Chapter 2
Anatomy of Normal and Degenerative Changes in the Brain

Samuel S. Giles, Rosemary Kusaba Byanyima, and Stanley Jacobson

Abstract This chapter reviews the normal anatomy of the human cerebrum. We then demonstrate the appearance of degenerative changes in the brain grossly and with CT and MRI images. We have focused on the effects on the cerebrum of major diseases that affect the cerebrum, namely: (1) CVA/strokes; (2) the Communicative diseases of malaria and HIV/AIDS and, (3) Non-Communicable Disease (NCD) the Neurodegenerative diseases-Alzheimer's' Disease, Amyotrophic Lateral Sclerosis, Frontotemporal degeneration/Picks, Huntington's' Disease, Parkinson's'. For each of the diseases we have included an illustrative case history. We have also listed the division of the NIH, WHO or the CDC and the organization which provides assistance to the patients and the families that are affected by these diseases.

Keywords Cerebrovascular accidents • Communicative diseases • Non-Communicable Diseases • Neurodegenerative diseases • Case history

Abbreviations

AD	Alzheimer's Disease
ALS	Amyotrophic Lateral Sclerosis
CDC	Center for Disease Control
CVA	Cerebrovascular Accident
DICOM	Digital Imaging and Communications in Medicine format
HD	Huntington's' Disease

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HIV/AIDS	Human immunodeficiency virus infection and acquired immunodeficiency syndrome
NCD	Non-communicable diseases
PD	Parkinson's' Disease
WHO	World Health Organization

Introduction

It is appropriate that this workshop was in Uganda discussing normal and abnormal findings in the brain in the region of Africa where genetic and fossil evidence supports a recent (<200,000 year) origin of modern *Homo sapiens* in Africa [1]. This was then followed by later population migrations and dispersal across the world as the "Out of Africa" model [2]. The fossil record further suggests that for over one half of mankind's life, *Homo sapiens* and their ancestors "Lucy" lived in sub-Saharan Africa [3, 4].

Data from the World Health Organization [5] and the Center for Disease Control [6] demonstrates the similarity in brain diseases seen throughout the world with major differences noted due to income disparities which directly affect public health and longevity. In sub-Saharan Africa currently HIV/AIDS, sleeping sickness, malaria, and sickle cell anemia are the common diseases in the region [7] with road traffic accidents becoming another common cause of injury to the brain in the African region [8, 9].

Data from the WHO shows that as the public health improves in low-income countries due to economic strengthening, there is a concomitant lengthening of one's life and a shift from the communicative diseases (lower respiratory infections, diarrheal diseases, HIV/AIDS, malaria, and TB; [5]) being the primary causes of death to the non-communicable diseases (NCD-Cardiovascular, Cancer, Respiratory, Diabetes, and Neurodegenerative diseases) being as the primary cause of death. The non-communicable diseases which are the most common cause of death in the mid- to high income countries include; cardiovascular disease, stroke and other cerebrovascular diseases, cancers and a concomitant rise of dementias including Alzheimer's disease [5].

Since the cerebral hemispheres are the region in the brain most commonly affected by degenerative diseases [10], we will focus our discussion on the diseases that most commonly affect the cerebrum. A detailed classification of disease affecting the cerebrum can be seen in *Principles of Neurology* [11]. We have reviewed the records of over 500 patients CT imaged at the Mulago Teaching Hospital in Kampala over the last several years and we noted the similarity in the common causes of disease in the brains there and in the United States – stroke and other cerebrovascular diseases, HIV/AIDS, Neurodegenerative diseases, (Parkinson disease, Alzheimer's) alcoholism, and motor vehicle accidents also becoming a major cause. In the US the accidents are primarily in automobiles while in Uganda and the lower income countries the accidents are primarily with the smaller motor cycles called "boda-bodas" in Uganda which are widely used throughout East Africa and in other lower income countries [12].

Our discussion will first review the normal anatomy of the cerebral hemispheres and we will then focus on the three major categories of diseases that affect the cerebrum. In Group One we have included the principle disease that causes degeneration in the brain, cerebrovascular/stroke, in Group Two we have illustrated the effects of the most common communicative diseases – malaria and HIV on the cerebrum, and in Group Three we include the major NCD, Neurodegenerative Diseases-AD, PD, HD, and ALS. There are other causes of cerebral degeneration including alcoholism, malnutrition, environmental toxins and trauma which are discussed elsewhere in this book.

Materials and Methods

With post-mortem examination of the brain limited in Uganda, in this chapter, we illustrate the gross features of degenerative diseases of the cerebrum with specimens from several sources- the anatomy laboratory at Tufts University School of Medicine, the Department of Pathology at Tufts Medical Center, and the Department of Neurology at University of Massachusetts in Worcester. The cases of malaria that we refer to in this book are all from Mulago Hospital in Kampala Uganda and were reviewed in the Department of Radiology at Mulago Hospital. We have included on our www.braindementia.net an illustrative video from one of the patients with malaria seen at the Kampala Imaging center in Kampala which illustrated many of the findings seen with cerebral malaria which are also discussed in other chapters in this book.

Virtual Patients

With the Health Insurance Portability and Accountability Act of 1996 (HIPAA US Department of Health and Human Resources [13]) limiting the amount of information that one can reveal from each patient, we have respected this policy and consequently created for this paper Eight Virtual Patients that illustrate the findings in each disease. A Virtual Patient is a patient created electronically or on paper from real patient data [14]. These Virtual patients are widely used for educating health care workers [15, 16]. Our virtual patients were created by a team effort combining the identified cause of death, with gross or CT observations, and the clinical expertise of our colleagues to create a plausible patient. For each case we will present first a short case history including medical and neurological information, and then we will illustrate the pathological findings with gross specimens and CT or MRI images from the actual patient under discussion or from a patient with similar findings.

Illustrative Video

We developed a video demonstrating a virtual patient with Cerebral Malaria and stored it on our website (Cerebral malaria, www.braindementia.net) from a case of cerebral Malaria which demonstrates cortical atrophy, a subdural, and dilation of the ventricles, We created a video using the OsiriX open software program (OsiriX: 2004) on a Macintosh PRO Processor: 2 × 3 GHz Quad-Core Intel Xeon Memory to organize the DICOM images (Digital Imaging and Communications in Medicine, the standard format used in CT and MRI imaging worldwide). The images were collected from a MX 16 Philips CT Scanner Philips. The video was created from the stack of DICOM images using QuickTime Pro. We also inserted labeled JPEG images to illustrate major findings in each movie using Adobe Photoshop and strung into the exported movie using QuickTime Pro.

Observations

Normal Anatomy of the Gross Brain (Fig. 2.1a–c from Jacobson and Marcus [17]). In Fig. 2.1a we have labelled the lateral surface of the brain with the frontal, parietal, occipital, and temporal gyri and sulci identified. In Fig. 2.1b on the medial surface of the brain we have identified the gyri and sulci in the frontal, parietal, occipital, temporal and cingulate gyrus of the brain. In Fig. 2.1c we review the insular region deep in the lateral sulcus.

Group One- CVA/Strokes

Worldwide, cardiac disease and stroke are the most common causes of death in the middle and upper income countries while in the lower income countries respiratory infections is the most common cause, followed by diarrheal disease, HIV AIDS and then ischemic heart disease, as the fourth most common, followed by malaria and then stroke [5].

In the USA as noted in the most recent data from the CDC in 2011, cardiac disease is the most common cause of death (597,689) with cancer as second (574,743), chronic lower respiratory diseases third (138,080) and CVA/stroke the fourth most common cause of death (129,476). Alzheimer's Disease is the 6th most common cause of death (83,494). Strokes also are the most common cause of degeneration in the brain and untreated hypertension in many cases is the root cause and can lead to strokes, ministrokes/TIAs, mild cognitive dysfunction and dementia. The following cases illustrate these points.

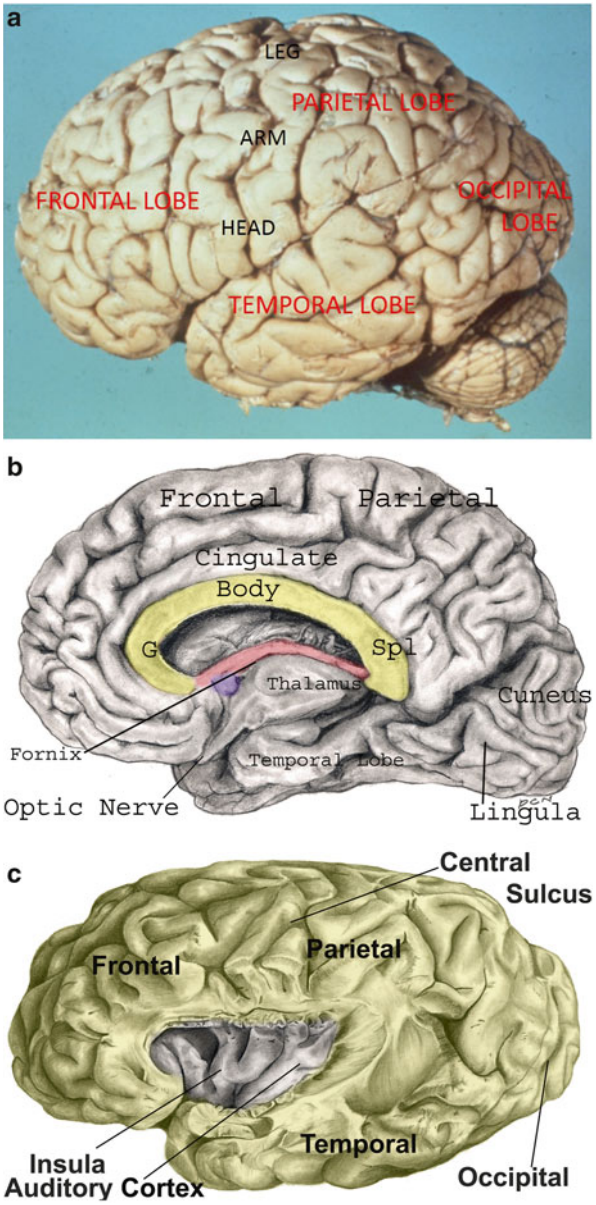

Fig. 2.1 Normal brain. (**a**) The lobes gyri and major sulci labeled in the frontal, parietal, occipital, and temporal gyri, and the motor strip identified on the lateral surface of the brain. (**b**) Medial surface with the corpus callosum, fornix, and gyri and cingulate sulci labeled and the gyri and sulci in the frontal, parietal, occipital and temporal lobe labeled. (**c**) Frontal and parietal operculum removed to reveal insular cortex and auditory cortex of temporal lobe (transverse temporal gyri). (From Jacobson and Marcus [17])

Case One: Cerebrovascular Accidents (CVA) (Figs. 2.2–2.4, Modified from Jacobson and Marcus 2003)

A 62 year old, Left-handed, untreated male with hypertension had an infarct in the territory of the middle cerebral artery on the left after carotid clamping for removal of plaque in the left common carotid. The patient progressed from a weakness of the right hand to complete right hemiparesis with right central facial weakness and a mixed aphasia. There was a subsequent recovery in the right lower extremity. Figure 2.2 is the post mortem examination of the brain of Patient One showing an infarct in the right operculum of the precentral gyrus and insula.

Figure 2.3a is an MRI which shows the appearance of a normal patient at the level of the frontal operculum, while Fig. 2.3b is an MRI which shows an infarct in the cortical territory of the left superior branch of the middle cerebral artery in the frontal lobe with similar neurological findings to Case One.

Figure 2.4 is a micrograph which demonstrates a lesion in the right medullary pyramid several years after a lesion in the medial most portion of the left motor strip with resultant atrophy of the corticospinal pathway and resultant upper motor deficit with increased reflexes, weakness of movements and some disuse atrophy of the right lower leg.

Although cardiac disease is still the most common causes of death in middle and upper income countries, there have been improvements due to better nutritional choices, exercise, stopping smoking, reducing salt intake and taking of medicine

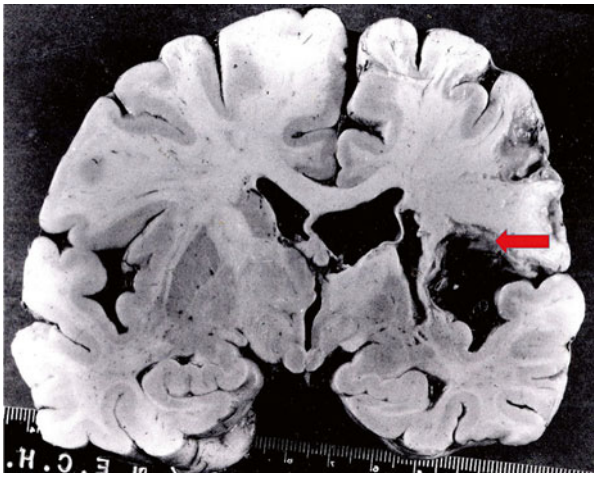

Fig. 2.2 CVA. This is a post mortem examination of the brain of Case One with a CVA showing an infarct in the left operculum of the precentral gyrus and insula (From Jacobson and Marcus [17])

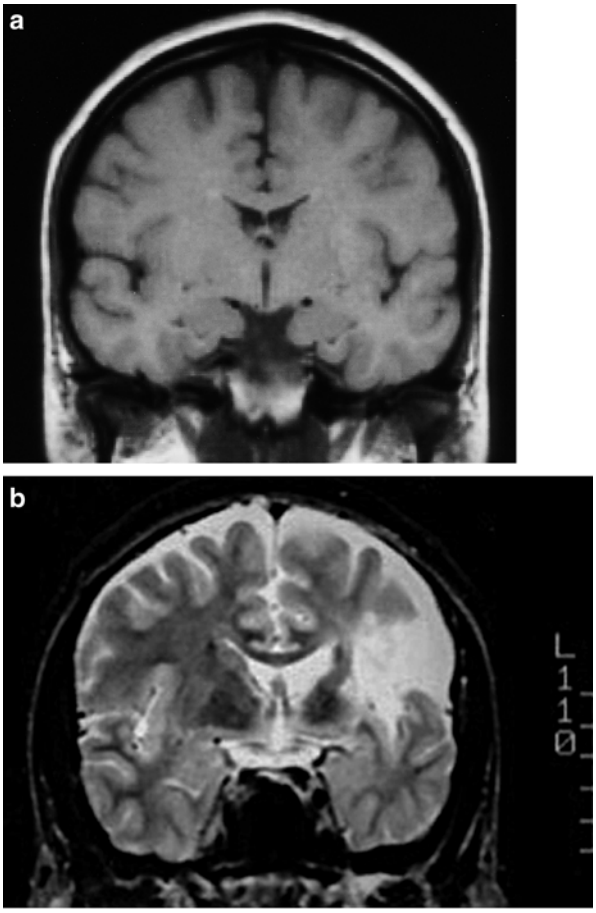

Fig. 2.3 CVA. (**a**) is an MRI which shows the appearance of a normal patient at the level of the frontal operculum, while (**b**) is an MRI which shows an infarct in the cortical territory of the left superior branch of the middle cerebral artery in the frontal lobe with similar neurological findings to Case One (From Jacobson and Marcus [17])

which will reduce the blood pressure. In lower income countries as shown in a recent article in Neurology [18] there is a critical need to alleviate the effects of hypertension, by encouraging life style changes, and reducing salt intake and when necessary treating patients with the inexpensive anti hypertensives (thiazides). The National Institute of Neurological Disease and Stroke of the National Institute of Health is dedicated to the eradication and treatment of stroke in the USA and the world www.ninds.nih.

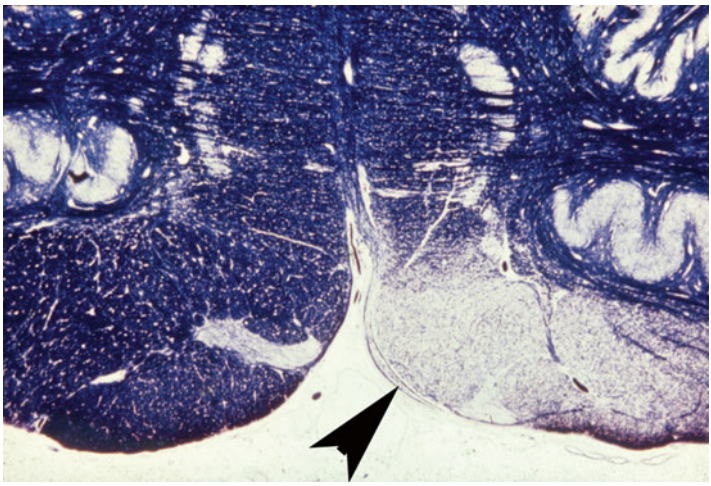

Fig. 2.4 CVA. This micrograph demonstrates a lesion in the right medullary pyramid several years after a lesion in the medial most portion of the left motor strip (controls the contralateral foot). This patient demonstrated atrophy of the corticospinal pathway and clinically demonstrated an upper motor deficit with increased reflexes, weakness of movements and some disuse atrophy of the right lower leg (From Jacobson and Marcus [17])

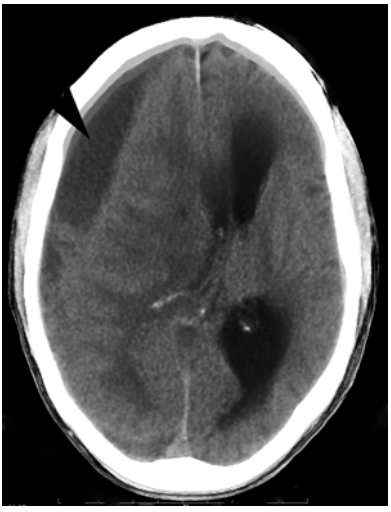

Fig. 2.5 Malaria. This CT is from a patient with a subdural hematoma and a displacement of the midline and compression of the lateral ventricles on cerebral malaria (From Kampala Imaging Center, courtesy of Dr. Rosemary Byanyima)

Group Two: Communicable Diseases, Malaria and HIV/AIDS

Case Two: Cerebral Malaria, Case developed by Dr. Erisa Mwaka Sabakaki, Fig. 2.5

A 32-year-old man presented with a history of fever, chills and weakness for 2 weeks along with generalized tonic-clonic seizures, occurring 2–3 times per day, for 5 days. He also had a history of loss of consciousness 2–3 times a day, each

episode lasting for 2–3 min. He complained of loss of power in the right upper limb for 4 days. He had had 4–5 episodes of severe vomiting during the duration of the illness. CNS examination revealed that he was conscious and oriented. There was no neck rigidity. Power in the right upper limb was 4/5. His sensory and motor systems were normal; there was no cranial nerve deficit. The other systemic examinations were normal. Biochemical and hematological investigations were normal. Peripheral smear for malarial parasite was positive and the patient was started on antimalarial drugs. CT of the brain revealed an irregular lesion, mixed hyper- and hypodense areas in the left high posterior frontoparietal region and the evidence of a subdural and subarachnoid hematoma in left frontoparietal region with surrounding hypodensity. Two days later, the patient complained of pain and swelling in the left lower limb. Venous Doppler of the limb showed deep vein thrombosis. The patient was treated aggressively with antithrombotics, antibiotics, antipyretics and anti-inflammatory drugs along with antacids. The patient completed the course of antimalarial drugs. He improved clinically. Follow-up CT scan of the brain done 1 month later showed a resolving infarct in the left frontoparietal region.

Figure 2.5 is a CT of a patient demonstrating a large subdural (arrow) external to the frontal lobe with a shift of the midline and the compression of the lateral ventricles on the right and enlargement of the ventricles on the left due to the presence of the *f. plasmodium* parasites in the subdural space and also in the adjacent parenchyma of the infected brain. It has been noted that the parasites sequester in cerebral capillaries and also produce additional intra- and perivascular pathology with retinopathy being very common [19, 20]. Malaria is caused by a bite from an infected female *anopheles* mosquito carrying the protozoan parasites of *falciparum plasmodium*. It affects over 650,000,000 people infected each year and causes 10 % of the deaths in the lower income countries including Uganda (1–3,000,000/year; [5]). It also is a major cause of poverty and hinders economic growth. There has been some progress in protecting children by providing mosquito nets but more help is needed, and there has been some progress in developing a vaccine. We have developed a video (Cerebral malaria, www.braindementia.org) from a case of Cerebral Malaria which demonstrates cortical atrophy, a subdural haematoma and dilation of the ventricles, a common finding in Malaria (www.cdc.gov/malaria).

Case Three: HIV/AIDS (Fig. 2.6)

A 38 year old female presented with left sided hemiplegia and weakness on the right side and dementia (Fig. 2.6). She has recently started on antiretroviral therapy with some success. Her CD4 was 455 cells/mm. The CT images shows lesions on the right (1) and left (3) rostral internal capsule and a lesion in the insular cortex on the right (3) all of which were consistent with HIV infection in the brain [21, 22]. These pathological findings are consistent with other studies that have shown similar infarcts due to HIV-associated *toxoplasmosis, tuberculosis* and *cryptococcosis* whose presence were not tested for in this patient. Our findings of dementia in this patient were supported by the brain atrophy which was noted with the widening of the sulci in the young woman. Poor care of patients with limitations in extensive investigations is not uncommon in LIMC settings. The cause of HIV is well documented. There is still no cure for HIV. There is antiretroviral medication which slows

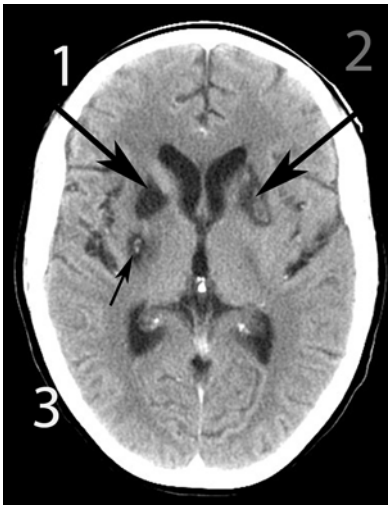

Fig. 2.6 HIV. This CT image of the brain is from Case Three. A 38 year old female presented with left sided hemiplegia and weakness on the right side and dementia. The CT images shows infarcts on the right (*1*) and left (*2*) in the rostral internal capsule and an infarct in the insula cortex on the right (*3*) due to the HIV infection. There is also significant evidence of brain atrophy with the widening of the sulci in this young woman (From the Kampala Imaging Center, courtesy of Dr. Rosemary Byanyima)

the progression from HIV to AIDS, and it can keep many people healthy for many years. However, these medicines are not widely available in poor countries. There are many groups working on developing a vaccine for HIV/AIDS and they have not yet succeeded, but there is a sense of optimism that there will be a vaccine 1 day.

Uganda is often held up as a model for Africa in the fight against HIV and AIDS [23, 24]. In Africa in most cases, HIV is spread heterosexually. Other causes include mother-to-child transmission, transfusion with infected blood or sharing needles in intravenous drug use. There are an estimated 1.2 million people living with HIV in Uganda, which includes 150,000 children. Strong government leadership, broad-based partnerships and effective and extensive public education campaigns using bill boards, newspapers, the radio, TV and internet are all contributing to a decline in the number of people living with HIV and AIDS. Uganda's success story must not detract from the consequences that AIDS continues to have across the country. An estimated 64,000 people died from AIDS in 2009 and over one million children have been orphaned by this devastating epidemic. The CDC has a very active surveillance and information upon the treatment of HIV (http://www.cdc.gov/hiv/topics/surveillance/) as does the WHO (http://www.who.int/hiv/en.)

Group Three (NCD) Neurodegenerative Diseases

Case Four: Alzheimer's Disease (AD) (Figs. 2.7 and 2.8)
A 64 year old male over the last 4 years had been having problems at work including inappropriate behavior, dress and memory problems. His changes in appearance and behavioral abnormalities including threatening his wife led him to be institutionalized by his family which was a very difficult experience for his wife and children

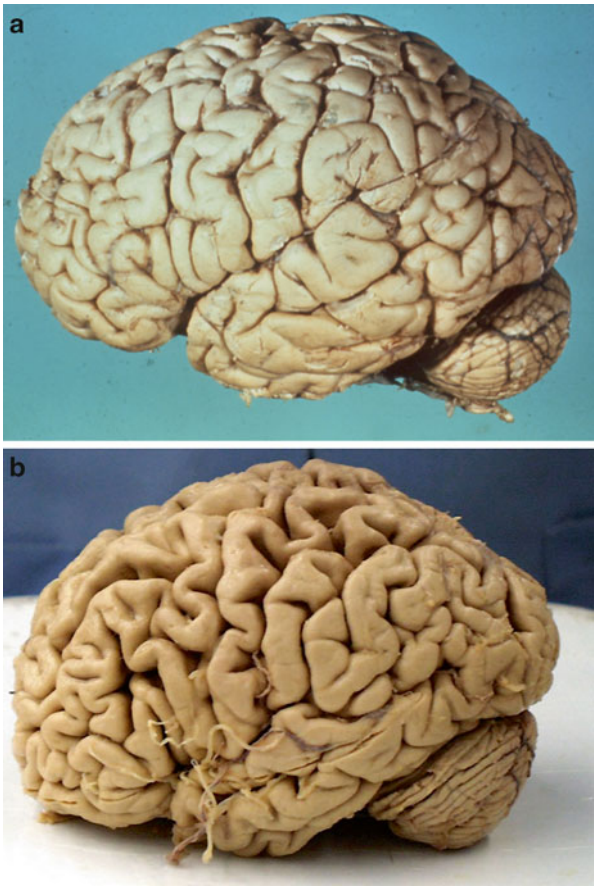

Fig. 2.7 (**a**) is the control, while (**b**) is from a patient diagnosed with Alzheimers' disease. In (**b**) from the patient with A Dnote the wide sulci throughout the brain which are a mark of extensive neuronal dropout. Compare the brain in (**b**) to that in Fig. 2.9b with frontotemporal degeneration (Courtesy of Dr. Stanley Jacobson)

(case developed by Drs. E. M Marcus and Stanley Jacobson). In Fig. 2.7a we show the appearance of a control brain while in Fig. 2.7b we show a brain from a patient diagnosed with Alzheimer's Disease showing major widening of the sulci throughout the brain due to the decrease in cortical gray matter/gyri which is the major pathology seen with this disease. In Fig. 2.8a we have included an MRI from a patient without AD at age 91 with a normal appearing hippocampus while in comparison we have included the MRI from a 71 year old male with severe AD. Figure 2.8b is from a 76 year old patient defined clinically as having AD and it shows severe atrophy of the hippocampus (from Marcus and Jacobson [25]). Please note that there is also atrophy in the hippocampus of the patients with AD enlargement of the ventricle due to the degeneration of the brain.

Alzheimer's disease is the most common cause of dementia and is a silent epidemic in US and much of the middle and upper income regions of the world. In the US there are over 5,000,000 affected individuals and it has deleterious effects on the personal and financial lives of the affected families. We were most fortunate at the

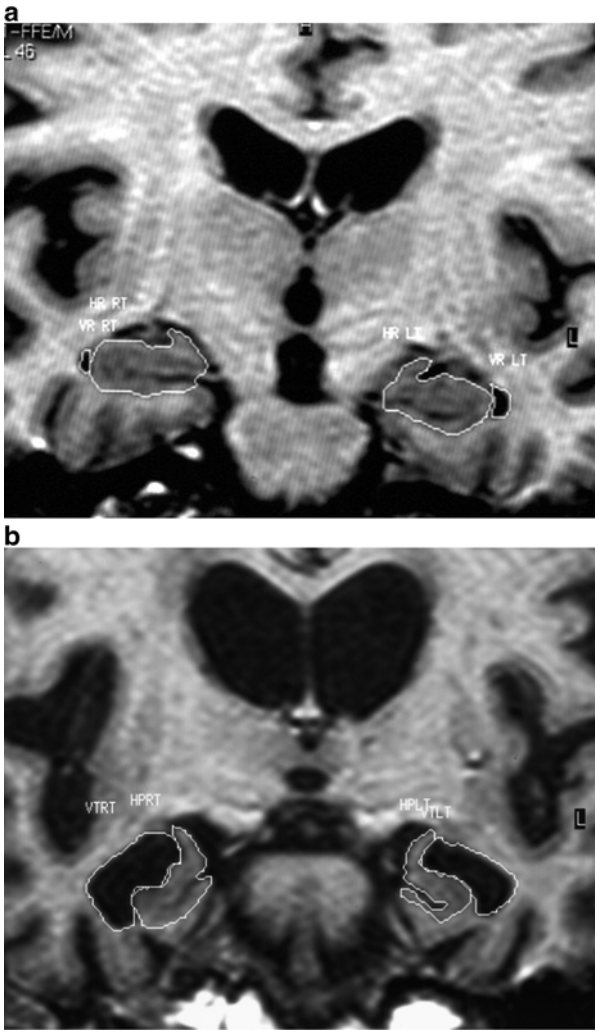

Fig. 2.8 Alzheimers' disease, MRI. In (**a**) we have include an MRI from a 91 year old male patient without AD at 91 with a normal appearing hippocampus; in (**b**) we have included the MRI from a 71 year old male with severe atrophy of the hippocampus (From Marcus and Jacobson [25]). Concomitant with the atrophy of the hippocampus there was an enlargement of the ventricular system due to the degeneration of the brain (From Jacobson and Marcus [17])

Ugandan workshop on Brain Degenerative Diseases to have Drs. Lee, Trojanowski and Schellenberg who have made great strides in reducing the effect of AD and Dr. Jeffrey Griffiths who described the heavy impact on the family and society of the AD patients. The Alzheimer's Organization is very active in supporting research, and helping families with this disease cope with its effects on affected individuals and their family (www.alz.org).

Case Five: Frontotemporal Degeneration/Picks Disease (Fig. 2.9)
This case is from the Gross Anatomy Laboratory at Tufts University School of Medicine. The patient was an 89 year old male. Figure 2.8 shows a photograph of the base of his brain demonstrating bilateral atrophy in the temporal and frontal

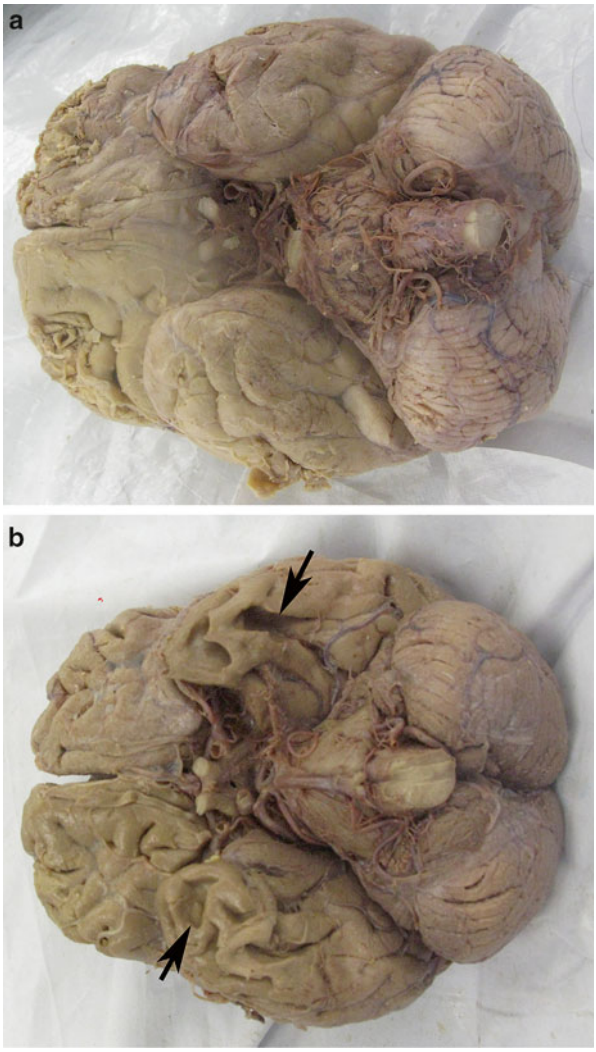

Fig. 2.9 Frontotemporal degeneration, Picks' disease. (**a**) The control brain. (**b**) The brain of this 89 year old male who demonstrated bilateral marked atrophy in the basal temporal and frontal lobes (*arrow*) with dementia and memory dysfunction which are the sign of this disease. The hippocampus was also atrophic (Courtesy of Dr. Stanley Jacobson)

lobes which also involved the hippocampus. He had changes in personality, language and memory. The hippocampus was atrophic [17]. This disease is similar to AD, but the regions in the brain that demonstrate atrophic degenerative changes are limited to the frontal and temporal lobes of the brain's regions. The Association for Frontotemporal Dementia is dedicated to treatment and control of this disease (www.theaftd.org).

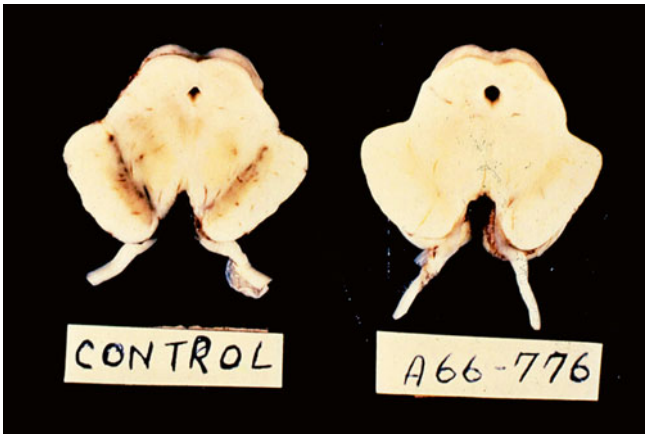

Fig. 2.10 Parkinson's disease. Note the normal appearance of the pigment in the substantia nigra of a 70 year old patient without disease (*left*), versus the marked loss of pigmentation in the substantia nigra pars compacta (*right*) (From Jacobson and Marcus [17]. Courtesy of Dr. Thomas Smith University of Massachusetts Department of Neurology)

Case Six: Parkinson's' Disease (Fig. 2.10, Modified from Marcus and Jacobson [25])

A 50 year old male developed a sense of fatigue and stiffness and lack of control of his left arm. He had a problem in writing and moving his leg. He said "I have to remember to lift it". When he walked there was a tendency to turn en bloc and there was decreased swinging of the arm. Over a period of a year he developed progression of the disease with cogwheel rigidity and micrographia with a pill rolling tremor at rest. Over the last 10 years he has undergone several different treatment regimens but the disease is still progressing with tremor at rest and rigidity and a slowly progressing dementia. There has been some discussion of whether he is a candidate for deep brain stimulation to stop the progression of the disease.

Parkinson's disease is the most common disease involving the basal ganglia (caudate, putamen and globus pallidus). The patient usually has several movement problems including a difficulty in walking, getting dressed, tying one's shoes, a tremor at rest and they may also develop dementia. They have a slow shuffling gait. The pathogenesis is the progressive loss of dopamine producing neurons in the pars compacta of the substantia nigra (Fig. 2.10). Figure 2.10A shows the normal appearance of the substantia nigra in a 70 year old patient without disease while in Fig. 2.10B shows the marked loss of pigmentation in the substantia nigra pars compacta in a patient with PD. In normal aging the rate of cell loss in the substantia nigra is 4 % per decade while in the PD patient it is about 45 % per decade. In the United State there are approximately 1,000,000 patients with the disease. Recently Drs. Lee and Trojanowski and colleagues [26, 27] have made great strides in understanding the basis of PD by determining that the transmission of a pathological α-synuclein gene initiates Parkinson-like neurodegeneration in transgenic mice.

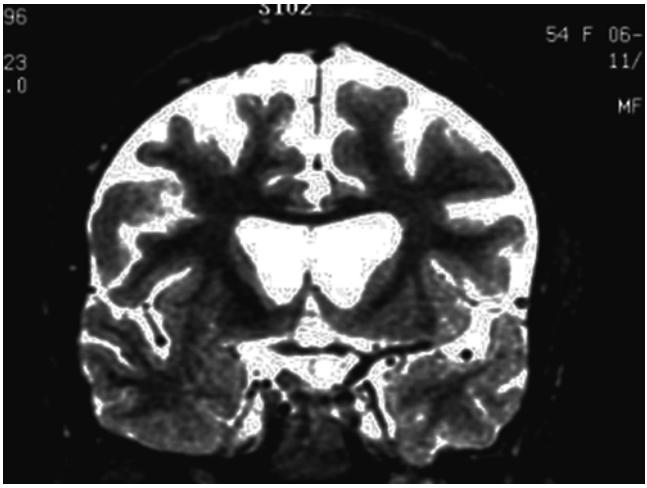

Fig. 2.11 This MRI is from 50 year old female patient who for several years had been noted to be nervous and had many restless movements. Her family felt that recently she was not thinking as clearly and had been undergoing a personality change (From Jacobson and Marcus [17])

This finding may lead to the development of an antibody to block this compound and mitigate the effects of PD. The Parkinson Organization (www.parkinson.org) website is a very helpful and describes this disease and the ongoing research aimed at the control and eradication of PD.

Case Seven: Huntington's' Disease [17] (Figs. 2.11–2.13)
A 50 year old female patient (Fig. 2.11) for several years had been noted to be nervous and had many restless movements. Her family felt that recently she was not thinking as clearly and had been undergoing a personality change. In addition, she demonstrated uncontrolled facial movements, including grimaces, head turning to shift eye position, and quick, sudden, sometimes wild jerking movements of the arms, legs, face and other body parts with restlessness and fidgeting. Additional behavioral changes may also occur in HD even before the movement problems. These can include: memory problems (dementia), behavioral disturbances, hallucinations, irritability, moodiness, paranoia and psychosis.

The MRI in Fig. 2.12a is from a normal patient while Fig. 2.12b is from a 45 year old patient with HD and shows enlarged ventricles and a thinning out of the cerebral cortex and basal ganglia especially noted in the rostral regions of the diencephalon around the anterior limb of the internal capsule. Patients with HD have enlarging of the ventricles, called "box car ventricles' and the thinning out of the basal ganglia. Figure 2.13 is the postmortem picture of the brain from a patient with HD with marked atrophy in the caudate and putamen with a dilation of the lateral ventricles. In this case there was the noted less involvement of the cerebral cortex.

Modern genetic analysis using recombinant DNA techniques has shown a defect in the short arm of chromosome 4 in patients with HD. The defect causes a part of DNA, called a CAG repeat, to occur many more times than it is supposed to.

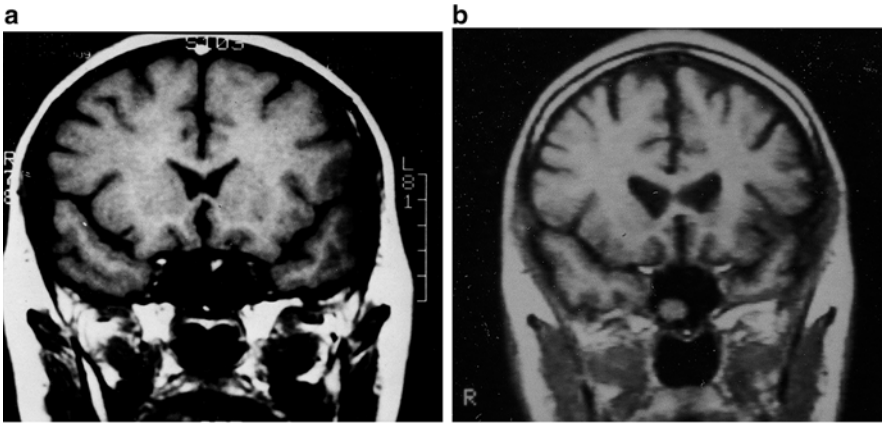

Fig. 2.12 Huntington's disease. (**a**) is from a normal patient in the mid-frontal region. (**b**) is from a 45 year old. patient with HD and shows a marked atrophy of the cerebral cortex and of the caudate nucleus in this patient with a familial history of the disorder and a significant increase in the CAG nucleotide repeats there is a thinning out of the cerebral cortex and basal ganglia especially noted in the rostral regions of the diencephalon around the anterior limb of the internal capsule. This patient with HD has enlarged ventricles, called "box car ventricles' and the thinning out of the basal ganglia (From Jacobson and Marcus [17])

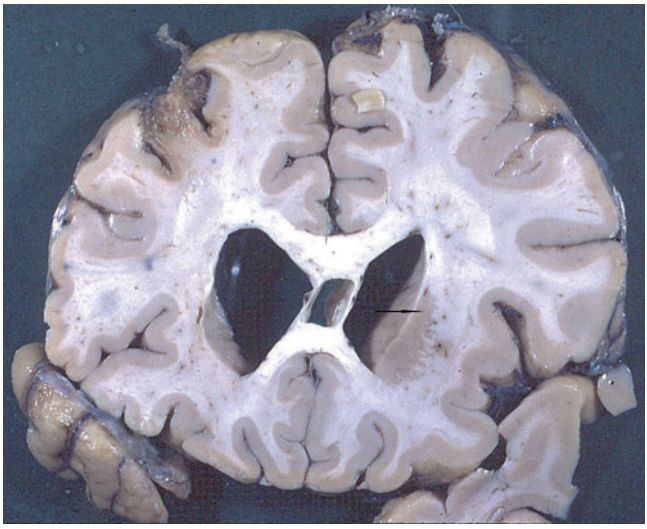

Fig. 2.13 A patient with Huntington's disease. There is marked atrophy in the caudate and putamen with a dilation of the lateral ventricles. In this case there was also less involvement of the cerebral cortex than the patient in Fig. 2.12 (Courtesy of Dr. Emanuel Ross)

Normally, this section of DNA is repeated 10–28 times. But in persons with Huntington's disease, it is repeated 36–120 times. As the gene is passed down through families, the number of repeats tends to get larger, especially where there is consanguinity. The larger the number of repeats, the greater are the chances of developing HD symptoms at an earlier age. Therefore, as the disease is passed along in families, symptoms develop at younger and younger ages. There are two forms of Huntington's disease. The most common is adult-onset Huntington's disease. Persons with this form usually develop symptoms in their mid-30s and 40s. An early-onset form of Huntington's disease accounts for a small number of cases and begins in childhood or adolescence. If one of the parents has Huntington's disease, there is a 50 % chance of getting the gene for the disease. If one gets the gene from one's parents, they will develop the disease at some point in your life, and can pass it onto their children [28]. Inheritance is autosomal dominant. There are, currently, no known methods to reverse the course of this disease, consequently current interventions focus on easing the burden of care on the affected patient and their family and genetic counseling (*Huntington's Disease Society of America*; www.hdsa.org).

Case Eight: Amyotrophic Lateral Sclerosis, ALS (Figs. 2.14 and 2.15)
Case W was a 66 year old man who originally presented for medical evaluation with a history of progressively increasing generalized muscle weakness involving both the upper and lower extremities. He initially noted weakness of his right hand manifested as difficulty with fine motor skills such as writing or buttoning a shirt or coat. He also noted a tendency to drop things when holding objects with the right hand. He subsequently noted lower extremity weakness involving proximal (thigh) muscles. He had difficulty rising from a chair and walking up stairs. He developed distal muscle weakness manifested as a foot drop, the so called "slapping" gait. Several months later, he developed dysarthria (slurring of speech) and dysphagia (difficulty swallowing) especially for thin liquids. This got progressively worse so that in the 2 weeks before admission to the hospital he frequently experienced choking and coughing when drinking liquids. At the time of admission the patient had significant cough, fever and dyspnea. On physical examination he had tachypnea with a respiratory rate of 24 breaths per minute. Chest exam revealed crackles at both bases. He was found to have significant hypoxemia. The patient's dysphagia (from bulbar muscle involvement) predisposed him to aspiration and hence pneumonia. His presentation of cough, fever, dyspnea, with crackles on physical examination was consistent with this diagnosis. This case was developed into a virtual patient by Drs. Scott Epstein, EM Marcus, Samuel Giles, and Stanley Jacobson to illustrate the deleterious effects of ALS and the illustrated brain is from the patient with ALS from the gross lab at Tufts University in Fig. 2.14. The brain shows atrophy bilaterally of the precentral and post central gyrus, premotor, and prefrontal cortex, but especially notable bilaterally is the motor strip which is very thin and has been called "razor thin" and with the resultant widening of the adjacent sulci. Compare this brain

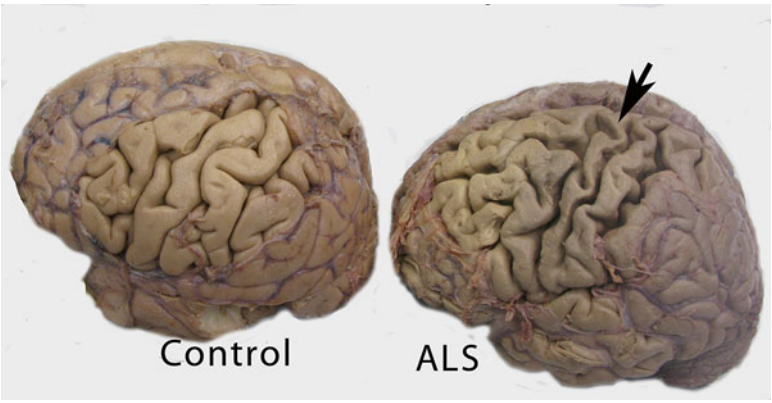

Fig. 2.14 ALS. Photograph of a brain on the *left* from a 70 year old patient without disease in the brain while the brain on the *right* is from a 66 year old patient, Case W, with ALS. The brain from the ALS patient shows atrophy of the precentral (*arrow*) and post central gyrus, premotor, and prefrontal cortex but especially notable bilaterally in the motor strip (*arrow*) which is very thin and has been called "razor thin"-compare to the brain from a 70 year old male who died of cancer (Courtesy of Dr. Stanley Jacobson)

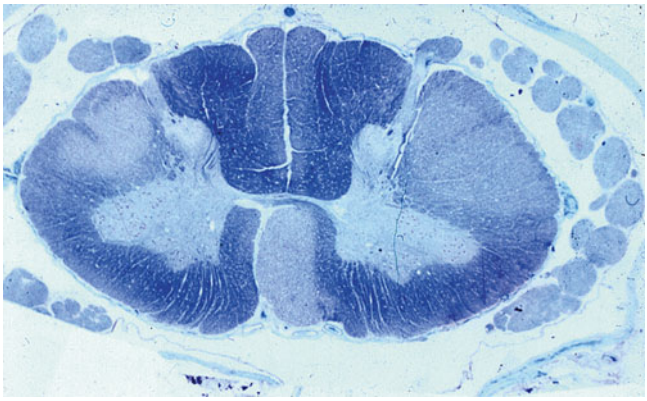

Fig. 2.15 A micrograph that shows the pattern of degeneration in the cervical spinal cord of a patient with ALS demonstrating degeneration bilaterally in the lateral corticospinal tract and in the anterior corticospinal tract on the left (From Jacobson and Marcus [17]. Courtesy of Dr. Jose Segarra)

from the patient with ALS to the control brain from a 70 year old who died of cancer. The atrophy in the prefrontal and post central gyrus, in addition to the precentral/motor cortex, produces degeneration in the upper motor neurons that form the corticospinal and corticobulbar pathways which originate from these cortical regions.

Figure 2.15 is a micrograph that shows the pattern of degeneration in the spinal cord of a patient with ALS in the motor, premotor and prefrontal cortices demonstrating degeneration in the lateral and anterior corticospinal tract. There was also degeneration of the lower motor neurons in the Ventral Horn Cells. There are about

20,000 people in the United States with this disease today where the disease is commonly linked to a famous baseball player, Lou Gehrig, who died from it in the 1930s hence Lou Gehrig's disease. Recently there have been major strides in understanding the underlying cause and prolonging the life of patients who come down with this disease but there is yet no cure insight. The deleterious effects of ALS and the ongoing research on this disease are well illustrated by the ALS Society of the US (www.als.org).

Conclusion

In this paper we have reviewed many of the anatomical and clinical features seen in the brain caused by the Communicable Diseases of malaria and HIV/AIDS, and the Non-Communicable Diseases including CVA/strokes and the neurodegenerative diseases of AD, PD, HD and ALS. We have also discussed the major strides made in reducing the effects of CVAs and malaria on the brain. We have discussed the effects on the families of the affected patients who presented with the neurodegenerative diseases of AD, PD, HD, and ALS. Finally, we have reported on the major strides made in dealing with the deleterious effects of these disease on the brain matter. Other chapters in this book have discussed the effects of HIV/AIDS, malaria, nutritional deficiencies on the brain.

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References

1. Tattersall I. Human origins: out of Africa. Proc Natl Acad Sci. 2009;106:16018–21.
2. Moreno E. The society of our "out of Africa" ancestors. The migrant warriors that colonized the world. Commun Integr Biol. 2011;4, J Urban Health. Suppl 2:256–65.
3. Johanson DC. Lucy (*Australopithecus afarensis*). In: Ruse M, Travis J, editors. Evolution: the first four billion years. Cambridge, MA: The Belknap Press of Harvard University Press; 2009. p. 693–7.
4. Johanson C, Wong K. Lucy's legacy: the quest for human origins. New York: Harmony Books; 2009.
5. World Health Organization, WHO, Data and Statistics, 2011.
6. Center for Disease Control (CDC). Leading causes of death in the United States Centers for Disease Control and Prevention. US Government, Washington DC. 2011.
7. Jamison DT, Feachem RG, Malegapuru A, Makgoba W, Bos ER, Baingana FK, Hofman KJ, Khama O. Disease and mortality in sub-Saharan Africa. 2nd ed. Washington, DC: World Bank; 2006.

8. Samuel JC, Sankhulani E, Qureshi JS, Baloyi P, Thupi C, et al. Under-reporting of road traffic mortality in developing countries: application of a capture-recapture statistical model to refine mortality estimates. PLoS ONE. 2012;7(2):7–11.
9. Ziraba AK, Kyobutungi C, Zulu EM. Fatal injuries in the slums of Nairobi and their risk factors: results from a matched case-control study. PLoS Med. 2011;2:163–70.
10. Love S, Louis DN, Ellison DW. Greenfield's neuropathology. 8th ed. London: Edward Arnold (Publishers) Limited; 2008.
11. Victor and Roper. Principles of neurology. 2008; 8th ed, McGraw-Hill, NY, 2014.
12. Lagarde E. Road traffic injury is an escalating burden in sub-Sahara Africa. PLoS Med. 2007;4:170–75.
13. Health Insurance and Portability Act, nih.US gov/hipaa/1996.
14. Virtual Patient Special Issue. Medical Teacher, vol 31. 2009.
15. Ellaway RH, Poulton T, Smothers V, Greene P. Virtual patients come of age. Med Teach. 2009;31(8):683–4.
16. Jacobson S, Epstein SK, Albright S, Ochieng J, Griffiths J, Coppersmith V, Polak JF. Creation of virtual patients from CT images of cadavers to enhance integration of clinical and basic science student learning in anatomy. Med Teach. 2009;31(8):749–51.
17. Jacobson S, Marcus EM. Neuroanatomy for the neuroscientist, 2nd ed. Springer. New York, 2011.
18. Chin JH. Stroke in Sub-Saharan Africa: an urgent call for prevention. Neurology. 2012;78:1007–8.
19. Cordoliani YS, Sarrazin JL, Felten D, Caumes E, Lévêque C, Fisch A. MRI of cerebral malaria. Am J Neuroradiol. 1998;19:871–4.
20. Taylor TE, Wenjiang JF, Carr RA, Richard O, Whitten RO, Mueller JG, Fosiko NG, Lewallen S, Liomba NG, Molyneux EM. Differentiating the pathologies of cerebral malaria by *postmortem* parasite counts. Nat Med. 2004;10:143–5.
21. Quinn TC. Epidemiology of human immunodeficiency virus infection and acquired immunodeficiency syndrome. In: Goldman L, Schafer A, editors. Cecil medicine. 24th ed. Philadelphia: Saunders Elsevier; 2011. Chap. 392.
22. Sterling TR, Chaisson RE. General clinical manifestations of human immunodeficiency virus infection (including the acute retroviral syndrome and oral, cutaneous, renal, ocular, metabolic, and cardiac diseases). In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2009. Chap. 121.
23. Genuis SJ, Genuis SK. AIDS prevention in Uganda why it has worked. Postgrad Med J. 2005;81:615–7.
24. Uganda Reverses the tide of AIDS, WHO, Data and Statistics 1998.
25. Marcus EM, Jacobson S. Integrated neurosciences a clinical problem solving approach. Boston: Kluwer; 2003.
26. Irwin DJ, Abrams JY, Schonberger LB, Leschek EW, Mills JL, Lee VM, Trojanowski JQ. Evaluation of potential infectivity of Alzheimer and Parkinson disease proteins in recipients of cadaver-derived human growth hormone. JAMA Neurol. 2013;70:462–8.
27. Luk KC, Kehm V, Carroll J, Zhang B, O'Brien P, Trojanowski JQ, Lee VM. Pathological α-synuclein transmission initiates Parkinson-like neurodegeneration in nontransgenic mice. Science. 2012;338:949–53.
28. NIMH. Top research advances NIMH, NIH, gov.; 2011.