



# Diagnostic Exercise

## From The Davis-Thompson Foundation\*

Case #: **150** Month: **September** Year: **2020**

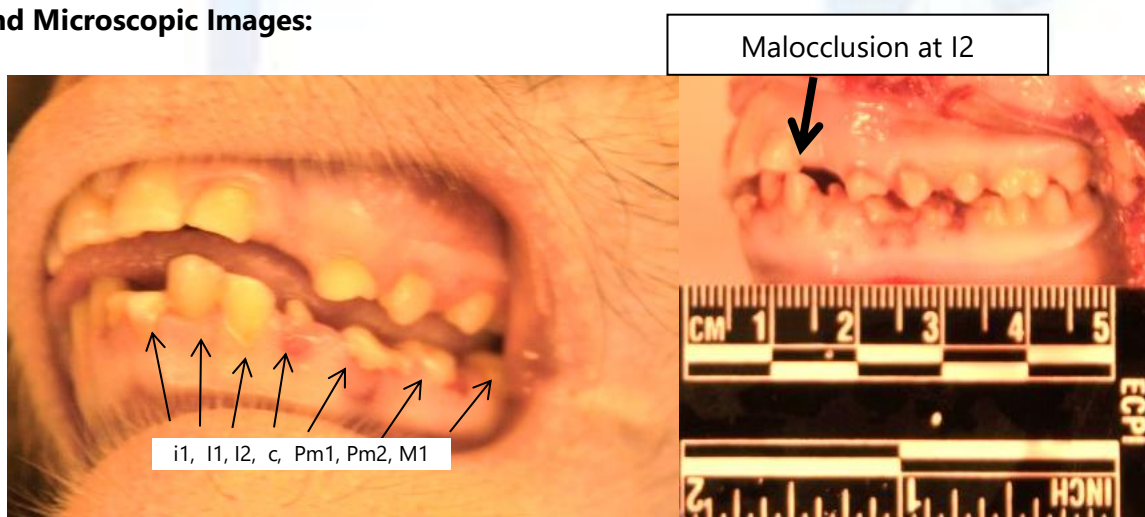
### Answer Sheet

**Contributor:** Erin K. Morris, DVM, Diplomate ACVP. WRAIR-NMRC. Forest-Glen Annex, MD.

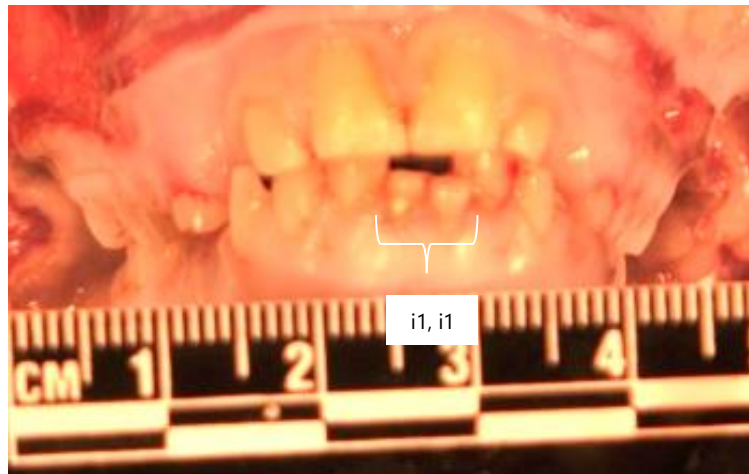
**Clinical History:** This 4-year-old female rhesus macaque, in good body condition, was euthanized and necropsied as a precautionary measure after receiving an “indeterminate” result when submitted for Herpes B virus status on serology, along with the presence of gingival ulcers on physical exam. The serum antibody status appeared positive by titration ELISA but could not be confirmed as positive or negative by Western Blot. PCR from swabs of oral ulcers were negative for Herpes B virus. There was no clinical history of oral pain or difficulty with eating.

**Necropsy Findings:** On the left buccal aspect of the mandibular arcade are multifocal to coalescing red to purple gingival erosions/ulcers up to 5 mm in diameter (Figure 1) starting at the deciduous canine (c) and involving the permanent premolars 1 and 2 (Pm1, Pm2) and the permanent molar 1 (M1). There is malocclusion of the permanent left upper and lower second incisor (I2) (Figure 2), associated with a 3-mm gap between the two permanent mandibular first incisors (I1), with two presumably retained deciduous teeth (i1) filling and projecting rostrally from the gap (Figure 3). The left lower deciduous canine (c) is markedly smaller compared to the right canine and upper canine (C). The left mandibular arcade involving premolars 1 and 2 (Pm1, Pm2) are markedly worn with complete loss of the cusps at a beveled angle from the lingual towards the buccal surface, with only 1-2 mm of visible crown above the gingiva. There are also multifocal exposed pulp chambers. Both left lower premolars are very mobile (loose) within the periodontal ligament.

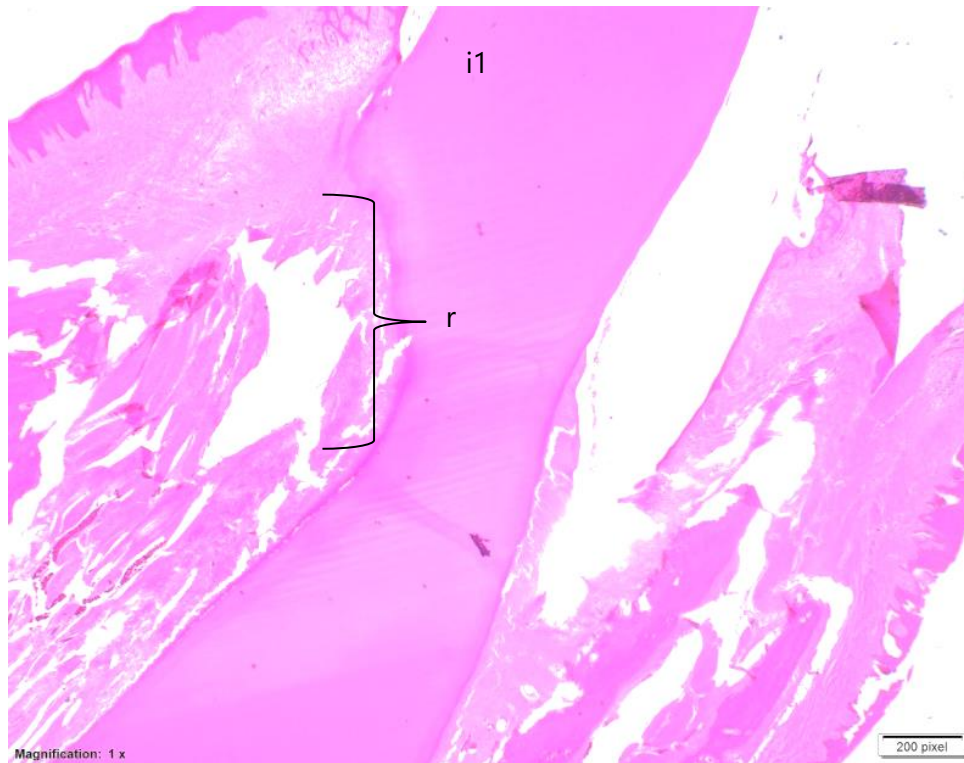
### Gross and Microscopic Images:



**Figures 1 and 2.** Gross photos. Mandibular gingiva showing ulcers and malocclusion.

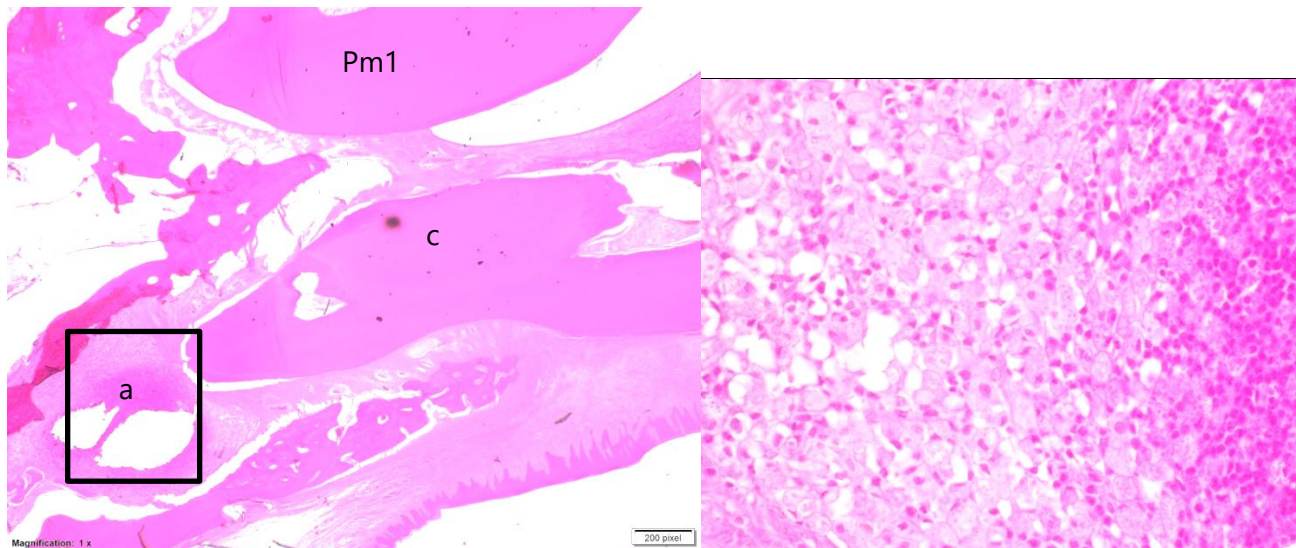


**Figure 3.** Gross photo. Retained mandibular incisors (i1).

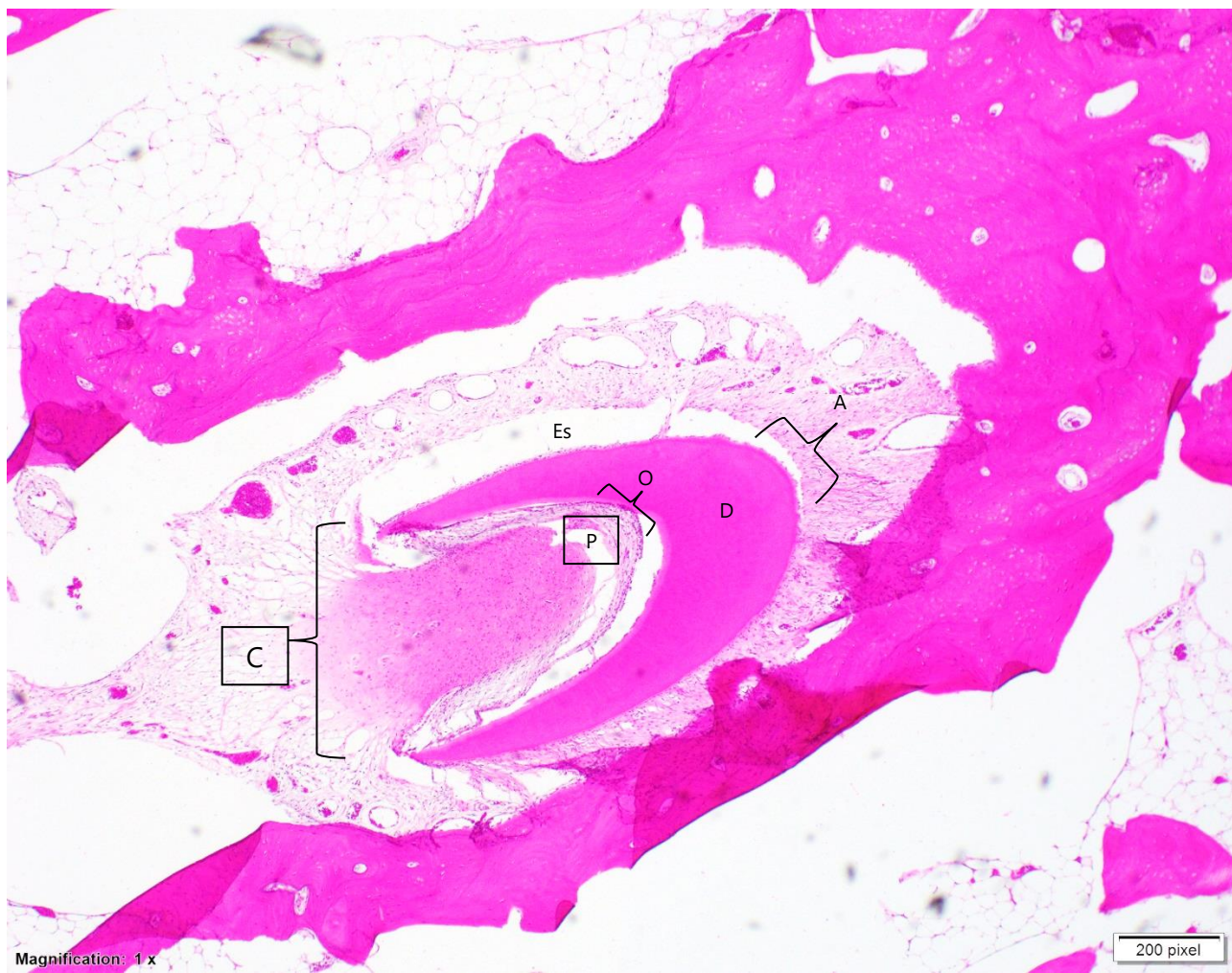


**Figure 4.** Deciduous incisor (i1) with partial inactive tooth resorption (r) with no odontoclasts. 40X, H&E.

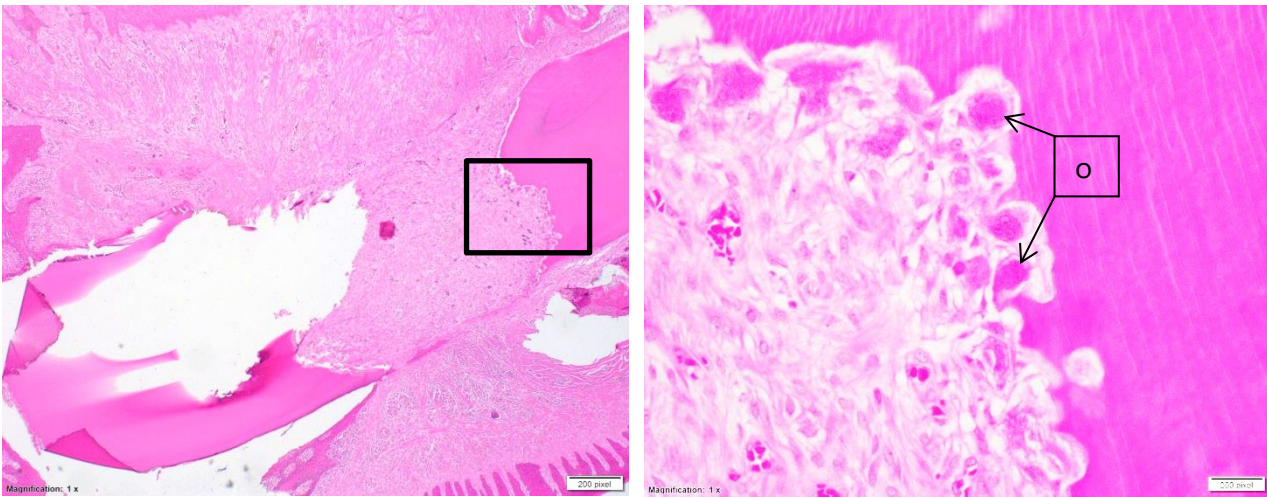




**Figures 5 and 6 (inset).** Canine (c) with apical abscess (a) (low magnification). At high magnification, the degenerate neutrophils on the right are surrounded by epithelioid macrophages containing eosinophilic globular material. 20X and 400X, H&E.



**Figure 7.** Developing permanent tooth (C) below deciduous canine ("c" in Figure 1). 40X, H&E. A=Ameloblasts, Es=Enamel space, D=Dentin, O=Odontoblasts, P=Pulp.



**Figures 8 and 9 (inset).** Subgingival root (tooth unspecified) with active odontoclastic (o) resorption. 20X and 400X, H&E.

### Gross morphological diagnoses:

1. Multifocal to coalescing ulcerative gingivitis of the canine (c) and premolars (Pm1 and Pm2) of the left mandibular arcade
2. Left mandibular and maxillary arcade malocclusion at I2
3. Retained left and right mandibular deciduous first incisors (i1), and left canine (c)

### Microscopic morphological diagnoses (based on the pictures shown):

1. Deciduous canine (c) and periodontal tissue, left mandibular arcade: Abscess, apical, chronic active, focal, marked, with woven bone formation.
2. Deciduous incisor (i1), left mandibular arcade: Root resorption, partial and inactive.
3. Subgingival root (tooth not specified): Root resorption, active, with odontoclasts.

**Possible causes:** Although this macaque was in good body condition and had no history of oral pain or difficulty eating, the presence of oral ulcers and an indeterminate Herpes B Virus serology results necessitated euthanasia as a precautionary measure due to occupational and colony health concerns. In this case, the gingival ulcers were the result of malocclusion. There was no apparent trauma to the jaw, so the malocclusion was most likely a result of retained deciduous teeth, possibly from a developmental defect, and possibly relating to ineffective guidance along the gubernaculum of the erupting tooth.

It is histologically difficult to determine if teeth are deciduous or permanent, unless of course, there is a permanent tooth viewed on examined histologic sections. Radiographs may be helpful in these instances. In general, deciduous teeth are much smaller than permanent teeth, as in this case.

Other possible causes of gingival ulcers in a rhesus macaque include:

1. Macacine herpesvirus 1 (B virus) (formerly Cercopithecine herpesvirus 1) - Vesicles and ulcers may occur on the dorsal surface of the tongue, on the lip, and the gingival mucosa; eosinophilic **intranuclear inclusion that peripheralize the chromatin with possible syncytial cells.**
2. Monkey pox – Cutaneous rash/pocks; syncytial cells, large eosinophilic **intracytoplasmic inclusion bodies.**
3. Simian varicella virus (Cercopithecine herpesvirus 9) - **Multiple vesicles** within epidermis that contain debris, erythrocytes, and rare **syncytial cells**; hyperplasia of basal cell layer; eosinophilic



Cowdry-type A **intranuclear inclusions in cells adjacent to vesicles**; necrotizing vasculitis in dermis with inclusions in endothelial cells.

**Comments:** This case serves as a good review of dentition, tooth formation, and eruption patterns in non-human primates, and a reminder that in addition to important viral causes, some gingival ulcers can be the result of routine dental disease in B Virus negative patients.

**The dentition formula for deciduous teeth** in a macaque is (i 2/2, c 1/1, m 2/2), while the formula for permanent dentition is (I 2/2, C 1/1, Pm 2/2, M 3/3).

The deciduous teeth erupt at the following mean intervals (days) but this varies somewhat based on which source is used:

Maxillary arcades: i1 = 20, i2 = 37, c = 71, m1 = 67, m2 = 155.

Mandibular arcades: i1 = 12, i2 = 24, c = 73, m1 = 73, m2 = 140.

All incisors should emerge by 2.5 months; all canines and molars should emerge by 4.25 months; and all second molars should emerge by 8.5 months of age. There is a 1 year wait time before the mandibular molars emerge (Kenney 1975).

When assessing age, there is large variation in **permanent dentition** eruption dates for female and male macaques (in years):

Female:

Maxillary arcades: M1 = 1.4, I1 = 2.5, I2 = 2.7, M2 = 3.3, Pm1 = 3.3, **C = 3.4**, Pm2 = 3.5, **M3 = 6.2**.

Mandibular arcades: M = 1.3, I1 = 2.4, I2 = 2.5, **C = 3.1**, M1 = 3.1, Pm1 = 3.4, Pm2 = 3.5, M3 = 5.7.

Male:

Maxillary arcades: M1 = 1.4, I1 = 2.5, I2 = 2.7, M2 = 3.3, Pm1 = 3.3, Pm2 = 3.5, **C = 4**, **M3 = 5.5**

Mandibular arcades: M1 = 1.4, I1 = 2.4, I2 = 2.5, M2 = 3.1, Pm1 = 3.7, Pm2 = 3.6, **C = 3.9**, M3 = 5.3 (Kenney 1975).

Female canines are much smaller than male canines, which may explain why they erupt earlier at 3-3.5 years of age. In the male, the canine is very large, long, and sharp, and is used for fighting, but it erupts closer to 4 years of age. The root of the canine is extremely long and extends to the ocular orbit. The lateral movement of the jaw is largely limited by the occlusion of the incisors. The upper canines interact with the mesial surface of the lower first premolar, the purpose of which is to shear or slice tough foods such as roots and fruit rinds (Kenney 1975).

**Tooth formation** occurs from the ectoderm and mesoderm during the development of the embryo as early as the sixth week of intrauterine life (in humans). In the macaque, fetuses as old as 70 days have calcified deciduous teeth. A **dental cap** containing the tooth bud forms a thin cord of cells called the **dental lamina**. The cap stage encloses undifferentiated cells, which form the dental papillae, and odontoblasts, which form dentin. The epithelial cells of the cap go on to form the enamel organ, which consists of ameloblasts. The developing tooth is enveloped in a dental sac, which later becomes the periodontal membrane, which contains cells that form cementum. When the cap becomes bell shaped, dentin and enamel are laid down to become the future cusp/edge. The dental lamina then disintegrates leaving no connection between the oral epithelium and the developing tooth, but prior to its disintegration it proliferates at its deepest point to form the successional permanent tooth germ. The dental lamina proliferates beyond the future pm2 to form the M1, M2, and M3 at a later time.

**Tooth migration** is guided by the remnant of the dental lamina, which appears as strands of epithelium in a band of connective tissues called the **gubernaculum**. In rhesus macaques, the gubernaculum persists as a tract between the developing tooth and the submucosa. This tract remains as soft tissue and guides the developing tooth in its eruption pathway, while the developing tooth is encased in alveolar bone that is laid down around it (Kenney 1975).

**Tooth eruption** is somewhat ambiguous but is believed to be initiated just after root formation starts. The root elongates at the same time there is a vertical increase in bone deposition at the tooth apex, and the erupting tooth moves at 0.04 mm per day. The **gubernaculum** may provide a path that directs deciduous tooth position in the arch. **When permanent teeth contact the apical part of the periodontal ligament of the deciduous tooth, then root resorption occurs until the periodontal ligament can no longer hold it in place, at which point the tooth is shed.** The permanent tooth placement is dictated by the guidance from the occlusal or incisal surface of the opposing tooth (Kenney 1975).

Teeth are also important because non-human primates use facial expressions as a means of **communication**. One of the most common facial expressions in rhesus macaques is the "silent bared teeth" face, which signifies differing rank with the lower-ranking or submissive animal performing the "silent bared teeth" face to the dominant animal. Another common facial expression used in dominance interactions include a "fear grimace" accompanied by a scream, heard in frightened animals and used to appease or redirect aggression (Rowe 1996). Dominant animals use a silent "open mouth stare" as a threat to other animals; this is accompanied by the tail sticking straight out behind the body with the monkey standing quadrupedally (Cawthon Lang 2005).

On a trivial note, the August 2007 issue of the *American Journal of Primatology* features a report called "Long-Tailed Macaques Use Human Hair as Dental Floss." Written by scientists at Kyoto University, in Japan, and Ubon Rajathanee University and Chulalongkorn University in Thailand, it builds on a report from the year 2000 that "two individual *Macaca fascicularis* monkeys in Lopburi, Thailand used human hair as dental floss" (Watanabe 2007).

## References:

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- Watanabe K, Urasopon N, Malaivijitnond S. . 2007. Long-Tailed Macaques use human hair as dental floss. Am J Primatol. Aug. 69:940-944.

The material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author, and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense.

The research was conducted under an approved animal use protocol in an AAALACi accredited facility in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the *Guide for the Care and Use of Laboratory Animals*, NRC Publication, 2011 edition

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**Editor-in-chief:** Claudio Barros

**Associate Editor for this Diagnostic Exercise:** Erin K. Morris