On Down — Down Syndrome

Secrets of the Sequence Video Series on the Life Sciences • Grades 9 — 12

Teaching materials developed by **VCU** Life Sciences

Virginia Commonwealth University

Classroom Tested Lesson

Video Description

"Secrets of the Sequence," Show 110, Episode 3

"On Down: Down Syndrome" – approximately 9 minutes viewing time

Scientists have known for some time that Down Syndrome, the most common chromosomal abnormality, is caused by an additional chromosome #21. However, new fetal stem cell research is demonstrating that it is not only the presence of this additional chromosome, but the altered expression of genes on other chromosomes that make the difference in the prognosis of an affected individual.

Ward Television
Producer: Fran Victor
Featuring: Dr. Lewis Leavitt, University of Wisconsin-Madison, Clive Svendsen, University of Wisconsin-Madison
Lesson Author; Reviewers: Robert Pyatt, Catherine Dahl; Dick Rezba
Trial Testing Teachers: Karly Wortman

National and State Science Standards of Learning

National Science Education Standards Connection

Content Standard A: Science as Inquiry

As a result of activities in grades 9-12, all students should develop:

- Abilities necessary to do scientific inquiry
- Understandings about scientific inquiry

Content Standard C: Life Science

As a result of their activities in grades 9-12, all students should develop understanding of

- Molecular basis of heredity
- Behavior of organisms

Content Standard G: History and the Nature of Science.

As a result of their activities in grades 9-12, all students should develop understanding of

- Science as a human endeavor
- Nature of scientific knowledge
- Historical perspectives

Selected State Science Standards Connections

Use http://www.eduhound.com (click on "Standards by State") or a search engine to access additional state science standards.

Virginia

BIO.5 The student will investigate and understand life functions of archaebacteria, monerans (eubacteria), protists, fungi, plants, and animals including humans. Key concepts include

e) human health issues, human anatomy, body systems, and life functions;

BIO.6 The student will investigate and understand common mechanisms of inheritance and protein synthesis. Key concepts include

c) cell specialization;
d) prediction of inheritance of traits based on the Mendelian laws of heredity;
e) genetic variation (mutation, recombination, deletions, additions to DNA);
h) use, limitations, and misuse of genetic information; and
i) exploration of the impact of DNA technologies.

Louisiana

Science as Inquiry
Understanding Scientific Inquiry

13. Identify scientific evidence that has caused modifications in previously accepted theories (SI-H-B2)
14. Cite examples of scientific advances and emerging technologies and how they affect society (e.g., MRI, DNA in forensics) (SI-H-B3)

Life Sciences
The Molecular Basis of Heredity

8. Describe the relationships among DNA, genes, chromosomes, and proteins (LS-H-B1)
12. Describe the processes used in modern biotechnology related to genetic engineering (LS-H-B4) (LS-H-B1)
13. Identify possible positive and negative effects of advances in biotechnology (LS-H-B4) (LS-H-B1)

Personal and Community Health

42. Summarize the uses of selected technological developments related to the prevention, diagnosis, and treatment of diseases or disorders (LS-H-G5)

Overview

Students will learn how stem cell research has provided scientists with the tools to make significant breakthroughs in the study of Down Syndrome. Until recently, the focus has been totally centered on Chromosome 21, the extra chromosome associated with Down Syndrome, and how it causes the symptoms seen in this syndrome such as impaired mental development. New technology has now made it possible to directly examine the function of genes in normal brain development. Using this technology, it appears in Down Syndrome that the extra copy of Chromosome 21 is altering the expression of genes on other chromosomes and their role in normal brain development. By comparing 33,000 genes in the stem cells from Down Syndrome fetal tissue to non-Down Syndrome stem cells, scientists are now able to see the differences in the way these genes control brain development between people with and without Down Syndrome. These differences in gene expression may also explain why there is a large degree of variation in the severity of Down Syndrome patients. These profound differences show up by looking at other chromosomes affected by this "downstream effect".

Testing: A sample related multiple-choice item from State Standardized Exams

A human zygote, like most other human cells, contains 46 chromosomes. How many chromosomes does a zygote receive from the mother?

A. 0
B. 23*
C. 46
D. 92

Source: Massachusetts 2004 Biology, Grade 10

Video Preparation

Preview the video and make note of the locations at which you will later pause the video for discussion.

Before Viewing

1. Ask: "What characteristics do people with Down Syndrome typically have?"
   "What else do you know about Down Syndrome?"

During Viewing

1. START the video.

2. PAUSE the video (4.25 minutes into the video) after the segment where Dr. Svendsen speaks about the key developments in researching Down Syndrome and just before the computer explanation of stem cell growth in a lab.

   Ask the following questions:

   - "What is the typical number of chromosomes in a child who has Down Syndrome?
     47 (46 chromosomes plus one extra chromosome 21)

   - **"**What were the key developments that made it possible for researchers to get a better understanding of Down Syndrome?"
     The mapping of the human genome.
     The ability to grow stem cells in a dish.

3. RESUME the video and play to the end.

After Viewing

1. Ask: "What are some common features of Down Syndrome mentioned in the video?"

   People with Down Syndrome have similar facial features (broad faces and upward slanted eyes).
   They will also have some form of mental impairment.
   They will develop a form of Alzeheimer's Disease during their life.
   They have an accelerated aging process.
   They have an extra copy of chromosome 21.

2. Ask: "What surprised the scientists about the genetic causes of Down Syndrome?"

   Down Syndrome is caused by having a third copy of chromosome 21 and consequently a third copy of all the genes on that chromosome. However, it also appears that the expressions of other genes on other chromosomes besides 21 are also affected in Down Syndrome. For example, the scientists in the video discovered that the expression of the genes for brain development is different in people with Down Syndrome and these genes are not on chromosome 21. This is called the "Downstream Effect".

3. Ask: "Why is stem cell research so important to the study of Down Syndrome?"

   Initially Down Syndrome studies were performed on mice, but mice do not even have Chromosome 21. The ability to grow stem cells from Down Syndrome fetal tissue and compare them to stem cells from non-Down Syndrome patients makes it possible to determine if replication of these cells occur in the same way. For example, it is now possible to view the development of stem cells into neuron cells, and it is clear that there are enormous differences in the rates of development between the Down Syndrome (DS) and non-DS stem cells.

Teacher Notes for the Student Activities:

Part I: Normal Human Karyotypes - students will examine a normal human karyotype and become familiar with examining the similarities of chromosome pairs.

Part II: Matching Chromosomes - Students will use these skills and take on the role of a scientist in assembling and analyzing a karyotype for an unborn child with Down Syndrome.

Part III (Optional): Other Anueploid Conditions - students will again act as scientists and assemble an unknown karyotype that could be one of three syndromes associated with an aneuploid state or an altered number of chromosomes in their karyotype.

Note: All of the karyotypes, photos of chromosomes, and Answer Keys for Teachers are found at the end of the lesson.

Preparation

Prepare copies of the handouts, karyotypes, and chromosome sets to be used.
For a class of 24 (12 pairs), you will need:

Part I	6 copies of the female karyotype
	6 copies of the male karyotype
Part II	6 copies of chromosome Set A
	6 copies of chromosome Set B
Part III	4 copies of aneuploid syndrome Set A
	4 copies of aneuploid syndrome Set B
	4 copies of aneuploid syndrome Set C

Note: If you choose to assign Part III as homework, you will need 8 of each set so every student has one of the three sets to take home.

Materials for Student pairs

- Index Cards

- Scissors
- Glue or glue stick
- White Paper
- Handout on Normal Human Karyotype, Part I plus 1 of 2 karyotypes (male or female)
- Handout on Matching Chromosomes, Part II plus 1 of 2 sets of chromosomes (Set A or Set B)
- Handout on Other Aneuploid Syndromes, Part III plus 1 of 3 sets of chromosomes (Set A, B, or C)

Procedure

Assign Student Pairs to work on all the activities. If time allows, you may want to conduct a short pre-activity game to match-up students with a partner.

Optional Pre-activity:

1. Students will each be given an index card with a picture of one of two paired chromosomes and will be instructed to find their match. Their match will be their lab partner.

2. Prepare the index cards ahead by cutting the matched chromosomes apart using a copy of one of the Part I karyotypes. Use the matched chromosomes that are most visually similar; for example on the XX karyotype, use 2, 6, 13 and others, to facilitate partners finding each other. Paste the separated chromosomes on different cards. (You may want to write the chromosome number on the back top left corner so that if the students have difficulty finding their match in a timely fashion, they can turn their cards over.) Make enough paired cards to accommodate the number of students in your largest class.

3. Make sure you shuffle the cards first so they are distributed randomly to students.

4. You may want to direct students to look carefully at the size, shape, and bands of each chromosome in order to find their match.

Conduct each of the following activities.

Part I: Normal Human Karyotypes

1. Once students have found their match, distribute the Student Handout: *Part I Normal Human Karyotypes.* Give half the student pairs the normal male karyotype and the other half the normal female karyotype.

2. Have students follow the instructions on the handout and answer the following questions.
    - *a)* What is a karyotype? *(A photograph of the chromosomes taken from a single cell. The chromosomes are matched into pairs based on their common size, shape, and banding pattern. The chromosome pairs are then arranged from the largest pair to the smallest and the sex chromosomes are placed last to form a karyotype.)*
    - *b)* How many chromosomes are in a normal human karyotype? *(46 total chromosomes. 44 autosomes and 2 sex chromosomes.)*
    - *c)* Which chromosome pair is different from the others? *(sex chromosomes)*
    - *d)* What are the names of the two types of chromosomes? *(sex chromosomes and autosomes)*
    - *e)* Is your karyotype for a male or female? How can you tell? (*Male has X and Y chromosomes, Female two X)*

f) Does this karyotype have the correct total number of chromosomes and chromosome pairs? *(Yes, in a normal human karyotype there will be 22 pairs of autosomes and one pair of sex chromosomes for a total of 46 chromosomes.)*

g) How is a karyotype used in medicine*? (To determine if a person has any differences in their total number of chromosomes which may cause a genetic syndrome with severe medical symptoms.)*

h) Pick any pair of autosomes (Chromosomes 1-22) on your karyotype and carefully draw that pair and label your pair with their number. In a few sentences describe the size, shape, and banding pattern of your chromosome pair.

Part II: Down Syndrome

1. Once students have completed Part I, distribute the Student Handout: *Part II Matching Chromosomes* and one of the two sets of Down Syndrome chromosomes (give half the students Set A and the other half Set B) to match.

2. In Part II students will use the information on normal karyotypes and chromosome pairs from Part I to do a matching activity and assemble a karyotype for a male or female with Down Syndrome. An ideal match should look like the karyotype answer keys provided for the teacher.

3. While we have simplified these karyotypes, they are still real ones taken from real people. As with any real data, parts of these karyotypes may be challenging for the students to assemble. Encouraging the students to begin by matching the most obvious chromosomes first, like the smallest ones, should help reduce the number of potentially difficult ones and the student's frustration. If the students get too frustrated with the matching of chromosomes, this exercise will lose its educational value.

4. When students have completed the Part II matching activity, have them answer the follow-up questions.

    a) Is this karyotype for a male or a female child? How do you know? (*Male has X and Y, Female has X X*)

    b) Does this karyotype have the correct total number of chromosomes and chromosome pairs? Explain in a complete sentence how you know this. *(*No, *in a normal human karyotype there will be 22 pairs of autosomes and one pair of sex chromosomes for a total of 46 chromosomes. This child has three of chromosome 21 for a total of 47.)*

    c) What inherited condition arises from this alteration in chromosome number? (*Down Syndrome)*

    d) What are the common characteristics or symptoms of individuals with this syndrome? *(See After Viewing Questions 1 for list)*

Part III (Optional) Aneuploid Karyotypes

1. If time allows, distribute the third student handout and one of the three other karyotypes of aneuploid conditions for each group to assemble. This exercise is designed for students to apply what they have learned in parts I and II to examining an unknown karyotype in an inquiry based exercise.

2. The same difficulties students face when working with real karyotypes should be considered from part II.

3. Once their karyotypes are assembled, students will answer the following questions. The answers will be specific to the unknown karyotype (Edwards, Turners, Trisomy X) they are given.

   a) Is this karyotype for a male or a female child? How can you tell?

   b) Does this karyotype have a normal number of human chromosomes? If not, what are the differences?

   c) What is the total number if chromosomes in your karyotype?

   d) What is the name for this condition?

   e) What are some of the symptoms associated with this condition?

4. Because this exercise asks students to take on the role of a scientist examining the karyotype, it may by an ideal situation to begin a discussion on genetic testing and the ethics surrounding the associated issues that arise. Further information about this subject can be found on Internet (See the American Society of Human Genetics homepage).

5. It is also important for students to realize in this section that having the gain of an extra chromosome or the loss of one can have dramatic results on a person's health. This can easily be seen in Down Syndrome where the presence of a third copy of chromosome 21 results in the severe health issues discussed in the video. So having a third copy of all the genes on a chromosome or missing a complete set of genes on a chromosome in the case of a monosomy is a drastic state. Not surprisingly then, most aneuploid conditions where a person has a monosomy or trisomy are normally fatal. Trisomy 21, 18, 13, X, and Y (where the male will have 48 total chromosomes with sex chromosomes XYYY) are the only viable trisomies. The only viable monosomy is Turners Syndrome (monosomy X). Trisomy X is a very special case then where an aneuploid condition results in no harmful symptoms and the females are essentially normal and healthy. Given a frequency of 1 female in 1,000, you may want students to think about how many potential women in their town could have this karyotype and be unaware of it.

Student Handout: Part I Normal Human Karyotypes

Background Information

The human genome is made of 3.2 billion chemical units or nucleotide bases and if stretched out it would be one very thin strand about six feet long. To squeeze all of this genetic information into a cell, the DNA is supercoiled or twisted many times on itself and bound by proteins to form structures called chromosomes. Chromosomes exist in pairs and each species has a distinct number of pairs in their genome; dogs have 39 chromosome pairs, cows have 30, cats have 19, and humans have 23 chromosome pairs. Because we get half of our genes from each of our parents, we get one set of 23 chromosomes from our father and one set of 23 chromosomes from our mother. In humans, the 23 pairs include a set of sex chromosomes (X and Y) and 22 autosome pairs (Chromosomes 1-22).

A karyotype is a photograph of the chromosomes taken from a single cell. Scientists can take a living cell, incubate it with growth factors in a laboratory to stimulate the cell to grow and divide, treat the cells with a chemical which stops their replication in metaphase of the cell cycle, extract the DNA in the form of chromosomes from those cells, and then stain the chromosomes with a dye. By looking under a microscope, the chromosomes can be paired up based on their similar size, shape, and unique dye pattern of each chromosome pair. Once each of the pairs has been identified, the chromosome pairs are arranged from the largest to the smallest with the sex chromosome pair last to form a karyotype. Karyotypes are used both by scientists studying genetics and sexual reproduction and by physicians because they can quickly identify chromosomal differences that may result in a genetic disorder with severe medical symptoms.

Procedure

In this first part, you'll examine a normal human karyotype and begin to appreciate the similarity of size, shape, and banding pattern of chromosome pairs for part II. Once you are given your karyotype, use it to answer the following questions.

a. What is a karyotype?

b. How many chromosomes are in a normal human karyotype?

c. Which chromosome pair is different from the others?

d. What are the names of the two types of chromosomes?

e. Is your karyotype for a male or female child? How can you tell?

f. Does this karyotype have the correct total number of chromosomes and chromosome pairs?

g. How is a karyotype used in medicine?

h. Pick any pair of autosomes (Chromosomes 1-22) on your karyotype and carefully draw that pair and label your pair with their number. In a few sentences describe the size, shape, and banding pattern of your chromosome pair.

Student Handout: Part II Matching Chromosomes

Background Information

In Part I you learned that a normal human karyotype contains 46 total chromosomes; 23 pairs of chromosomes with one chromosome of each pair donated from each parent. However, some people can have alterations in the total number chromosomes in their genome which can cause a genetic disorder or syndrome. These karyotypes are called aneuploid or having an incorrect number of total chromosomes. You are already familiar with one such condition from the video, Down Syndrome.

Individuals with Down Syndrome have an extra copy of chromosome 21, called a Trisomy, giving them a total of 47 chromosomes. Down Syndrome occurs once in every 600 to 700 births, making it the most common genetic disorder. Most individuals with Down Syndrome have characteristic features such as upward slanted eyes, broad flattened face, short neck, and a prominent tongue. Muscle coordination is often impaired in these individuals, resulting in poor posture and balance and speech difficulties. Heart disease is found in forty percent of these individuals, along with a near twenty-fold increase in the risk of kidney malformation, thyroid abnormalities, diabetes, and leukemia. Neurological retardation and impaired immune systems render these individuals more susceptible to infection and disease. In the early l900s, Down Syndrome patients rarely lived to reach the age of twenty, as they only had a life expectancy of about 10 years. With the advances of modern health care, most individuals, excluding those with irreparable heart damage, live to reach adulthood. Although it is still shorter than normal adults, their life expectancy has increased to about 55 years.

While the exact causes of Down Syndrome are not known, the presence of an extra copy of chromosome 21 in a gamete is caused by non-disjunction. During meiosis, chromosomes divide to create eggs or sperm with one half the total number of chromosomes of a mature cell created by sexual reproduction. In our case, our fathers give us 23 chromosomes and our mothers give us 23 for a total of 46 chromosomes in our cells. Non-disjunction occurs when one set of chromosomes fails to separate during meiosis resulting in one gamete with two copies of chromosome 21 and one gamete with none. When the gamete with two copies is fertilized by a normal gamete with the normal one copy, the embryo then has three copies of chromosome 21 resulting in Down Syndrome.

Because many people with Down Syndrome are born with heart defects and other medical problems, it is important to identify a child as having Down Syndrome as quickly as possible. This is often done before a child is born through an Amniocentesis. Amniocentesis is a procedure where a sample of amniotic fluid and cells is collected from the space surrounding the baby in its mother's womb. These cells will be grown, DNA extracted, and stained in order to examine the child's karyotype and look for a normal or altered number of chromosomes. These karyotypes are extremely important then for the physicians and parents to use to guide their care of the newborn if they do have Down Syndrome.

In this section, you and your partner will take on the roll of a scientist assembling a karyotype of an unborn child. One of each pair of chromosomes has already been identified and your job is to finish the karyotype and to make the diagnosis of a normal karyotype or Down Syndrome. These are real karyotypes from real people so the assembly may be difficult due to poor staining of some chromosomes with the dye or twisting of the chromosomes under the microscope. Do your best and start with the easy to identify pairs first.

Procedure

1. Cut out each chromosome on the attached sheet.

2. Match the pairs of chromosomes.

3. Arrange and number the matched pairs in a pattern similar to your example of a normal karyotype from Part I: Make sure to match all chromosomes even if you have extra chromosomes.

4. Use glue or a glue stick to paste your final karyotype arrangement.

5. Using your matched karyotype, answer the following questions:

   a) Is this karyotype for a male or a female child? _____How do you know?

   _____

   b) Does this karyotype have a normal number of human chromosomes? _____What is different?

   _____

   c) What condition arises from this alteration in chromosome number?

   _____

   d) What are the common characteristics or symptoms of individuals with this syndrome?

   _____

   e) What special needs would the parent have to meet in order to provide for this child?

   _____

Student Handout: Part III Other Aneuploid Syndromes

Background

As you saw in the last section, Down Syndrome is one of many aneuploid conditions in which an individual has an altered number of total chromosomes. Many of the most common aneuploid conditions seen in humans involve the gain or loss of a single chromosome. In the case of Down Syndrome, the individual has an extra copy of chromosome 21 for a total of 47. A condition where there is an extra copy of a single chromosome is called a trisomy (tri meaning three); someone with Down Syndrome is said to have Trisomy 21. When there is a loss of a chromosome, the condition is termed a monosomy (mono meaning one). There are several aneuploid conditions, but common ones besides Down Syndrome are Turners Syndrome, Edwards Syndrome, & Trisomy X.

Turners Syndrome is characterized by a single sex chromosome (45 total chromosomes) and is also called monosomy X. Without a Y chromosome, all individuals develop into females and individuals with Turners Syndrome typically are short with an average height of four feet eight inches, have heart and kidney defects, and are sterile. Monosomy X affects 1 in 2,500 females.

Edwards Syndrome is characterized by a third copy of chromosome 18 (47 total chromosomes) and is also called Trisomy 18. Individuals with Trisomy 18 are born with severe heart defects, low birth weight, mental retardation, and typically don't live more than a year. Edwards Syndrome affects 1 in 3,000 live births.

Trisomy X is characterized by a third copy of the X chromosome (47 total chromosomes). This affects 1 in 1,000 females however there are no abnormal signs or symptoms associated with this condition. These females are normal and healthy.

When a karyotype is ordered on an unborn child, the scientist assembling and reading it has many possible outcomes to consider. The karyotype could be normal with 46 chromosomes or one of the aneuploid conditions such as Down Syndrome, Edwards Syndrome, Turners Syndrome, or Trisomy X. Because each condition is associated with unique symptoms ranging from a shortened lifespan due to severe birth defects in Edwards Syndrome to no adverse symptoms at all in Trisomy X, a doctor needs a clear and accurate karyotype in each case to correctly treat each patient and syndrome.

In this third activity, you will again act as scientists and assemble an unknown karyotype. As before, one of each chromosome pair has already been identified and you need to find its match. In this activity, however, any of the karyotypes discussed so far are possible including a normal number of chromosomes, a monosomy, or a trisomy.

Procedure

1. Cut out each chromosome on the sheet.
2. Match the pairs of chromosomes.
3. Arrange and number the matched pairs in a pattern similar to your example of a normal karyotype from Part I. Make sure to match all chromosomes even if you have extra chromosomes.
4. Use glue or a glue stick to paste your final karyotype arrangement.
5. Using your matched karyotype, answer the following questions:
    a) Is this karyotype for a male or a female child?

    b) Does this karyotype have a normal number of human chromosomes?

    c) What is the total number if chromosomes in your karyotype?

    d) What is the name for this condition?

    e) What are some common characteristics or symptoms associated with this condition?

Additional Resources

Because Web sites frequently change, some of these resources may no longer be available. Use a search engine and related key words to locate new Web sites.

Lesson karyotypes adapted from *http://worms.zoology.wisc.edu/zooweb/Phelps/karyotype.html*

http://gslc.genetics.utah.edu/units/disorders/karyotype/downsyndrome.cfm

http://www.ndss.org/

http://www.nads.org/

http://web.indstate.edu/thcme/anderson/JJ.html

http://whyfiles.org/shorties/144downs_alz/

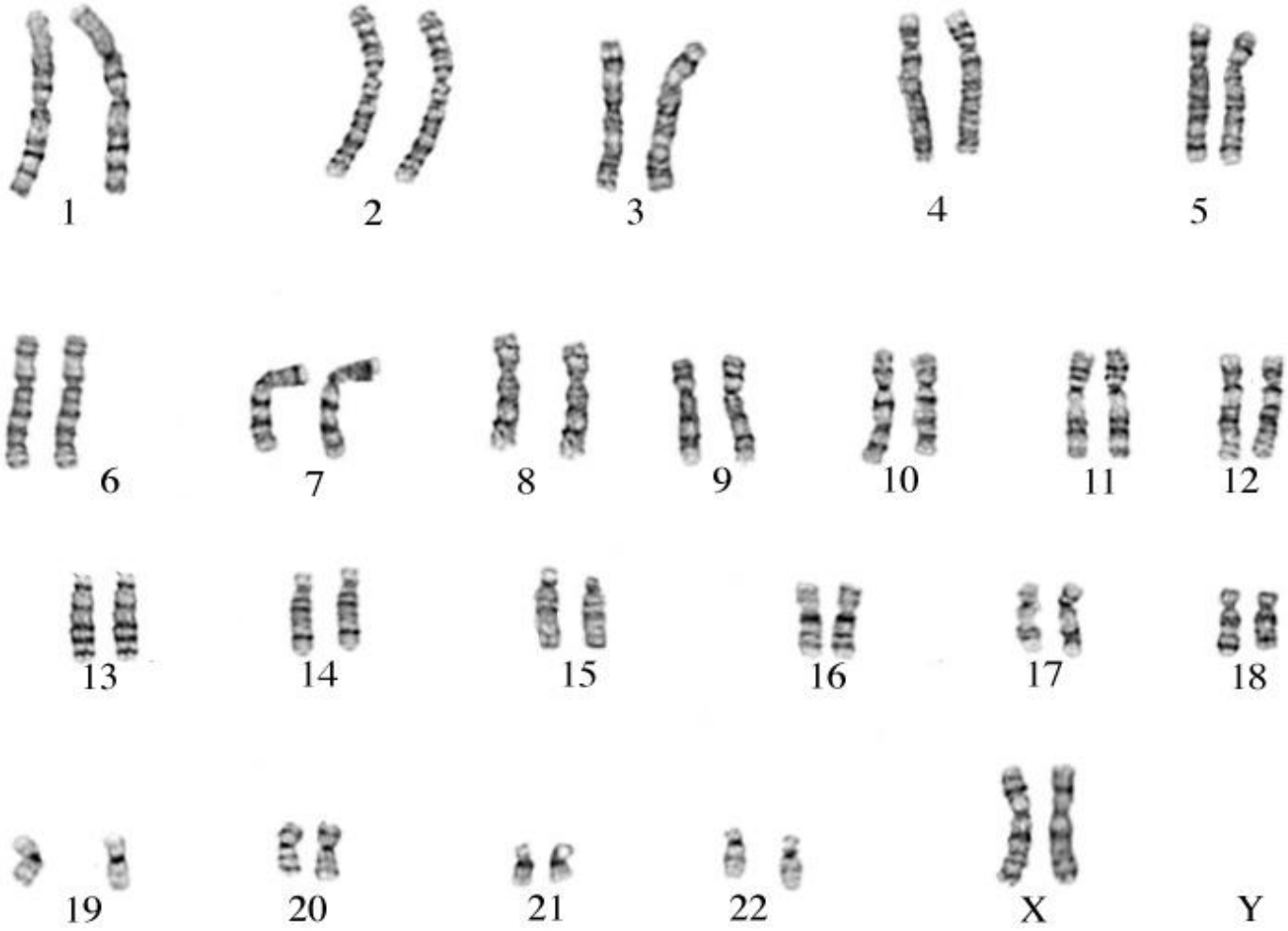
http://www.badgerherald.com/news/2002/02/04/stem_cells_provide_i.php

http://gslc.genetics.utah.edu/units/disorders/karyotype/flash/karyotype_try_it.swf

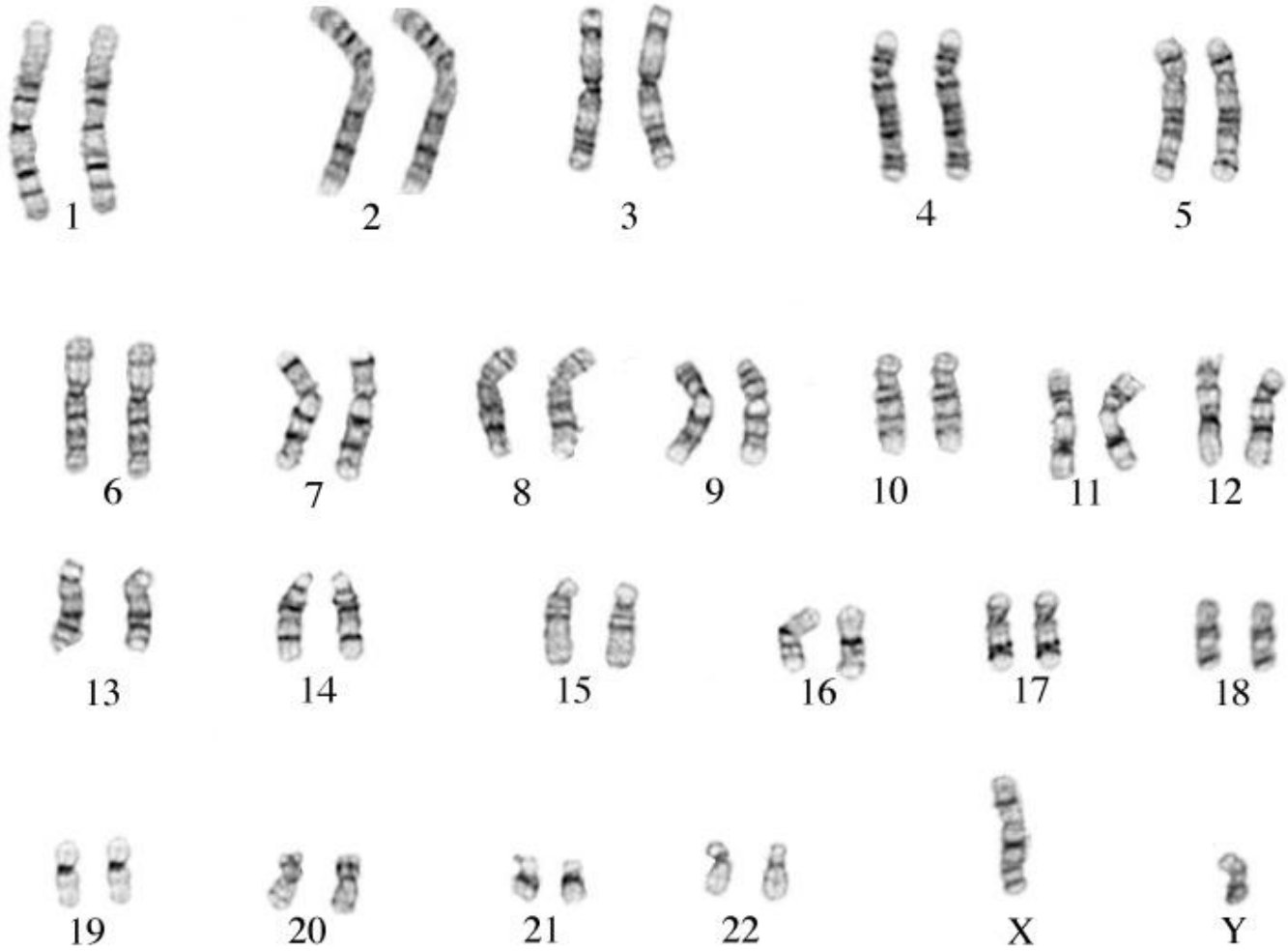
Genomic Revolution
http://www.ornl.gov/sci/techresources/Human_Genome/education/education.shtmL
This Web site of the government-funded Human Genome Project has links about genomics, the history of the project, and more.

Secrets of the Sequence Videos and Lessons
This video and 49 others with their accompanying lessons are available *at no charge* from www.vcu.edu/lifesci/sosq

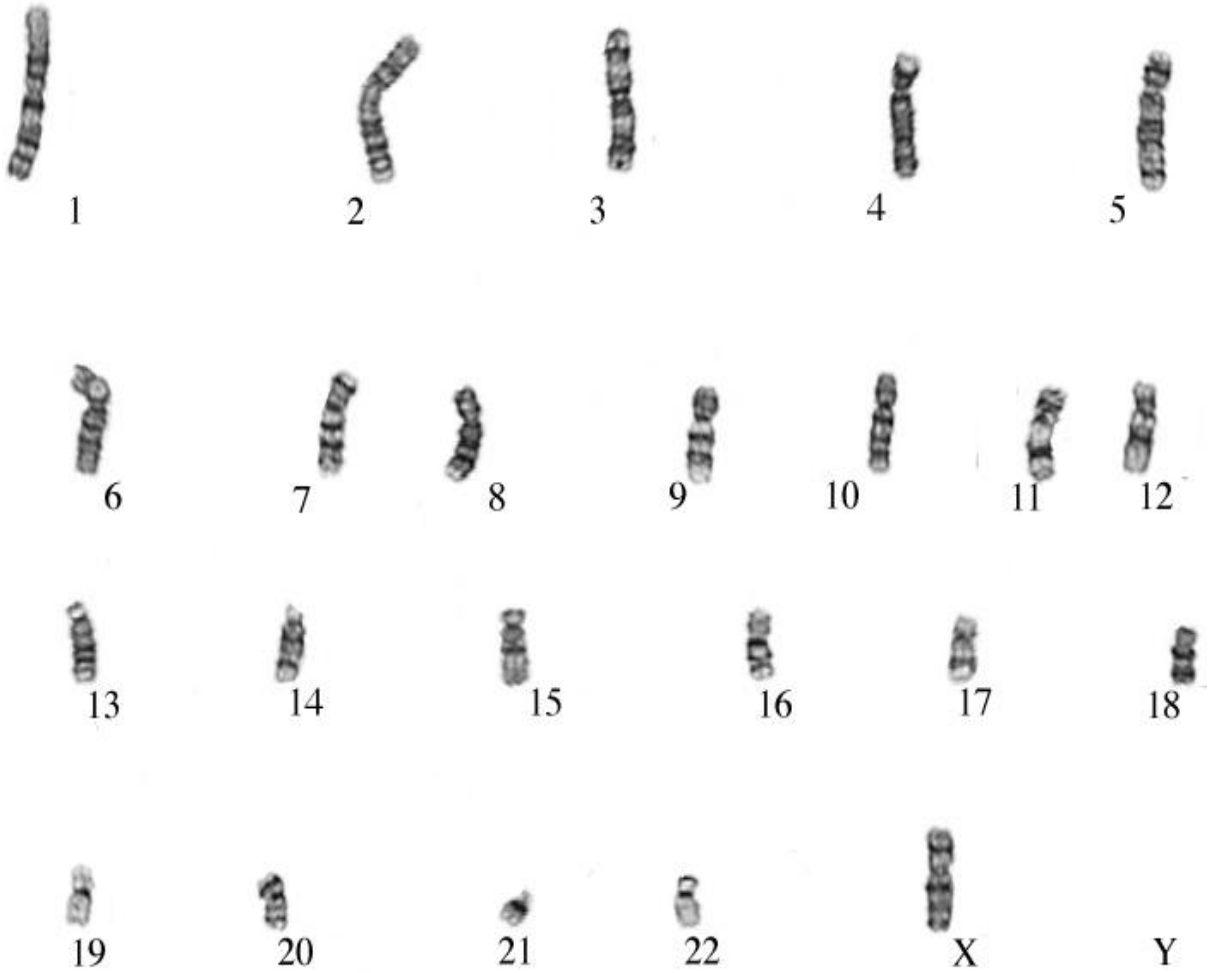
Part I Chromosome Set A



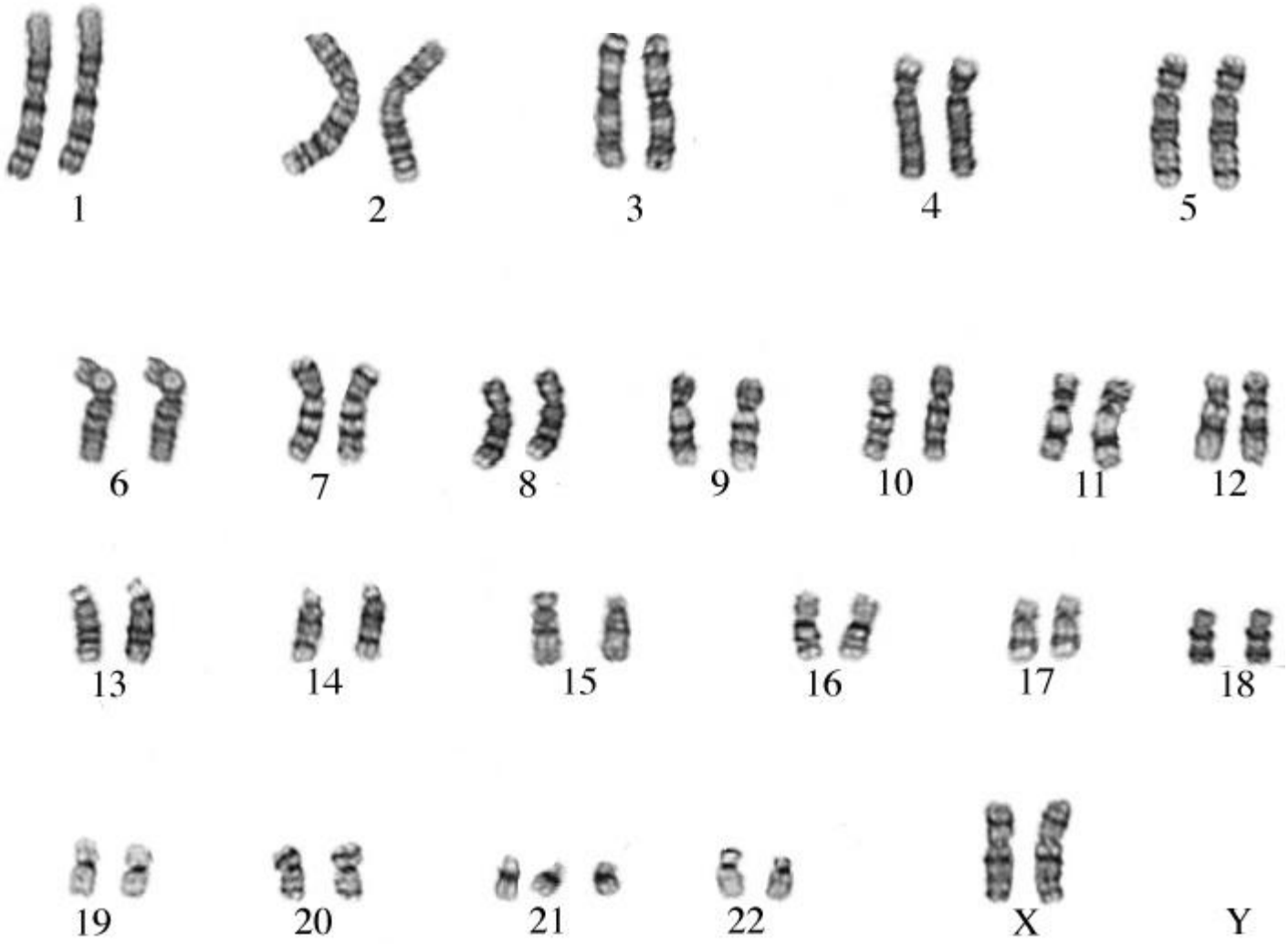
Part I Chromosome Set B



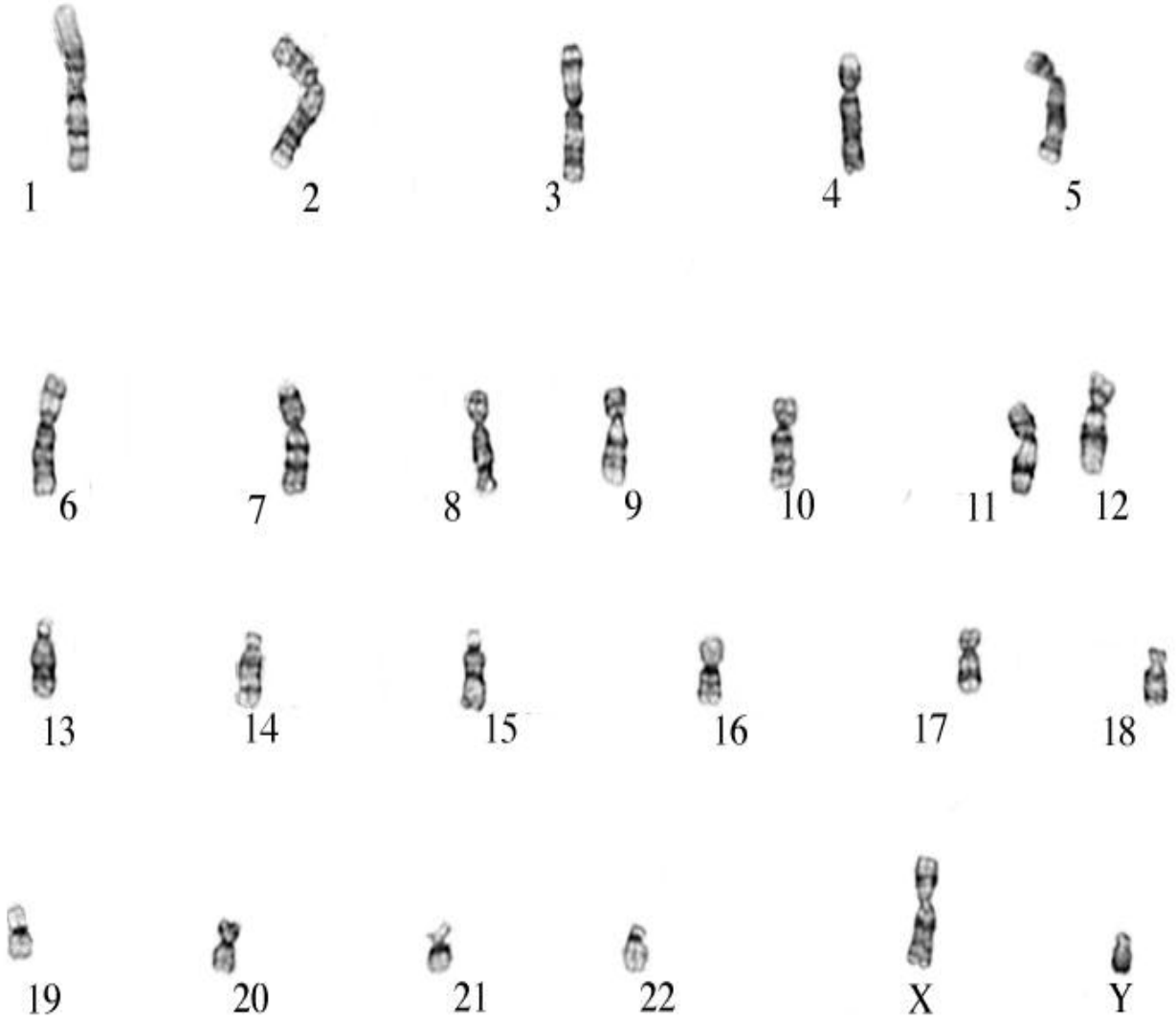
Part II: Matching Chromosomes A



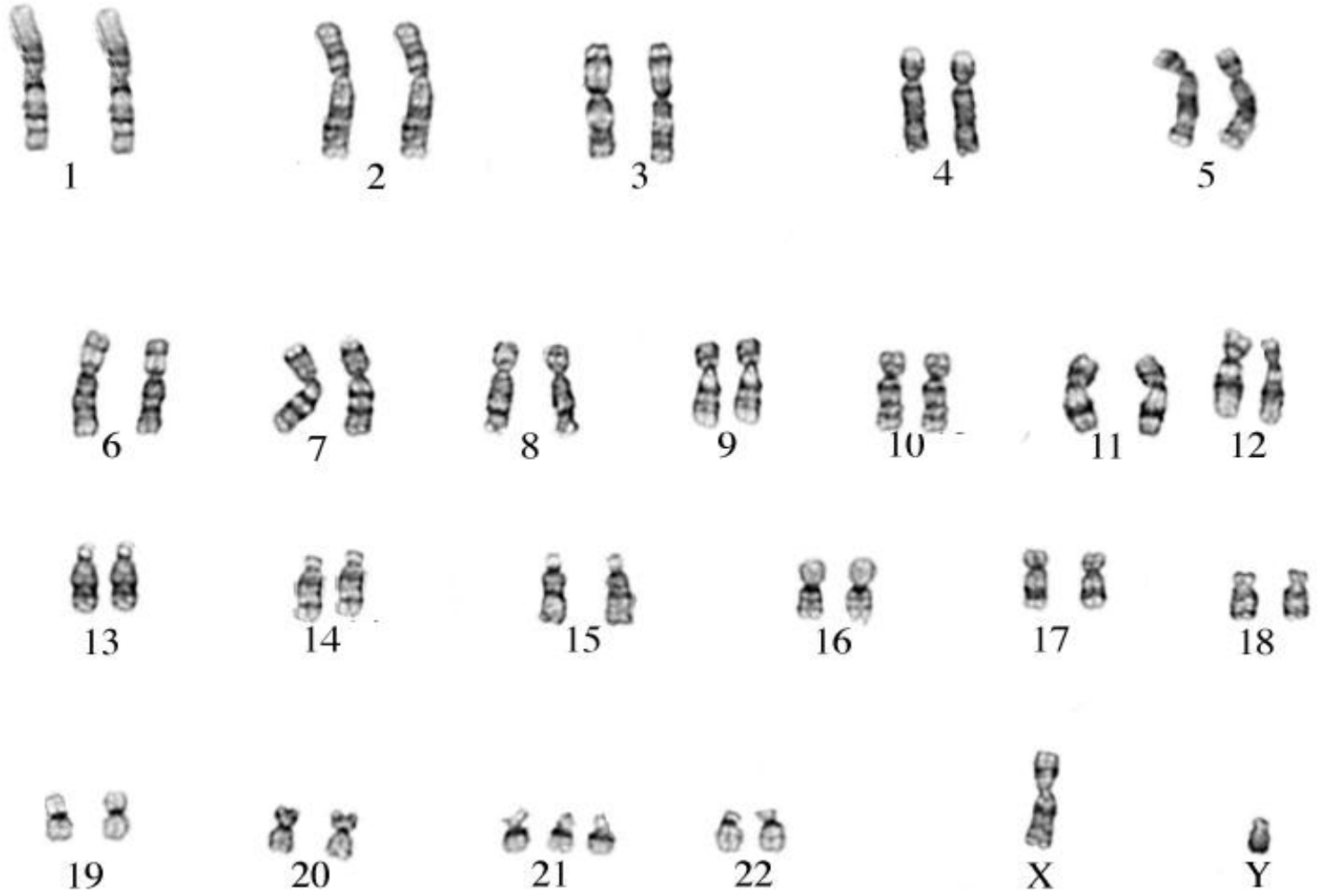
Answer key for:
Part II: Matching Chromosomes A



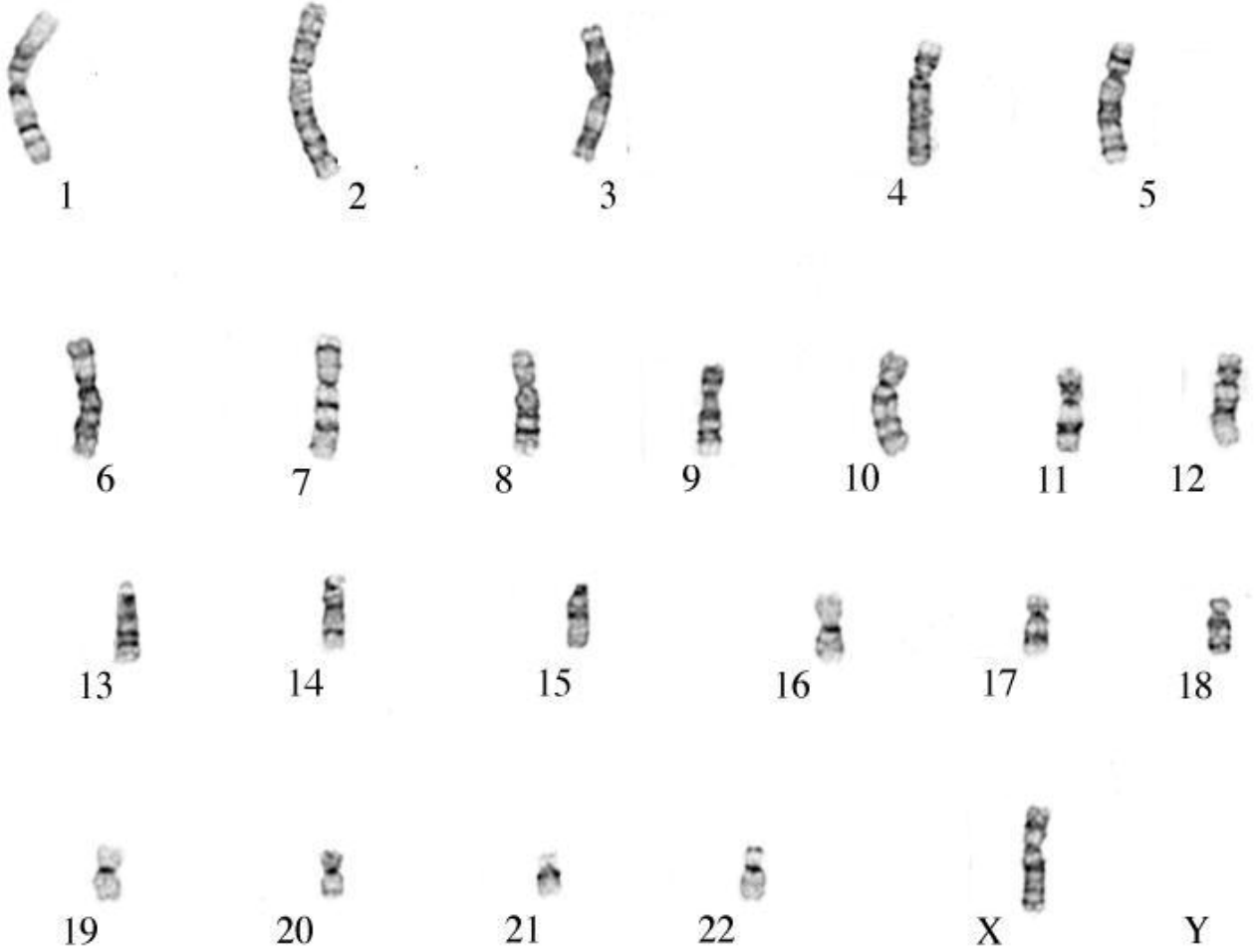
Part II: Matching Chromosomes B



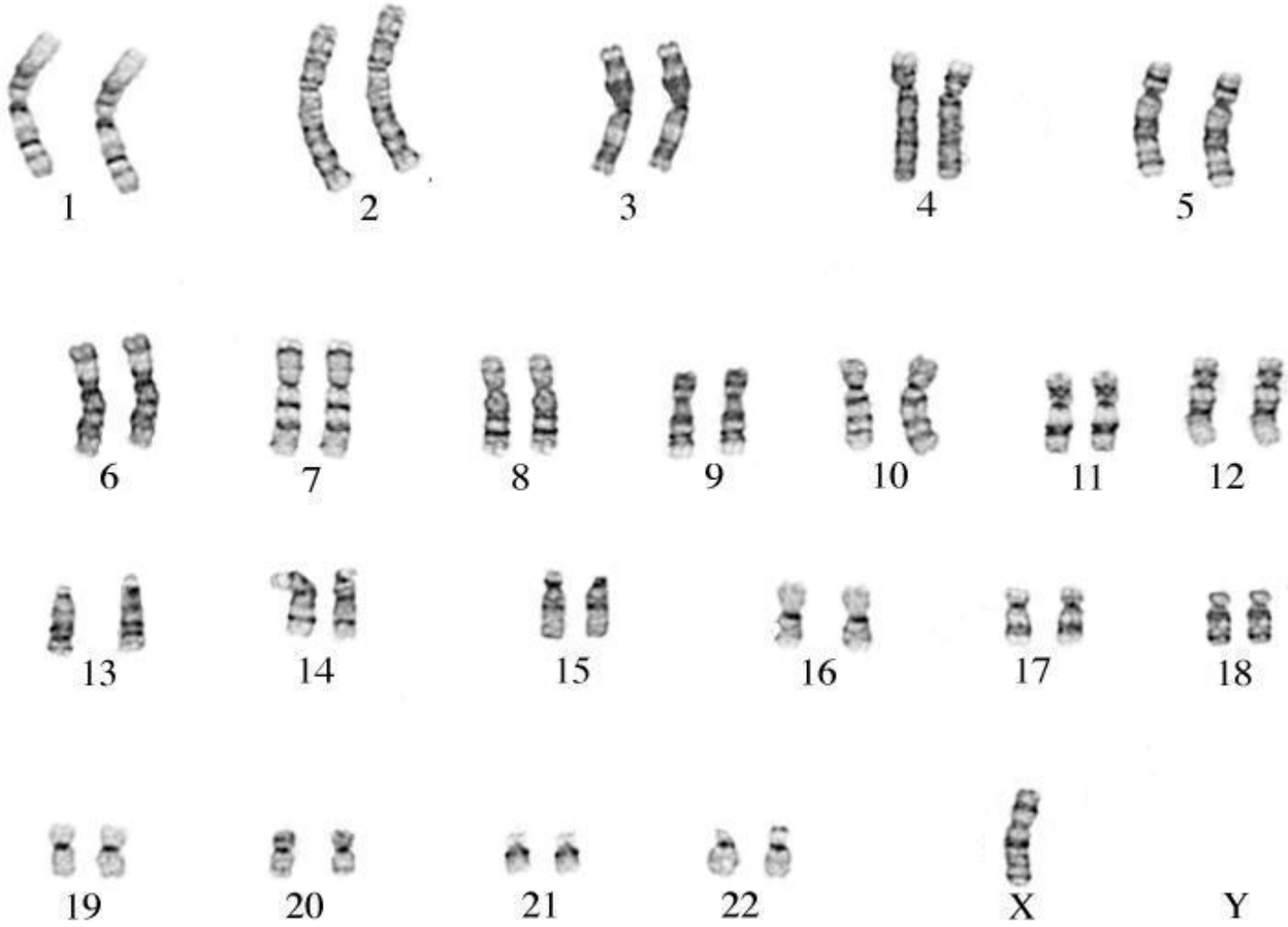
Answer Key for
Part II: Matching Chromosomes B



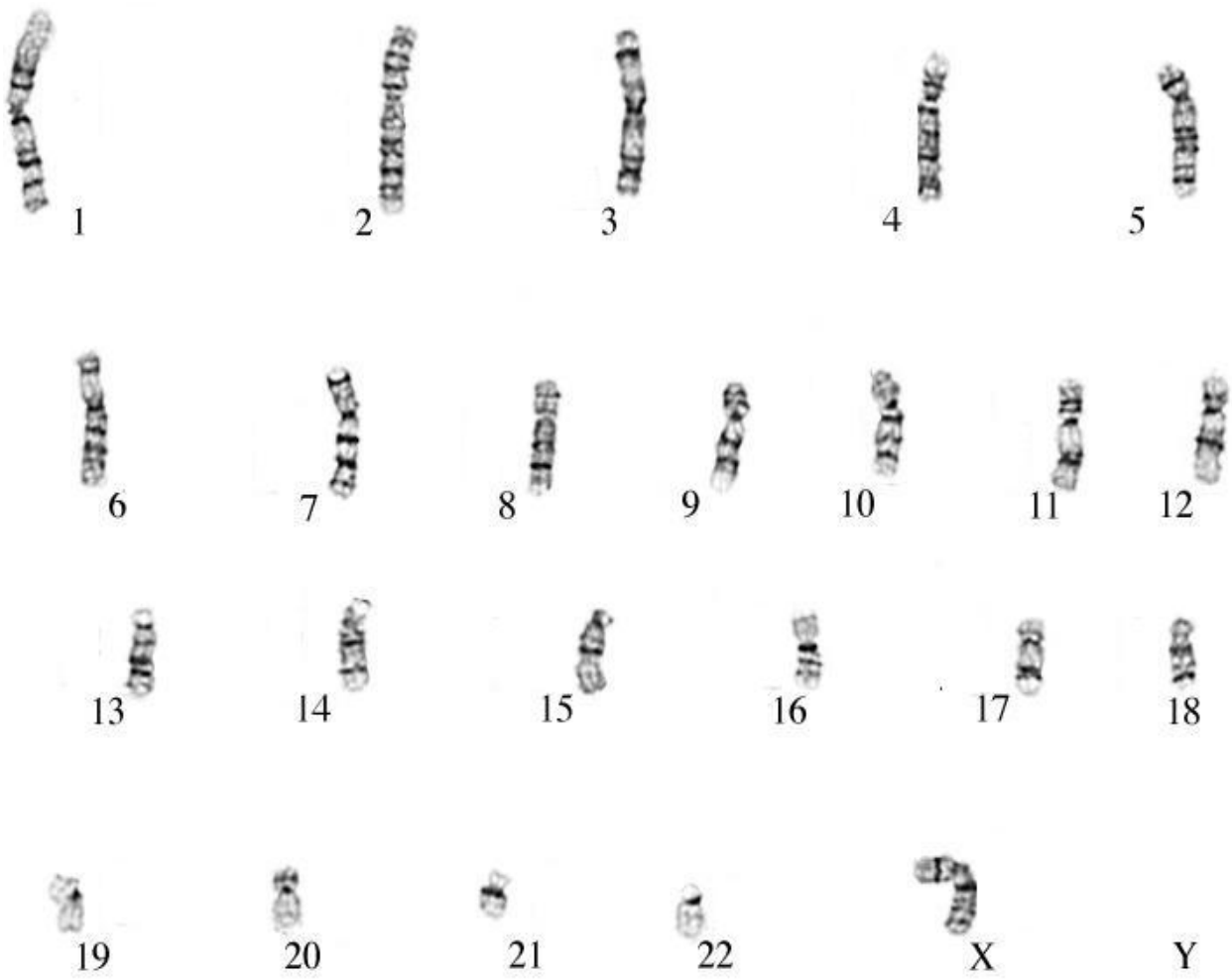
Part III: Other Aneuploid Syndromes A



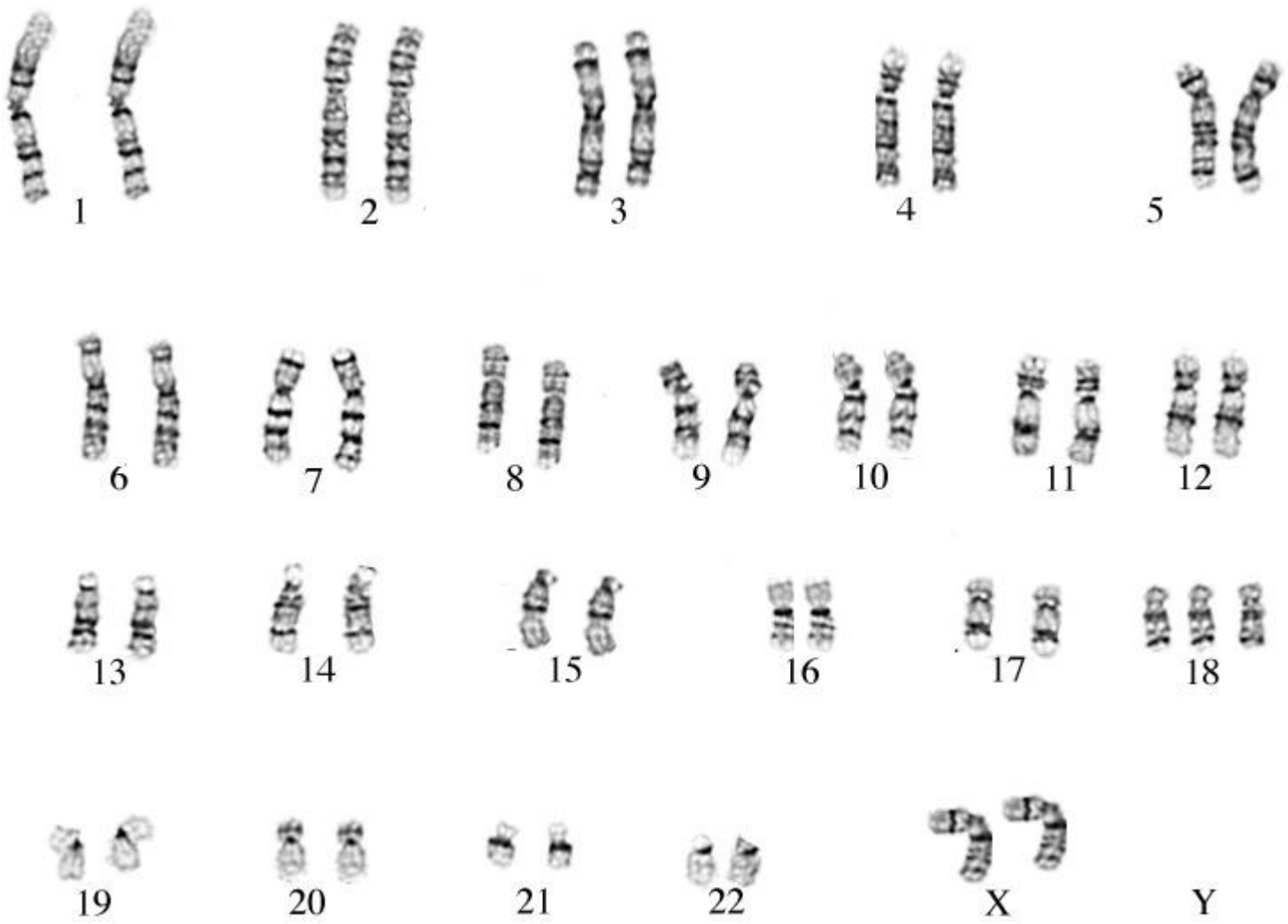
Answer key for
Part III: Other Aneuploid Syndromes A



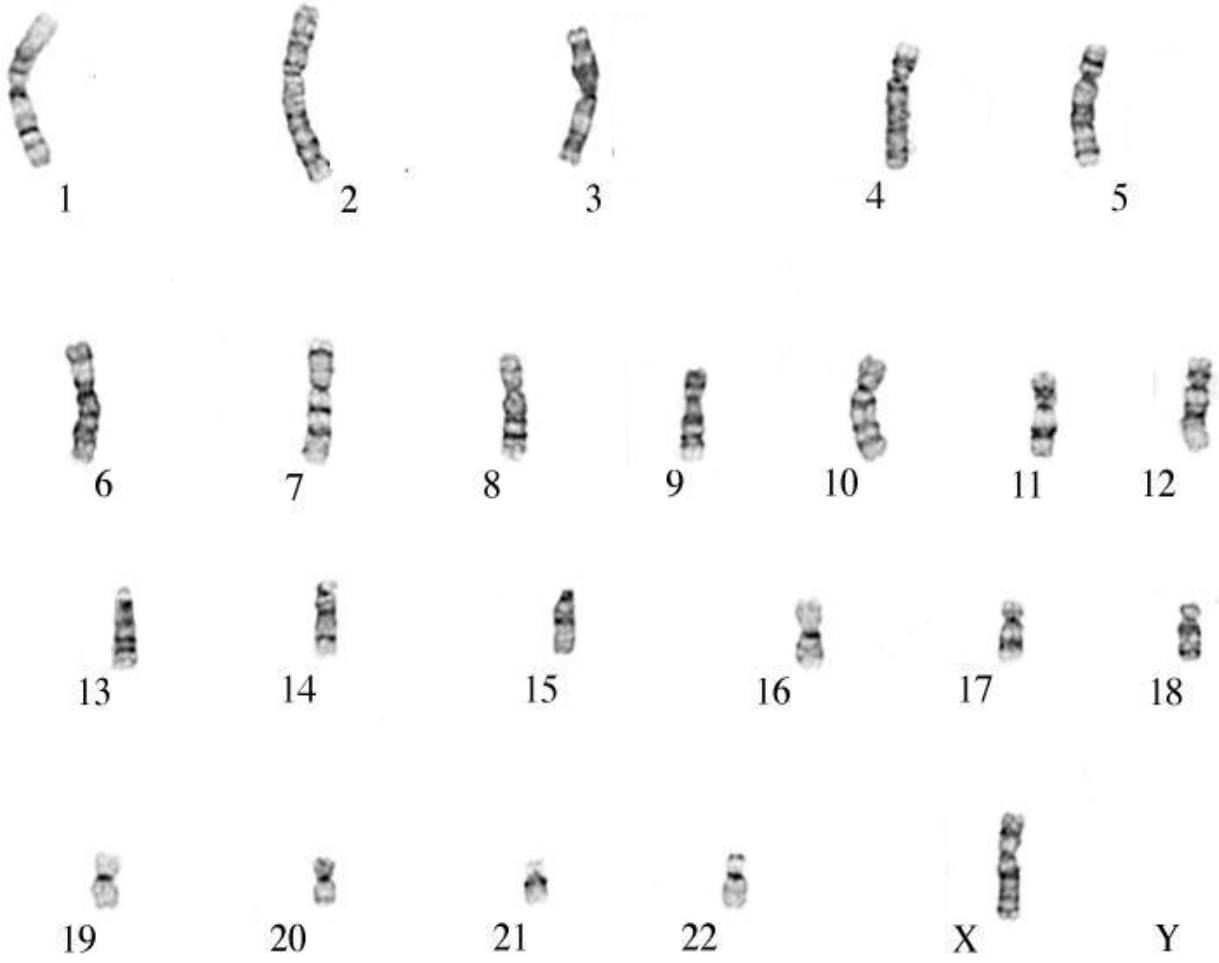
Part III: Other Aneuploid Syndromes B



Answer key for
Part III: Other Aneuploid Syndromes B



Part III: Other Aneuploid Syndromes C



Answer key for
Part III: Other Aneuploid Syndromes C