ICE - Calculating Antiderivatives

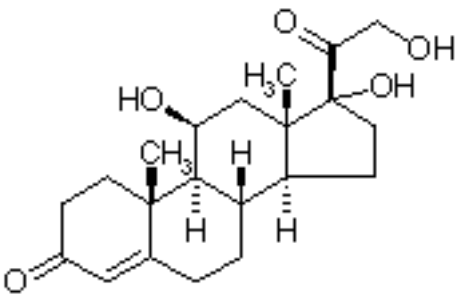

Figure 1: Molecular structure of cortisol.

Cortisol (see Figure 1[1]) is a glucocorticoid hormone that is naturally produced by the adrenal glands (see Figure 2[2]) in response to stress.

When a human with a normally-functioning endocrine system perceives a threat, coticotrophin-releasing hormone (CRH) is released throughout the brain, and in very large quantities within a structure at the base of the brain called the hypothalamus (see Figure 3[3]). The CRH released by the hypothalamus travels to the nearby pituitary gland (see Figure 3) where it stimulates the release of adrenocorticotrophin hormone (ACTH).

Figure 2: Perceptions of threat trigger production of ACTH by the pituitary gland. ACTH triggers production of cortisol in the adrenal glands, which are located on top of the kidneys.

ACTH travels from the pituitary gland to the outer layers (cortex) of the adrenal glands (see Figure 4[4]) which are located on the kidneys. The presence of ACTH stimulates the kidneys to produce cortisol.

In a human being with a normal functioning endocrine system, the levels of cortisol are reduced to zero as soon as the threat is perceived to have passed. However, scientific studies have documented elevated levels of cortisol in humans who have taken certain substances (such as 3,4-methylenedioxymethamphetamine

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[1] Image source: http://www.genome.ad.jp/kegg/catalog/cpd_steroid_hormone.html
[2] Image source: http://www.cnn.com/
[3] Image source: http://www.humboldt.edu/
[4] Image source: http://lancelot.bms.ac.edu/

and alcohol) who engage in some types of competitive activity (such as long-distance running) and who are suffer from certain medical conditions (principally Cushing's Disease). Even the stress experienceded by college students at particularly busy periods of the semester may elevate levels of cortisol in the body by a significant amount.

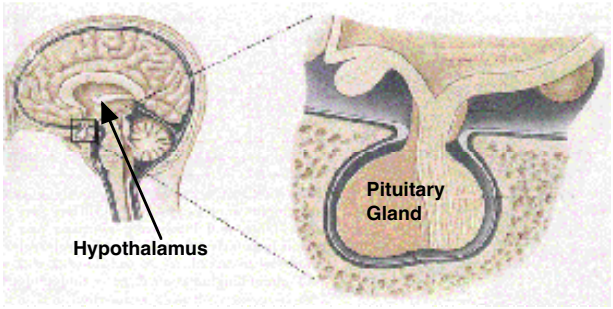

Figure 3: Location of hypothalamus and pituitary gland in human brain.

Although cortisol is a hormone that is naturally produced by the human body, prolonged exposure to high levels of cortisol have been linked to a number of mental and physical problems. These include:

- ***Possible permanent damage to the hippocampal formation in the brain[5]. (A number of animal studies [6] have suggested that the hippocampal formation is important in regulating the production of cortisol. If the hippocampus is damaged, then the capacity of the body to regulate subsequent cortisol production may also be impaired.)***
- ***Impairment of memory and learning ability[7].***
- ***Mood alteration[8].***
- ***Depression[9] and other psychiatric and neurological disorders[10].***
- ***Psychosomatic disorders (such as chronic fatigue syndrome)[11].***
- ***Immune system suppression[12].***

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[5] Source: L. R. Ember. (1998) "Surviving stress." *Chemical and Engineering News*, **76**(21): 1-13.

[6] For example, see: R. F. McGiven, P. Rittenhouse, F. Aird, L.D. Van der Kar and E. Redei. (1997) "Inhibition of stress-induced neuroendocrine and behavioral responses in the rat by prepo-thryrotropin releasing hormone 178-199." *Journal of Neuroscience*, **17**(12): 4886-4894.

[7] Source: J.W. Newcomer, G. Selke, A.K. Melson, T. Hershey, S. Craft, K. Richards and A.L. Alderson. (1999) "Decreased memory performance in healthy humans induced by stress-level cortisol treatment." *Archives of General Psychiatry*, **56**(6):527-533.

[8] Source: J. Smyth, M.C. Okenfels, L. Porter, C. Kirschbaum, D.H. Hellhammer and A.A. Stone. (1998) "Stressors and mood measured on a momentary basis are associated with salivary cortisol secretion." *Psychoneuroendocrinology*, **23**(4): 353-370.

[9] Source: B.J. Carroll, G.C. Curtis and j. Mendels. (1976) "Neuroendocrine regulation in depression." *Archives of General Psychiatry*, **33**(11): 1039-1044.

[10] Source: F. Holsboer, A. Grasser, E. Friess and K. Wiedemann. (1994) "Steroid effects on central neurons and implications for psychiatric and neurological disorders." *Annals of the New York Academy of Sciences*, **746:** 345-359.

[11] Source: J.C. Pruenessner, D.H. Hellhammer and C. Kirschbaum. (1999) "Brunout, perceived stress, and cortisol responses to awakening." *Psychosomatic Medicine*, **61**: 197-204.

• ***Take a minute or two to reflect on what you've just read, and what you have been through over the last few weeks. How do you feel mentally and physically? Could any of this be attributed to the effects of elevated levels of cortisol in your system?***

Figure 4[13] shows a graph[14] of the plasma cortisol concentration in a normal, healthy adult who is living in a relatively stress-free environment. The "total cortisol concentration" is defined to be the area under this curve for the entire 24 hours of the day.

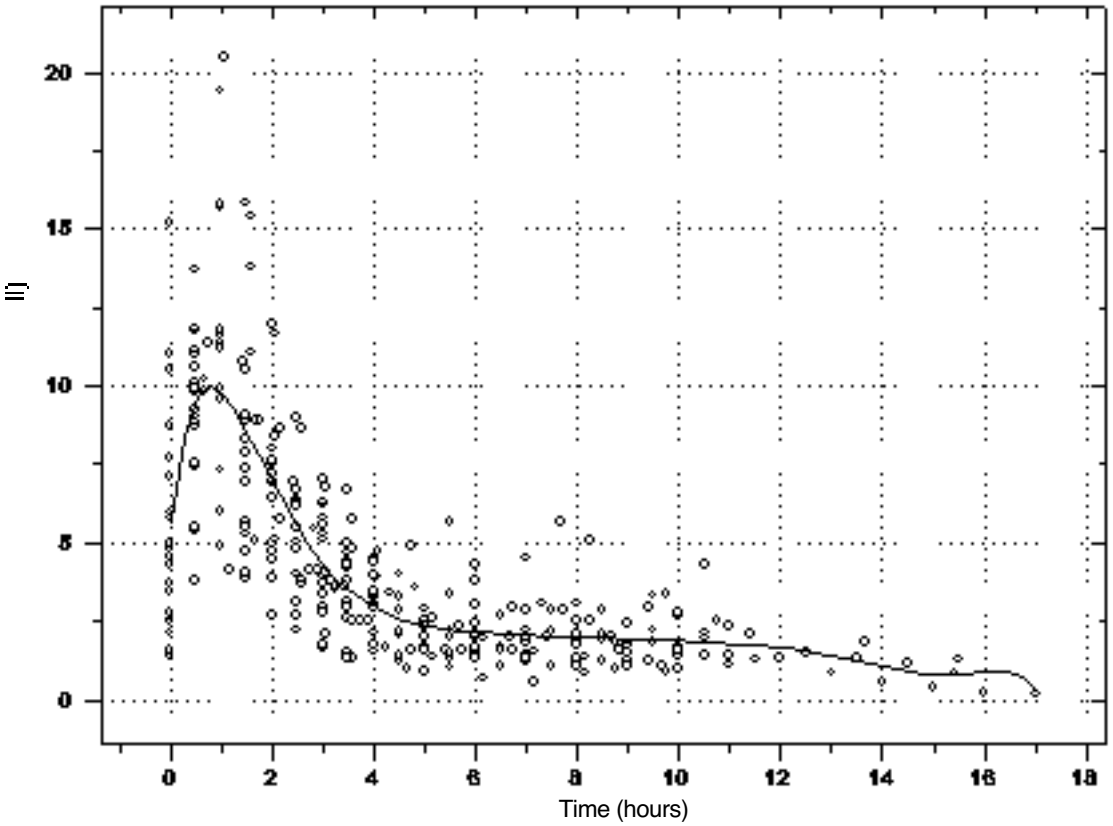

Figure 4: Cortisol production for a healthy adult in a reasonably stress-free environment.

Let T represent the hour of the day, and $m(T)$ represent the cortisol concentration in units of micrograms per deciliter (μg/dl).

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[12] Source: R. Glaser, B. Rabin, M. Chesney, S. Cohen and B. Natelson. (1999) "Stress-induced immunomodulation. Implications for infectious diseases." *Journal of the American Medical Association*, **281**(24): 2268-2270.

[13] Source: http://www.ibl-hamburg.com/pics/cortis1.gif

[14] Only the first 18 hours are shown in the graph. After the eighteenth hour of the day, the cortisol concentration in all experimental subjects was essentially zero.

- ***Three functions are given below. Each of the functions approximates the graph shown in Figure 4, although some do a better job of approximating the patterns in Figure 4. Find an antiderivative for each of these functions and use the antiderivatives to calculate three estimates for the total cortisol concentration. Record your results in the table given below.***

  - **Polynomial:**

$$m(T) = -0.00071 \cdot T^4 + 0.02317 \cdot T^3 - 0.1939 \cdot T^2 - 0.3213 \cdot T + 7.7849$$

  - **Exponential:**

$$m(T) = 11.6649 \cdot (0.7884749407)^T$$

  - **Rational:**

$$m(T) = \frac{20}{T + \frac{4}{3}}$$

Cortisol concentration, $m(T)$ (μg/dl)	Antiderivative	Estimate for total cortisol Concentration (μg·hours per dl)
Polynomial		
Exponential		
Rational		

• ***Figure 4 is reproduced below. Sketch the three cortisol concentration curves over the given graph. Of the three cortisol concentration functions given (polynomial, exponential and rational) which would you expect to give the most accurate*** **total cortisol concentration*?***

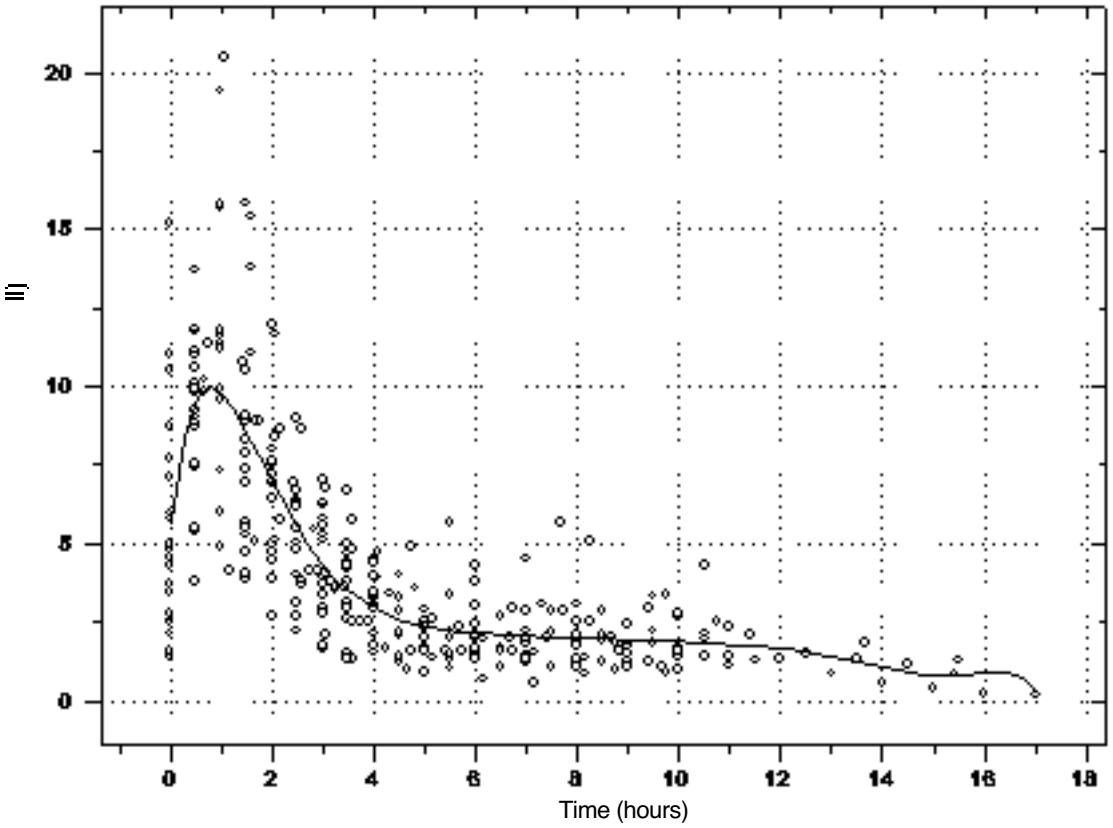

Figure 4: Cortisol production for a healthy adult in a reasonably stress-free environment.

• ***What is the best estimate of the total cortisol concentration (in units of microgram hours per deciliter) for a healthy adult living in a relatively stress-free situation?***