A Bench to Bedside Primer

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Editor's notes:

This four-page "primer" (a booklet of basic principles) highlights a scientific interest of the teacher producing it in ONE of three physiology topics: cardiovascular (CV), renal (REN), or gastrointestinal (GI) physiology. This primer should be readable by middle to high school students or the general public to help inform them about the organ system, diseases that affect it, and basic and clinical research being done on it.

This resource can be used as a sample of the primer a teacher wishes to have their students produce or as an educational tool to explain basic and clinical research.

Website URLs listed in this resource were current as of publication, but may now be obsolete. If you know of a replacement URL, please suggest it in the resource's "Comments" section.

Disclaimer:

The Endocrine System: Regulating the Body with Hormones

An Overview of the Endocrine System

Remember that awkward time in middle school when boys' voices were changing and girls were developing curves? Did you ever wonder why? These changes – known as ***puberty*** – are a small part of what the endocrine system can do.

The endocrine system is instrumental in regulating mood, growth & development, cell function & metabolism, along with sexual function and the reproductive process. All of this is done through the release of chemical messengers called ***hormones***. These hormones are released in one part of your body (such as the brain), travel through the bloodstream and act on a specific target cell in another part of your body (such as the pancreas). Islet cells in the pancreas are one of the most important targets as they produce insulin, which is needed for our cells to produce energy.

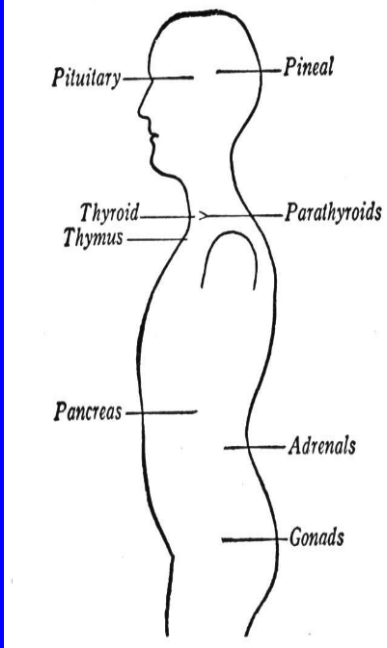

FIG. 467. *Location of the Principal Endocrine Glands* [1]

The endocrine system is composed of the following glands, organs, & tissues:

- Hypothalamus
- Pituitary
- Thyroid
- Parathyroid
- Adrenal
- Pineal
- Thymus
- Pancreas
- Testes/Ovaries
- Kidneys
- Stomach
- Liver
- Skin
- Heart
- Placenta
- Adipose (fat)

References:

Jenkins, G.W., Kemnitz, C.P., Tortora, G.J. (2010). *Anatomy and Physiology – From Science to Life.* (2nd ed.). Hoboken, New Jersey: John Wiley & Sons, Inc.

Tortora, G.J. & Derrickson, B. (2012). Principles of Anatomy and Physiology. (13th ed.). Hoboken, New Jersey: John Wiley & Sons, Inc.

FACTS ABOUT DIABETES

The most common endocrine disorder, affecting 25.8 million children and adults in the United States

What is *Diabetes*?

Diabetes is a condition in which your body is either unable to produce insulin, doesn't produce enough, or can't use it properly. There are **2** main types: ***Type 1***(insulin dependent)& ***Type 2*** (non-insulin dependent)

What is *Insulin*?

Insulin is a hormone produced by the pancreas that allows glucose to enter our cells. As we eat carbohydrates, our body digests them into small sugar molecules called ***glucose***. The cells use glucose to make energy.

Type 1 Diabetes

- **Who:** Children, young adults
- **Cause:** Autoimmune disease in which the body destroys the pancreatic Beta cells, no insulin produced
- **Symptoms**: excess urination, excess thirst, increased hunger, weight loss
- **Treatment:** insulin injections for life

Type 2 Diabetes

- **Who:** Any age
- **Cause:** Overweight, inactivity
- **Symptoms**: Any of Type 1, plus frequent infections, blurred vision, cuts/bruises don't heal
- **Treatment**: diet, exercise, oral medication

Potential Cure for Diabetes

Type 1

- **Pancreas transplant**
  Successful, but must be on immunosuppressant drugs
- **Islet cell transplant**
  Still in trial stage

Type 2

- **Monitor diet, exercise**
- **Weight loss**

Complications

- Increase risk of heart disease
- Increase risk of stroke
- Blindness
- Kidney failure
- Nervous damage
- Limb amputation

References:

Medline Plus: http://www.nlm.nih.gov/medlineplus/diabetestype1.html
Kids Health: http://kidshealth.org/parent/diabetes_center/diabetes_basics/type1.html
American Diabetes Association: http://www.diabetes.org/

Endocrine Research: The Importance of Genes, Hormones, and Islet Cells in Type 1 Diabetes

Researchers investigating autoimmune diseases involving the endocrine system have found a link between hormones and genes located on the X-chromosome. An autoimmune disease is caused by the body's immune system attacking its own healthy cells and tends to be hereditary [3]. Thyroid autoimmune diseases such as Graves Disease and Hashimoto's thyroiditis are found most often in females, while Type 1 diabetes is seen more in young males. Although the exact cause of these diseases is unknown, it seems to be primarily determined by genes in the HLA region of Chromosome 6 [2]. HLA is human leukocyte antigen, which determines immune responses within the body. The arrangement of genes in this region can lead to a difference in whether or not the body's immune system looks at a particular cell as a threat [4]. If it is viewed as such, the immune system attacks. The results of this study suggest that the X-chromosome interacts with a specific gene form resulting in Graves Disease, Hashimoto's thyroiditis, or Type 1 diabetes, depending on whether estrogen or testosterone is present [2].

In a rather interesting finding biologists at Georgetown University have discovered that spermatogonial stem cells in mice – from which sperm develop in the testes – can be coaxed into becoming pluripotent stem cells in the laboratory. Pluripotent stem cells can become any type of cell during embryonic development [6]. In this case, scientists have been able to produce pancreatic islet cells – specifically insulin producing β-cells. Once injected in the mice, these islet cells began producing insulin. Since the cells originated from the mice, there were no signs of rejection. Although this is only good for males, scientists believe similar results can be achieved using the female egg stem cells [1].

More current research is focused on islet cell transplantation as a potential cure. The University of Illinois at Chicago has achieved transplantation success through a modification of the Edmonton Protocol – a group of immunosuppressant drugs. The Edmonton Protocol originated in the 1990's when the University of Alberta in Canada began transplanting islet cells into diabetics as a means of eliminating the need for insulin injections. While the Canadian transplants showed some success, the patients needed to have multiple transplant procedures. The patients in the UIC study have all achieved insulin independence with fewer islet cells [5].

The above research studies are an important part of identifying the underlying cause and potential cure for Type 1 diabetes. This disease affects individuals from the very young to the old, with a range of complications such as kidney disease, eye disease, blindness, & cardiovascular disease. In order to intervene early and possibly prevent Type 1 diabetes we must look at the genetic factors involved. At the very least, we must make every attempt to treat this disease and eliminate the potential life threatening complications.

References:

1. Arnold, Carrie. "Sperm May Hold Cure for Diabetes." *Science Now*. December 13, 2010. Accessed July 22, 2011, from http://news.sciencemag.org/sciencenow/2010/12/sperm-may-hold-cure-for-diabetes.html

2. "Fathers Play The Key Role in Transmitting Susceptibility To Autoimmune Diseases To Their Daughters." Accessed July 17, 2011, from http://www.the-aps.org/press/archives/01/22.htm

3. MedlinePlus: Autoimmune Diseases. Accessed July 22, 2011 from http://www.nlm.nih.gov/medlineplus/autoimmunediseases.html

4. Mehers, K and Gillespie, K. (2008). "The Genetic Basis for Type 1 Diabetes" *Br Med Bull (2008) 88(1): 115-129 doi:10.1093/bmb/ldn045.* Accessed July 19, 2011, from http://bmb.oxfordjournals.org/content/88/1/115.full

5. University of Illinois at Chicago (2008, June 10). "Promising Advances in Islet Cell Transplants for Diabetes." *Science Daily*. Retrieved July 22, 2011, from http://www.sciencedaily.com/releases/2008/06/080609141225.htm

6. *Stem Cell Information.* National Institutes of Health, U.S. Department of Health and Human Services (2010). Accessed July 25, 2011 from http://stemcells.nih.gov/info/faqs.asp

Clinical Research Trial:
Islet Cell Transplantation in Type 1 Diabetes

Who?

- Are you a Type 1 diabetic?
- Are you tired of finger sticks and needle pokes?
- Are you sick of counting carbs and measuring insulin?

What?

- The National Institute of Allergy & Infectious Diseases is currently recruiting for a global Phase III clinical trial of islet transplantation (NCT00434811). The first two phases of clinical trials showed promise in allowing type 1 diabetics to be insulin free; however, this was short lived, as not all patients remained so. This phase of the trial will use new methods of transplantation and immunosuppressant medications in the hope of achieving long-term insulin independence. If you are between the ages of 18 and 65 and insulin dependent for at least 5 years with the onset of the disease before age 40, this may be for you.

Why Phase III?

- Phase I and Phase II showed the ability of islet transplantation to reduce the need for insulin injections, but it was short-term for most
- Phase III will determine the safety and effectiveness of islet transplantation combined with a new immunosuppressant regimen
- Phase III will use up to 3 separate islet transplants with different immunosuppressants at each stage

Is it Safe?

Possible safety concerns include:

- Worsening of diabetic retinopathy
- Adverse events related to surgery
- Adverse effects from immunosuppression
- Adverse effects from a change in immunosuppression regimen

Rationale:

- Type 1 diabetes is generally treated with insulin either by injections or through a pump. Although this allows for long-term survival, it is not the same as having a working pancreas. Since normal blood sugar control cannot be guaranteed, most type 1 diabetics often develop vascular problems, which may lead to blindness, kidney failure, and limb amputation. This Phase III clinical trial aims to determine if a new immunosuppressant regimen will make islet transplantation more effective in long-term control of blood glucose level.

Need More Information?

- ***Islet Transplantation in Type 1 Diabetes* @ Clinical Trials .gov**
  http://clinicaltrials.gov/ct2/show/NCT00434811?term=NCT00434811&rank=1
- **The Clinical Islet Transplantation Consortium** http://www.citisletstudy.org/