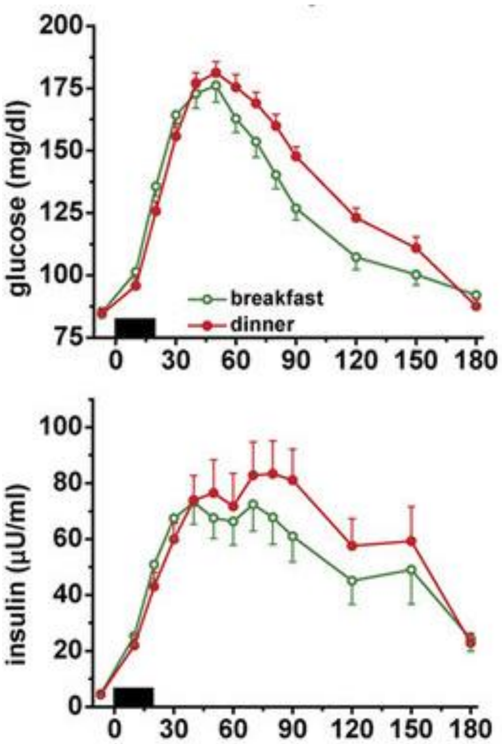
5. Metabolism throughout the day: Solutions

Insulin is a hormone produced by the pancreas. As a result of insulin's action, glucose gets taken up from blood into tissues, where it is stored and utilised to get energy.

The graphs below come from a study[1] in which blood glucose (left graph) and insulin levels (right graph) of healthy individuals were measured after identical meals were eaten at breakfast time and at dinner time. On the x-axis, time is in minutes; the black bar represents the 20-min test meal; and the data is the average of 8 individuals.



Interpret the graph. What is happening with blood glucose and insulin after a meal? What similarities and differences between breakfast and dinner are observed? You could use the concepts from "Regulation of metabolism by cell signalling" resource.

When the meal is digested, glucose is absorbed into intestine and transported into the blood – thus its levels there gradually increase, reaching a peak about one hour after the start of the meal. Glucose then gets taken up by different tissues, so its concentration in the blood gradually goes down until it comes back to the pre-meal level after about 3 hours. Glucose uptake from the blood into tissues is mediated by insulin: this hormone's level in the blood peaks around the same time as glucose (as it is released in response to it) but then plateaus for some time before falling back as well.

Comparing meals at different times of the day, an interesting pattern can be noticed. Glucose concentration starts, peaks and ends at the same level but it declines significantly slower after dinner than after breakfast (e.g. 90min after dinner the concentration of glucose was 150mg/dl, compared to only 125mg/dl after breakfast), resulting in overall higher glucose concentration in the blood throughout the *measured period (i.e. area under the curve Is greater). Insulin concentration falls more slowly after dinner as well, but also it peaks at a higher value and stays at its peak for longer: in the morning, insulin started going down 75min after the meal, whereas at dinner it stayed high up until 90min.*

You would have noticed the difference in postprandial (after a meal) blood glucose and insulin decline between breakfast and dinner. Other studies have shown similar patterns[2]: for example, during constant glucose infusion over 30 hours, lower glucose tolerance (how fast glucose goes down) is observed at night, i.e. levels of blood glucose at night are elevated compared to daytime when the sugar is supplied at a constant rate throughout the day-night cycle. This all points to glucose levels being affected by the time of day, and the mechanism behind this is our body's circadian rhythms. Why do you think such time-of-day differences in how blood glucose levels are maintained exist?

The **circadian** clock is an endogenous biological mechanism that drives roughly 24h cycles in various physiological processes.; This clock allows our body (and individual cells) to modulate responses to stimuli throughout the day.

Thanks to circadian rhythms, our body not only responds to but also anticipates the external changes that happen throughout the day. Usually we don't eat food during the night. However, to maintain proper function our tissues need glucose for energy 24/7. Therefore, higher levels of glucose in the blood must be maintained in the evening, and more glucose from the body stores (e.g. from glycogen in the liver) can be released in order to last through the night.

To find out how circadian rhythms link the external environment with our physiology, watch this short simple cartoon introduction:

https://www.youtube.com/watch?v=2BoLqqNuqwA

The video mentions that shift workers have an increased risk of some diseases, including type 2 diabetes. How do you think that fits with the studies mentioned above?

When shift workers eat during their night shifts, this could add extra glucose to that which the body is already programmed to release. As glucose tolerance at night is reduced, this could result in shift workers getting and/or maintaining higher blood glucose levels. Chronic prolonged high blood glucose is one of the defining features of diabetes.

References

1. Morris, C., Yang, J., Garcia, J., Myers, S., Bozzi, I., Wang, W., Buxton, O., Shea, S. and Scheer, F. Endogenous circadian system and circadian misalignment impact glucose tolerance via separate mechanisms in humans. *Proceedings of the National Academy of Sciences* 112, E2225-E2234 (2015).
2. Cauter, E., Desur, D., Decoster, C., Fery, F. & Balasse, E. Nocturnal Decrease in Glucose Tolerance During Constant Glucose Infusion. *The Journal of Clinical Endocrinology & Metabolism* 69, 604-611 (1989).

Circadian clocks and metabolism, recommended extra resources

1. A “Naked Scientist” podcast exploring circadian rhythms from many perspectives: https://www.thenakedscientists.com/podcasts/naked-scientists/clock-science-circadian-rhythm

   A great introduction into basic mechanisms in the beginning, followed by a very relevant discussion of recent studies on links between body clocks and obesity/diabetes (https://www.thenakedscientists.com/articles/interviews/body-clocks-obesity-and-diabetes)
   Other topics covered include sleep and light exposure, as well as an evolutionary perspective on circadian rhythms.

2. The Nobel Prize in Physiology and Medicine 2017 was awarded for the discovery of the molecular basis of circadian rhythms to three scientists who worked on the fruit fly Drosophila to discover genes involved in the animal clocks. Find out more about their discoveries in this 6-min video: https://www.youtube.com/watch?v=M-Tdvu3N8dA&feature=youtu.be&t=27