stroke is not due to a stress response. We believe that there is evidence that there is a stress hyperglycemic response in the early stages of acute stroke. The nature of the stress response, and in particular the influences of central centers in the brain on the response, has yet to be elucidated.

References

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Response
We thank Drs Tracey and Stout for their comments on our study. In accordance with our results, these authors have found no association between plasma norepinephrine and blood glucose in patients with acute ischemic stroke. However, as they point out, there are two main differences between their findings and ours: (1) they have found a relationship between cortisol—which we did not measure—and glucose levels and (2) in hyperglycemic patients who were not known to have diabetes, glucose levels dropped consistently after the acute period. Drs Tracey and Stout regard these findings as convincing evidence that hyperglycemia was caused by stress in these patients.

However, as the authors themselves state, norepinephrine and epinephrine are much more sensitive to stress than cortisol. Several studies in humans indicate that circulating norepinephrine and epinephrine, administered exogenously and leading to high physiological concentrations, do not alter plasma corticotropin and cortisol.2, 3 Furthermore, although Tracey and colleagues found a significant correlation between cortisol and glucose, the strength of the relationship was modest \((r^2=.25)\). Moreover, elevation of cortisol only, without a concomitant rise in epinephrine and glucagon, would not be expected to cause hyperglycemia in the acute phase.4

We have checked the glucose levels after 2 weeks in our patients with latent diabetes and in those with idiopathic hyperglycemia. Patients with latent diabetes had similar values during the acute stage and after 2 weeks. In agreement with Tracey and colleagues, patients with idiopathic hyperglycemia showed a decrease in the mean glucose level of 1.1 mmol/L. However, 67% of these patients still had an elevated (ie, ≥7.7 mmol/L) blood glucose after 2 weeks. Furthermore, normalization of the blood glucose after the acute stage in some patients does not exclude the possibility that factors other than stress (eg, increased insulin resistance) may have caused temporary hyperglycemia. Also, sustained elevation of blood glucose after the acute phase may be caused by increased insulin resistance, independently of epinephrine, glucagon, and cortisol levels. However, the insulin clamp technique, which was not used in either study, is mandatory to obtain reliable data on insulin resistance.4, 5

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References

Nailfold Capillary Microscopy in Lacunar Infarction

Nailfold capillary microscopy is a useful, noninvasive procedure that allows the direct observation of in vivo microvascular abnormalities in the skin. Various capillaroscopic abnormalities have been described in different cardiovascular, endocrine, rheumatic, and neuropsychiatric diseases. A constant typical capillaroscopic pattern, generally characterized by a diffuse microangiopathy, has been described in a few diseases. In particular, in systemic sclerosis (scleroderma), nailfold capillary microscopy shows a characteristic pattern that includes loss of capillaries, tortuous and enlarged capillary loops, and bushy loops. In neuropsychiatric diseases, capillaroscopy revealed some capillary abnormalities; however,
Hyperglycemia in the acute phase of stroke and stress response.
F ‘Tracey and R W Stout

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