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Diabetes Update:

Insulin receptors... key

Insulin binding: a matter of sensitivity

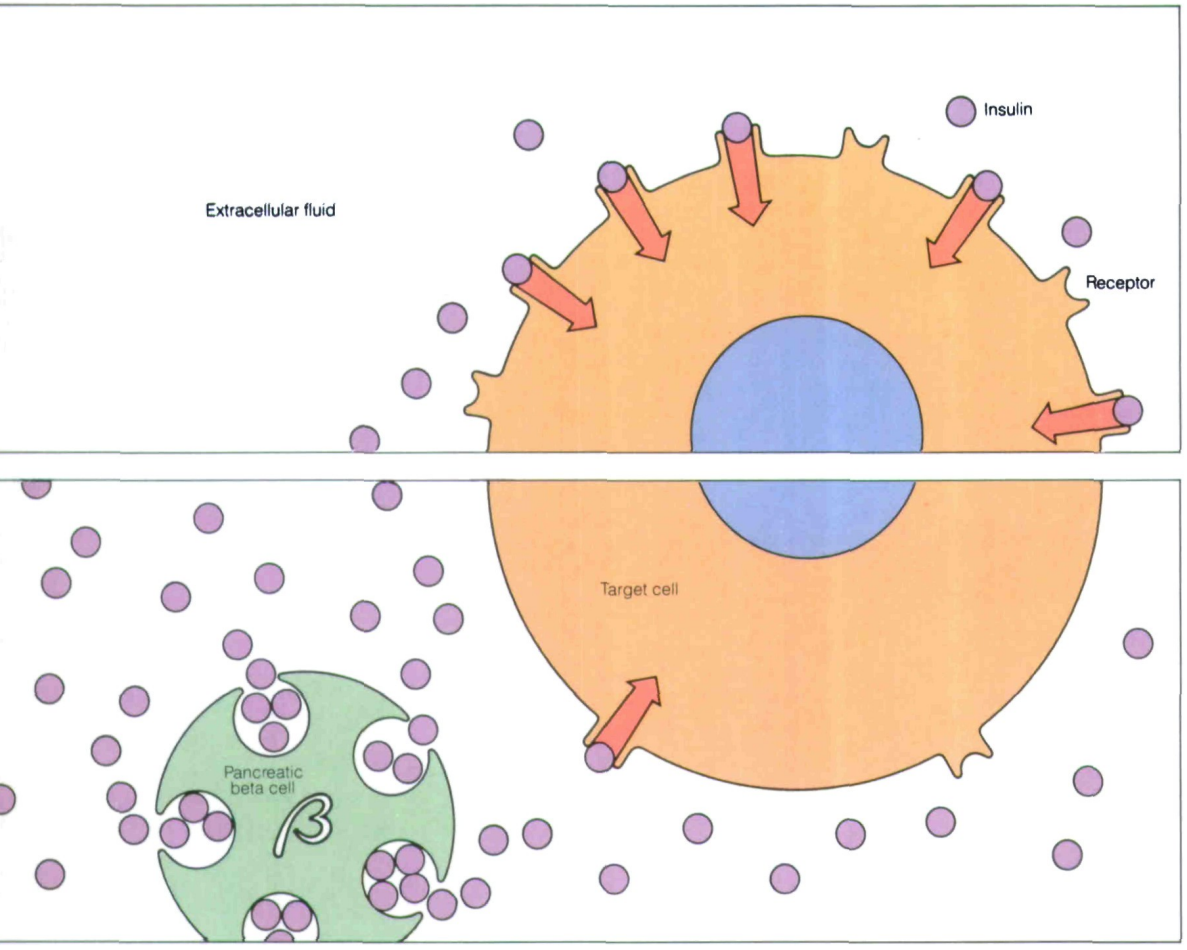
Normally, a glucose challenge elicits an appropriate beta-cell response—release into the bloodstream of insulin, which then binds to receptor sites on the cell membrane. This binding initiates a process that converts glucose into metabolic energy and/or stores it as glycogen in the liver and as fat in adipose tissue. With this activity, plasma values of glucose and insulin return to normal fasting levels.

Receptor regulation: a question of numbers

The number of insulin receptor sites varies inversely with the fasting plasma insulin level, that is, the more insulin present, the lower the number of receptor sites.

In normal nondiabetics, the cell membrane's response to insulin increases until 10% of the available receptors are occupied. Whereas, in a recent study of diabetic patients, the receptor occupancy of the erythrocyte, an accessible model of the target cell, was only 5.5%.

The number of insulin receptors largely determines the level of insulin utilization and glucose metabolism in non-insulin-dependent diabetic patients. Where there are fewer receptors, there are lower levels of insulin binding and higher levels of glucose and circulating free insulin.



Insulin released from a pancreatic beta cell gains access to target cell through binding mechanism of receptor sites.

In hyperinsulinemia, the pancreatic beta cell maintains adequate or even surplus secretion of insulin, but insulin receptors decrease in number and there is decreased binding on target cell.

Blood glucose control: achievable through receptor regulation

A primary therapeutic goal in non-insulin-dependent diabetes is control of blood glucose. Effective diet and appropriate exercise remain the cornerstones of therapy and have been shown to increase the number and affinity of insulin receptor sites.

A new understanding of sulfonylureas

Recent research suggests that one of the dominant effects of sulfonylureas is to increase the number and affinity of receptor sites rather than just stimulate insulin secretion.

After only a few weeks on sulfonylureas, patients seemed to have a more normal glucose tolerance, even though insulin secretion was not increased. It is now clear that at least part of this effect was due to an increase in the number and affinity of receptor sites.

Treatment with diet and sulfonylureas brings about a diminution of hyperglycemia and a return toward normal insulin binding; this result is associated with increases in the receptor sites per cell.

Unfortunately, this return to normal fasting glucose levels does not occur in non-insulin-dependent diabetes. Plasma levels of glucose and insulin often remain high. The resulting hyperglycemia and hyperinsulinemia are related to decreased binding by receptor sites.

A high plasma insulin level has been associated with decreases in the number and affinity of insulin receptors. The result: a state of relative insulin resistance.