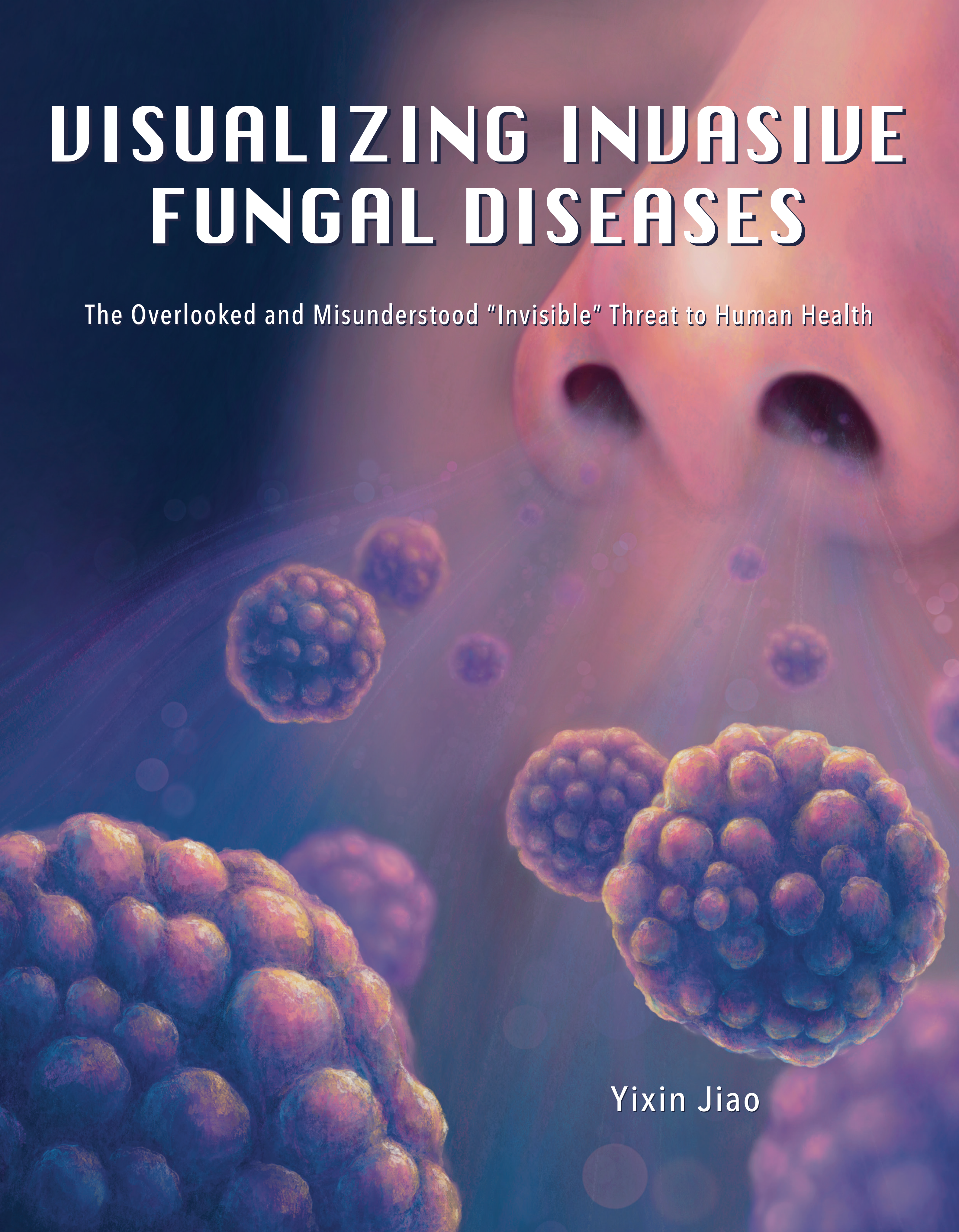
VISUALIZING INVASIVE FUNGAL DISEASES

The Overlooked and Misunderstood "Invisible" Threat to Human Health



Yixin Jiao

Hi, I'm Yixin Jiao

and I thrive in this happy place where art and science converge. Prior to my education in scientific illustration, I completed my Bachelor's degree in Biological Sciences at Rutgers University in New Jersey. While working as a teaching assistant there for a human anatomy lab course, I created a series of anatomical illustrations for the students as additional study aids. The positive response my illustrations received memorably flipped a switch in me that this was something I'd like to continue to do. They say ideas are only as good as our ability to communicate them– and I am thrilled to be part of a community of visual storytellers who work to transcend barriers in scientific communication to make science and medicine more accessible.

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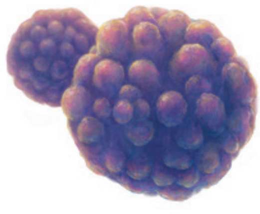

Visualizing Invasive Fungal Diseases

The Overlooked and Misunderstood “Invisible” Threat to Human Health

by

Yixin Jiao

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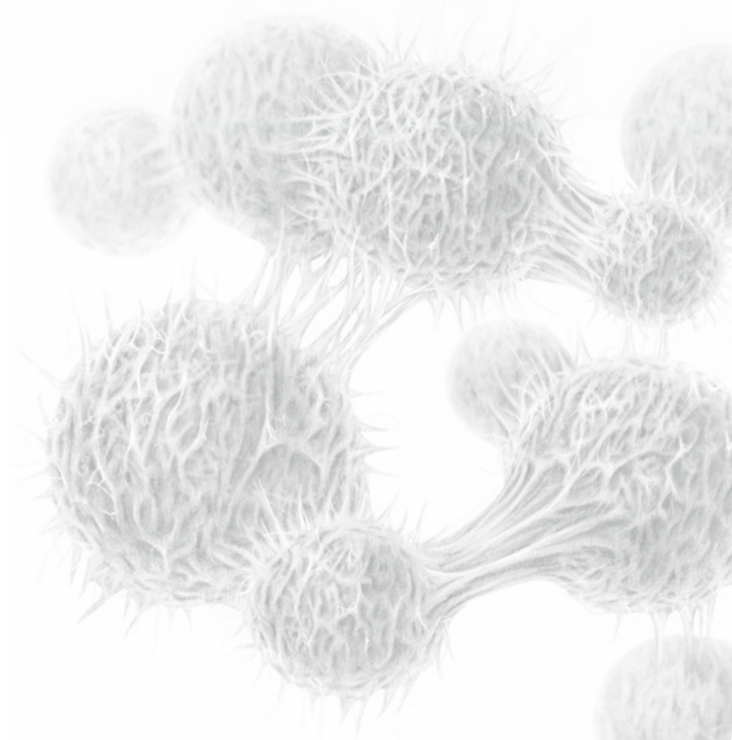


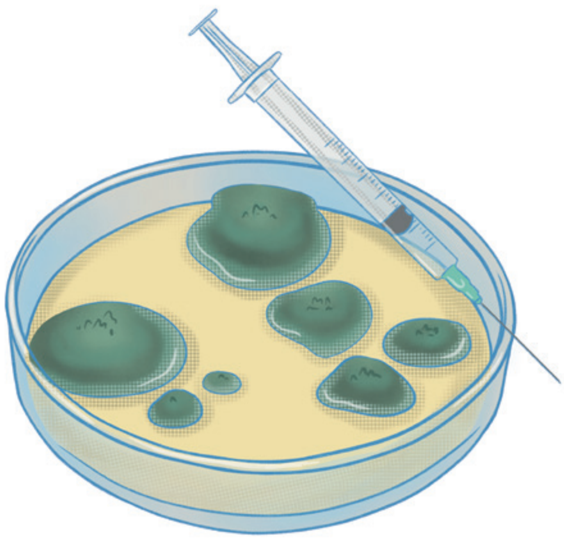


Fig. 1: Penicillium mold colonies grown on petri dish.

PREFACE

"The role of the infinitely small is infinitely large."

-Louis Pasteur

In more ways than you'd expect, humanity is deeply intertwined with fungi.

Ancient civilizations as early as 10,000 B.C. in Mesopotamia and Egypt harnessed yeasts and experimented with fermentation– creating breads, alcohols, and giving way to many foods and drinks we love today.

One of the most impactful fungal contributions to mankind is the use of *Penicillium* molds in the development of antibiotics in 1928 by Scottish physician and microbiologist Alexander Fleming *(Fig. 1)*. Penicillin, nicknamed the first wonder drug, is used to combat numerous bacterial infections and has since its conception, enabled control over many infectious diseases and thereupon saved countless lives. Subsequently, the technology used in the production of penicillin has been molded by the modern pharmaceutical industry, which continues to use fungi in drug development with various medical applications.

However, our relationship with fungi is a delicate balance– although fungi have proven to provide benefits to human life, there are certain outlying fungal species that do quite the opposite. Fungi have inflicted upon staple crops that humans depend on– the Great Potato Famine in Ireland during the 1840's is a notable example of the devastation fungi can cause. But even more frightening are those that directly cause human disease and death. Commonly known "problem" fungi are those that cause superficial fungal infections– those associated with undesirable conditions like athlete's foot, ringworm, and yeast infections. Yet the more destructive fungi, causing debilitating invasive infections, are far from the public eye in comparison.

The COVID-19 pandemic has made us more alert and wary of the infinitely small and unseen threats in the world. Still, the dangers of fungal pathogens are continued to be overlooked and misunderstood.

Furthermore, this delicate balance between humanity and fungi has been significantly disrupted in recent years (shifting the status quo towards the fungi's side). The COVID-19 pandemic has increased the population of individuals at risk for severe fungal infections (Shishido et al., 2022). Several strains of fungi have also recently developed resistance to antifungal drugs, causing further complications in treating the infected as previous medications become obsolete. Additionally, the rise in global temperatures over the years has also impacted the spread of fungal diseases (Casadevall et al., 2019). Areas where fungi could not easily thrive in the past, have unfortunately seen an increase in infections as climate change has given way for fungi to populate new uncharted territories.

I'd like to contribute to the hefty responsibility of scientific communicators in addressing these invasive fungal diseases with the visualization of the effects pathogenic fungi have on the human body. Through scientific illustration, I set out to educate those in the public sphere to garner more attention and resources towards harnessing these fungal threats in the future.

INTRODUCTION

Invasive Fungal Diseases?

Globally, infectious diseases are of great concern to human health, with bacterial and viral infections causing or contributing to millions of deaths every year. However, an additional cause of infectious disease has been on the rise– fungi. To many, poisonous mushrooms are what comes to mind in conversations about dangerous or harmful fungi, yet the most threatening and critical fungi are "invisible", in that they are microscopic molds and yeasts that are also exceedingly neglected.

Invasive fungal diseases (IFDs) are caused by opportunistic fungal pathogens, meaning these fungi primarily are not pathogenic and many are commonly found in the environment, as well as on and within the human body. Only when contracted by the critically ill or by patients with weakened immune systems do these fungi pose a serious threat. For example, *Aspergillus fumigatus* is a fungus found throughout soil, plant matter, and dust, and most people inhale *Aspergillus* spores on a daily basis without developing an infection; however, in immunocompromised patients, *Aspergillus* can cause severe pulmonary infections and disease that can be lethal.

Additionally, IFDs are an increasing public health threat as there is also a rapid evolution of antifungal resistance, as medications become less or ineffective in treating fungal infections, coupled with limited access to proper diagnosis and treatment.

Although cause for concern, not enough resources are directed towards research and public awareness on these fungal infections, resulting in a lack of data on the burden of these infections worldwide (WHO, 2022). In October 2022, the World Health Organization published the first-ever list of priority fungal pathogens (FPPL) that pose the greatest threat to public health. The list ranks the top 19 most prevalent fungal pathogens into three categories: critical, high, and medium priority *(Fig. 2 and Fig. 3)*. Through this report, the WHO aims to bring these opportunistic fungi into the spotlight with the goal of strengthening the global response to this growing public health threat. The WHO also proposes new approaches for healthcare professionals, policy makers, and other stakeholders revolving around building up fungal disease surveillance, bolstering investments in research and technologies, and improving interventions for prevention and disease control.

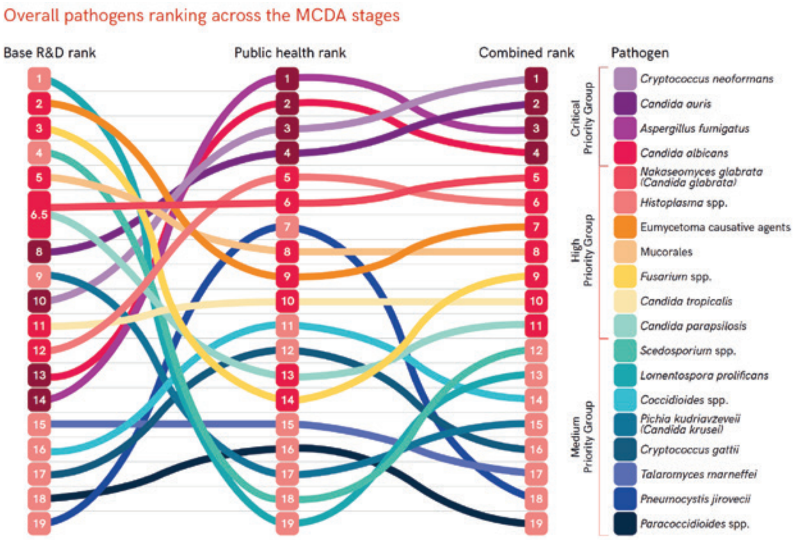
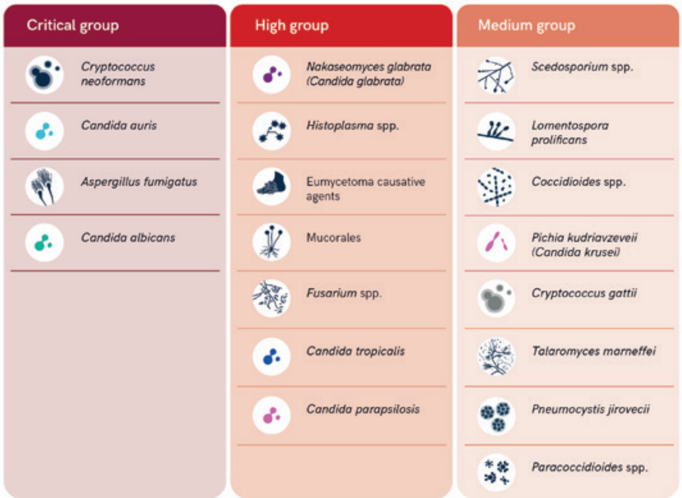


Fig. 2: WHO graph breaking down factors that determine pathogen ranking.
Source: WHO FPPL.



Critical group	High group	Medium group
Cryptococcus neoformans	Nakaseomyces glabrata (Candida glabrata)	Scedosporium spp.
Candida auris	Histoplasma spp.	Lomentospora prolificans
Aspergillus fumigatus	Eumycetoma causative agents	Coccidioides spp.
Candida albicans	Mucorales	Pichia kudriavzeveii (Candida krusei)
	Fusarium spp.	Cryptococcus gattii
	Candida tropicalis	Talaromyces marneffei
	Candida parapsilosis	Pneumocystis jirovecii
		Paracoccidioides spp.

Fig. 3: Table summarizing the WHO fungal priority pathogens list. Source: WHO FPPL.

About the Project

In the timely fashion of this newly released WHO report, I have been working with guidance from my external advisor, Dr. Dimitrios P. Kontoyiannis of The University of Texas MD Anderson Cancer Center in Houston, Texas, to highlight the contents of the WHO FPPL document and to distill this vital information to patients and to the general public.

Dr. Kontoyiannis is the Chair in Clinical Care and the Deputy Head in the Division of Internal Medicine. He is considered a world-wide leading expert in mycology, and is the recipient of many national and international awards for his research in medical and translational mycology. Dr. Kontoyiannis studies antifungal pharmacology, host defenses against fungi, and fungal pathogenesis through the development of model organisms best suitable for studying medically important opportunistic mycoses, such as fruit flies and zebrafish. His research group is credited for contributions to the advancement of novel diagnostics in fungal treatment and diagnosis detection of antifungal resistance, which has been a current rising public health concern.

With the WHO FPPL document on hand and Dr. Kontoyiannis' support, I worked my way through understanding these fungal threats and what they do to the human body– to ultimately create a series of educational scientific illustrations in the form of infographics for four fungal groups from the fungal pathogen priority list: *Cryptococcus*, *Candida*, *Aspergillus*, and *Mucorales*. From the WHO report's ranking, *Cryptococcus*, *Candida*, *Aspergillus* were ranked the top three most critical pathogens respectively, and *Mucorales* was ranked as a high priority pathogen. The illustrations aim to serve as vehicles of education, with a focus on communicating the risk factors and clinical manifestations of each fungus to patients, laymen, and healthcare professionals seeking an overview on these underrepresented pathogens.

A challenge in tackling this subject for visualization is navigating and condensing complex medical information released from scientific researchers (the WHO) into a form that is digestible and clear for general consumption, while retaining enough information for understanding the significance of fungal pathogens. The objective is for my illustrations to successfully meet this challenge and adequately serve as a tool to help bring this pressing current event in the scientific community to a larger audience. The journey through the creation of these illustrations from conception to completion, and all the artistic experimentations, decisions, and problem-solving in between have been documented in this thesis.

I. THE FUNGI

GETTING UP CLOSE AND PERSONAL WITH THE "INVISIBLE"

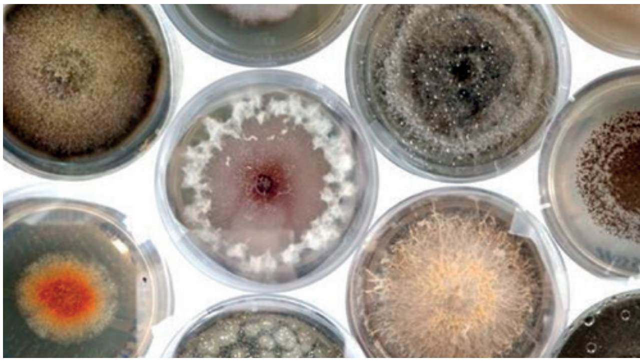
What are Fungi?

Fungi are a group of eukaryotic organisms that range from microorganisms including single-cellular yeasts and multicellular molds to complex macroscopic structures like mushrooms. A frequent misconception is that fungi are members of the plant kingdom, but they are actually within a separate kingdom of their own, apart from both plants and animals. Unlike plants which have cell walls composed of cellulose, fungi have chitinous cell walls which successfully prevents dehydration while providing structural strength. They also lack chloroplasts and are heterotrophic, similar to animals, meaning fungi absorb nutrients and energy from other sources, such as plants or animals, instead of synthesizing them. Fungi are also characterized by their ability to reproduce by both sexual and asexual means, with some reproducing through spore dispersal and others multiplying through fragmentation or budding.

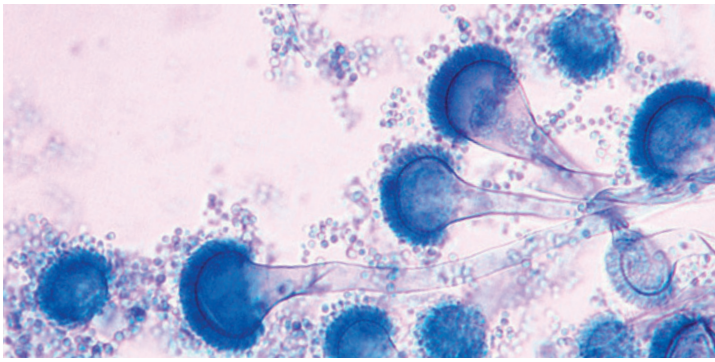
The four pathogenic fungi of interest are all microorganisms; *Cryptococcus* and *Candida* are both single-cellular yeasts, and *Aspergillus* and *Mucorales* are multicellular molds. These organisms are not visible with the naked eye on a cellular level, but can be observed as fungal colonies without magnification.

During the research phase of this project, I became fascinated by the morphology of these microscopic fungi, which range from simple spherical pill-like forms to those with complex flower-like structures. Seeing these images gave me a better understanding of the organisms behind the infectious diseases and it "put a face to the name", so to speak.

Amanita muscaria mushroom spotted while hiking at the Nationaal Park De Maasduinen in the Netherlands.



A collection of petri dishes containing various fungal cultures. Source: Rowena Hill, Queen Mary University of London.



Aspergillus fugimatus viewed under light microscopy. Source: LIFE Worldwide.

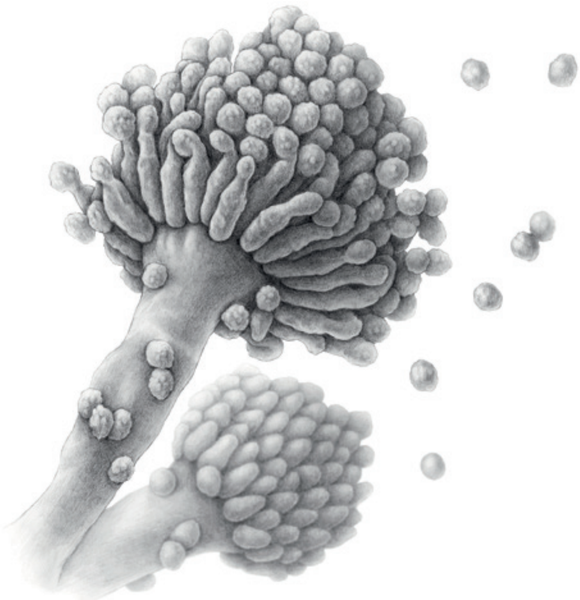


Fig. 4: Graphite rendering of *Aspergillus fumigatus.*

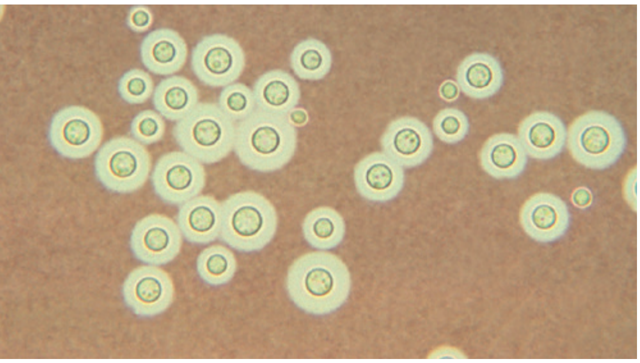


Fig. 5: Photomicrograph of *Cryptococcus neoformans* prepared with India ink staining. Source: Leanor Haley, CDC.

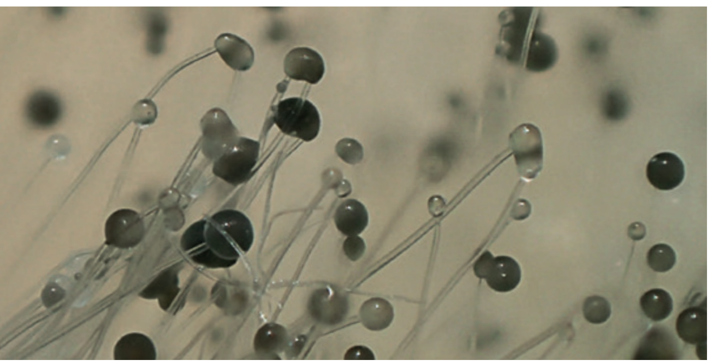


Fig. 6: Photograph of "pin-molds" of the Order *Mucorales.* Source: Robert Siegel, Stanford University.

Although the main focus of the infographics are the diseases resulting from these fungi, the storytelling is incomplete without providing information on the source of the infections, the fungi themselves. Patients and laymen would appreciate being able to visualize these fungi, instead of having a theoretical idea of the "invisible" threats behind these illnesses.

For this reason, my goal was to visualize these microorganisms up close and in detail. Scanning electron microscopes (SEMs) allow for high resolution observation of the surface structures of specimens with magnification up to 500,000 times. Thus the SEM images of these fungi were ideal references for the illustrations I had in mind.

To fully capture the details of these fungi, I chose to illustrate them using graphite in order to fully render the range of values and textures present in the magnified images. This technique also allows sharp precise lines to be made, which was ideal for representing the details of the fungi.

The first fungus I took on illustrating was *Aspergillus fumigatus (Fig. 4)*, because I found the morphology of this organism the most interesting out of the four. *A. fumigatus* is a mold with long

Fig. 7: Graphite rendering of *Cryptococcus neoformans.*

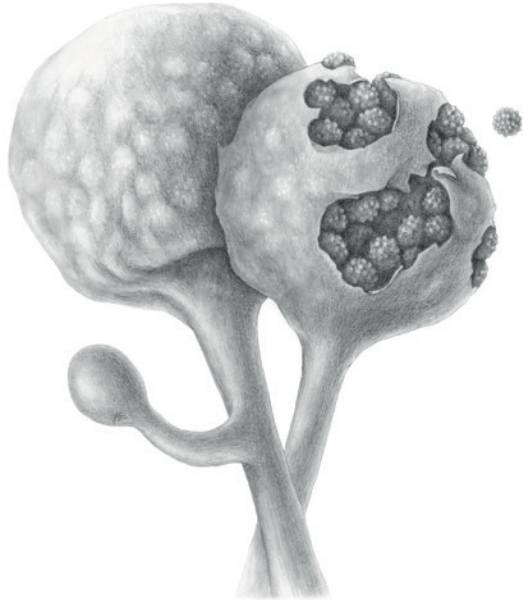


Fig. 8: Graphite rendering of a *Mucorales* species.

filamentous branches (hyphae) that form stalk-like projections called conidiophores. At the distal end of each conidiophore are phialides in which the conidia (spores) are formed, extending outward in long chains.

Cryptococcus neoformans was up next and the morphology of this fungus was a bit more difficult to capture using graphite *(Fig. 7)*, as it is an encapsulated yeast. Under lower magnifications, *C. neoformans* appear as smooth round cells *(Fig. 5)*, but the SEM images reveal that the capsule surrounding the cell is composed of polysaccharide chains that create a spiky appearance. With the addition of some highlights added with Adobe Photoshop, the spherical nature of the yeast and the irregular projections of the capsule were successfully rendered.

Mucorales is an order of fungi, commonly coined "pin molds" due to the pin-like shape of the spherical sporangia at the end of their long filamentous hyphae stalks *(Fig. 6)*. The sporangia are sacs where the sporangiospores (spores) form and mature. The walls of the sporangia disintegrate when the spores are mature and are ready to be released. For the *Mucorales* illustration

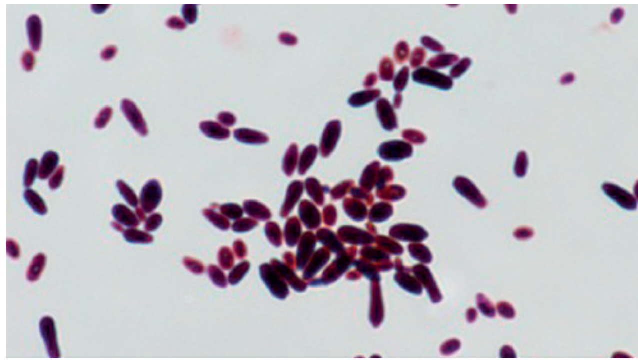


Fig. 9: Colony of *Candida auris* viewed under the light microscope. Source: MICROCOSM.

(Fig. 8), I wanted to depict one intact sporangium and a ruptured one revealing the mature spores which are contained inside.

Illustrating *Candida auris* was the most straightforward of the four fungi, the cells of this yeast are round or ovoid *(Fig. 9)*. To make the drawing more compelling, I also wanted to show some of the cells in the process of budding. Drawing *Candida (Fig. 10)* was a good practice in the fundamentals of illustrating light and form, as I took care to observe where the highlights, midtones, core shadows, and reflected light would appear for each of the round yeast cells.

Fig. 10: Graphite rendering of *Candida auris.*

Fig. 11: Colorized illustration of *Cryptococcus neoformans.*

Colorizing the Fungi:

I then chose to colorize the graphite illustrations derived from the greyscale SEM photographs to create a more visually pleasing image with the layouts of the final infographics already in mind. Graphite combined with digital colorization, produces a product that retains the feel and texture of traditional illustrations, but also serves as a quick way to add color on top of a greyscale registration of the subject, making this my technique of choice for these fungi illustrations.

Microscopically, these fungal cells are mostly transparent with only slight coloration. Only when viewed as a colony does the collective have a discernible color, yet even then the color of the colonies is influenced by various factors. The artistic decision was made to use the commonly observed color of the fungal colonies when colorizing the fungi themselves: *Cryptococcus* is yellow *(Fig. 11)*, *Mucorales* is often dark in color *(Fig. 12)*, *Candida* is pink *(Fig. 13)*, and *Aspergillus* is blue-green. Although not entirely true to reality, the colony color is the most representative and can help bridge the relation between how these fungi are perceived microscopically and macroscopically.

Following experimentation with color values, the choice to apply color modestly was made, which also reflects the somehow "colorless" transparent reality of these fungal cells. To create a more attractive product, the use of a purple reflection light, especially visible in the *Aspergillus* fungus illustration *(Fig. 14)*, was used to give more dimension to the image. The use of this purple reflection light also pushes the idea of transparency as this light also appears to shine through the fungus.

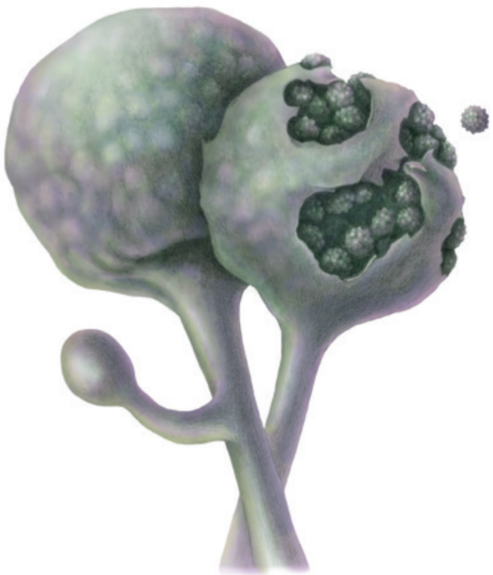


Fig. 12: Colorized illustration of *Mucorales.*

Fig. 13: Colorized illustration of *Candida auris.*

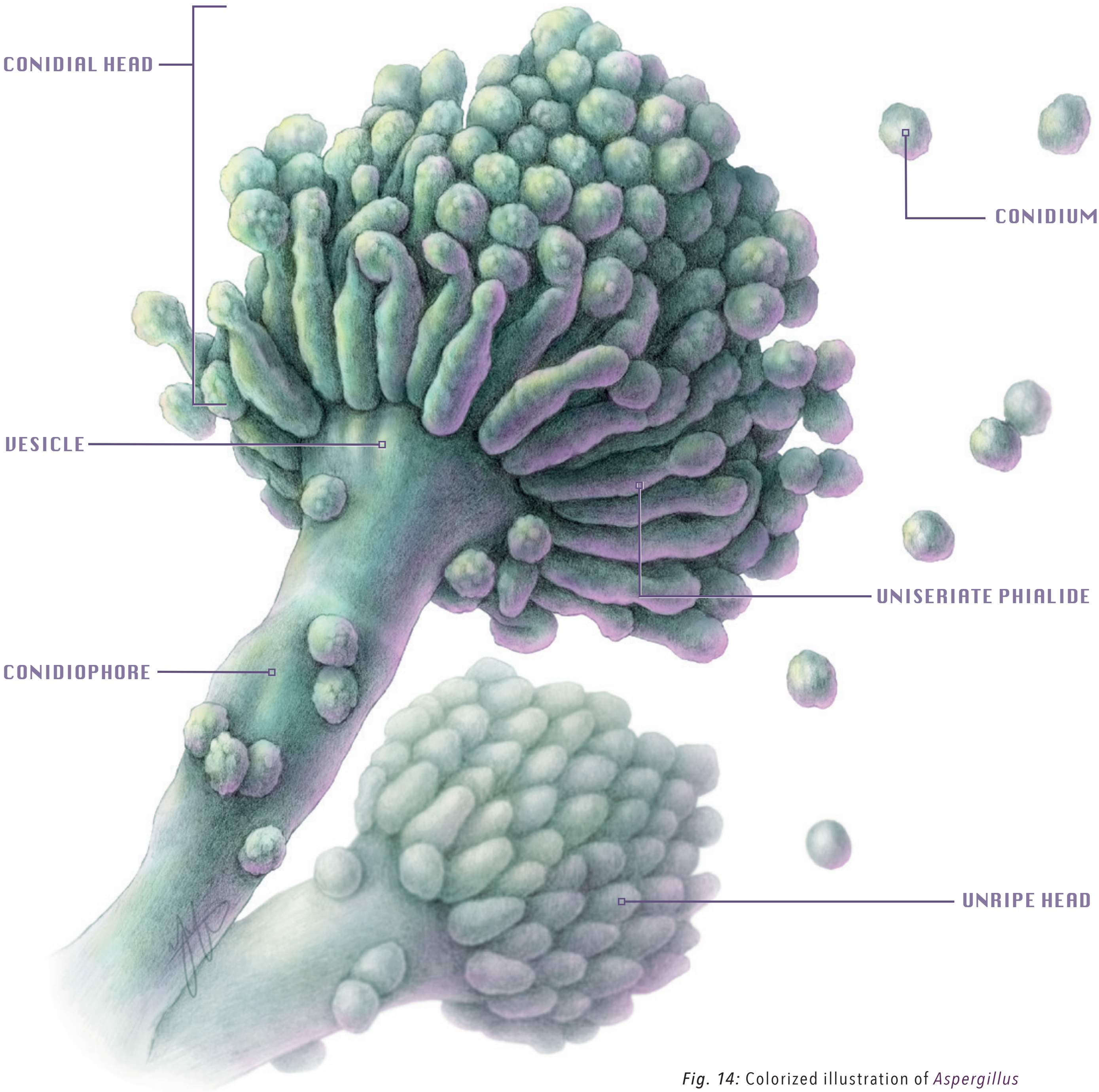


Fig. 14: Colorized illustration of *Aspergillus fumigatus* with labeled structures.

II. THE PATIENTS

PATIENT DIVERSITY

Progressive ideals of inclusivity have become a hot topic in the world of scientific illustration in the past few years, breaking through a past of illustrations predominantly depicting white males. The use of diversity in scientific illustration serves more of a purpose than simply representing minority groups, but has scientific significance. This can be seen when visualizing certain medical conditions that present themselves differently in patients of different ethnicities, or when certain surgical procedures are modified to better meet the anatomical differences and needs when operating on a specific demographic of patients. The example that comes to mind of the implications of creating inclusive material in the medical sphere is how patients with dark complexions experience misdiagnosis for Lyme disease due to the lack of awareness that the telltale rash signifying the disease manifests differently in black patients (Palmieri, 2019). The consequence of these delayed diagnoses includes neurological complications often with long-lasting and severe symptoms.

For these four patient oriented infographics, I was given free reign on how to depict the model patients shown on each spread. It was important to me to make the conscious and deliberate choice to show the patient as the centerpiece of each infographic. After several concept sketches *(Fig. 15)*, a diverse group of patients was illustrated, covering different ethnicities and genders, to reflect the indiscriminate nature of these invasive fungal diseases *(Fig. 16-19)*.

Some additional considerations were made in the decision of how to depict a more "representative" and inclusive patient specifically for the *Cryptococcus* and *Candida* posters.

Due to the heavy burden that cryptococcal infections disproportionately place upon HIV/AIDS patients (WHO, 2022), an emphasis on representing this group of patients was at the forefront while creating the *Cryptococcus* infographic. The decision was ultimately made to depict a black man as the model patient for this spread *(Fig. 16)*.

Fig. 15: Early concept sketches for the *Aspergillus* infographic.

Fig. 16: Illustration of the *Cryptococcus* patient.

Black individuals account for a greater percentage of new HIV diagnoses in comparison to other ethnicities, as well as make up a large proportion of total HIV/AIDS infections (Laurencin et al., 2018). What makes matters more difficult for black HIV patients is the stigma against HIV and homosexuality within the black community. The idea to make a black man the face of this poster also intends to push against this negative discrimination individuals in this group may experience. Providing representation of black HIV patients can possibly also aid in sparking conversations about the secondary risks of HIV/AIDS infection within this community to raise prevention, awareness, and support.

Through a more artistic lens, the decision to represent a person with a darker complexion benefits the illustration– with the rich brown skin tone complimenting the warmth of the yellow used throughout the page. Alternatively, the portrayal of a patient of lighter complexion may appear washed out against the soft yellow background and give an undesired pale or sickly look for the illustrated patient.

Although illustrations of commonly-seen attractive, youthful people are visually more appealing and arguably eye-catching, an elderly woman was chosen to be depicted as the patient for Candidiasis *(Fig. 17)*. As these fungi primarily infect immunocompromised patients, it makes sense to illustrate one of the most immunocompromised groups– the elderly.

This decision was further supported by the sighting of several news articles while writing this thesis, one from the National Public Radio reads, "The potentially deadly *Candida auris* fungus is spreading quickly in the U.S.".

It was a surprise to see the subject of my thesis in the news and it was more of a surprise to learn that the fungus has been spreading rapidly through

Fig. 17: (Right) Illustration of the *Candida* patient.

Fig. 18: Illustration of the *Aspergillus* patient.

nursing homes and long-term healthcare facilities across the nation, and causing infections primarily in the elderly population.

This sudden wave of media attention for these *Candida* infections has been beneficial in spreading word about the severity of fungal infections, but social media such as Tiktok has also contributed to the spread of misinformation on this fungus. The popular show *The Last of Us*, about a fungus that causes people to turn into zombies, was released at the same time as news of the spread of the deadly fungus *Candida* reached the general public. People on social media voiced their concerns that like in the show, *Candida* will rampantly spread throughout the population and cause death.

Occurrences like these are prime examples of the importance of accurate scientific communication, since according to the WHO report, *C. auris* is unlikely to become a problem for healthy people who do not have catheters or other medical lines entering their bodies (and furthermore, infections from this yeast thankfully do not turn people into zombies).

It is also of note to mention that all four of the patients have been intentionally illustrated as visually healthy, generally attractive, with a neutral expression on their faces. This was done with the audience of these infographics in mind: patients, who perhaps have already undergone prior hospitalizations for conditions that put them at risk for fungal infections, are likely riddled with anxiety. Seeing images of other sick individuals and wondering "Is this going to be me?" can cause additional mental distress to already shaken people. The illustration of calm model patients serves the purpose of evoking a sense of ease in audiences that could be potential patients of these fungal infections.

Fig. 19: (Left) Illustration of the *Mucorales* patient.

SPORE/FUNGAL INHALATION AND THE PULMONARY SYSTEM

In order for a fungus to cause infection, it must first enter the human body. For many fungi that reproduce through the dispersal of spores, the common mode of entry into the body is through inhalation. As the spores travel through the air, they can be breathed in by an unsuspecting human host. Of the target fungal groups for this project, *Cryptococcus*, *Aspergillus*, and *Mucorales* invade the body through initial fungal inhalation. To include visual information of this shared mode of entry, illustrating the lungs *(Fig. 20)* was a necessary component in telling the story of fungal pathology in patients infected with *Cryptococcus*, *Aspergillus*, and *Mucorales*.

An obstacle when illustrating the lungs was the fact that I had illustrated the patients first, and now was faced with fitting lungs for each patient in the correct orientation and perspective. Given that the patients were illustrated in positions that deviated from the standard frontal and lateral views, it was a challenge in itself to find adequate anatomical references of the lungs in the orientations needed. In the scope of this project, the patients were already fully illustrated at this stage and the decision to work with the fixed positions determined by these illustrations was made. As the anatomical atlases available to me did not show the lungs in the positions needed, I turned to 3D models of the lungs available on Sketchfab as suitable references. 3D models are effective tools for this purpose, as the models can be turned and viewed from all angles. However, there are limitations to using 3D models as references, as 3D models themselves are also interpretations– with many missing realistic textures and possibly depicting erroneous anatomy.

The learning point here for future applications is to illustrate the patient and organs simultaneously and to reconstruct the skeletal features of the figure as a guide in placing the organs. In this case, marking the locations of the clavicles, sternum, and ribcage is useful in determining the correct perspective and placement of the lungs. By initially utilizing this method, problems with organ placement could have been reduced or eliminated, thus resulting in less revisions required during the illustrating process. Another solution is to find reliable references of the anatomy in the desired position before elaborating to ensure that there are enough supporting resources to avoid mistakes and incorrect anatomy. The value of using anatomical specimens as references was made explicit to me throughout this thesis, as having access to these specimens would allow for observation of the forms from all angles and provide reference for the look-and-feel of the organs.

The lungs were illustrated digitally on Adobe Photoshop in a semi-elaborated style to be able to accurately capture the anatomy, but with a technique that allows easier application of changes and feedback in comparison to illustrating by traditional means. Through several rounds of feedback from my mentors, the illustrations of the lungs with correct form for three different positions was achieved: mostly frontal viewed from the left for *Aspergillus (Fig. 20.1)*, a more lateral angle viewed from the right for *Cryptococcus (Fig. 20.2)*, and a mostly left lateral view of the lungs for *Mucorales (Fig. 20.3)*. Further adjustments of the form of the lungs were made while investigating the placement within each patient, for example, revising the shape of the apex of the superior lobe of the right lung to better fit relative to where the clavicles of the patient would be for the *Cryptococcus* infographic.

Partially changing the opacity of the lungs with masks in Adobe Illustrator, helped to create depth and to implement the structure within the body. In scientific illustration, objects of greatest contrast are seen as coming out towards the viewer and objects with less contrast are pushed backwards. This method allowed the lungs to be placed within the thoracic cavity of the patients instead of appearing to be pasted on top of the patients' chests *(Fig. 21)*.

For each of these illustrations, I also chose to show the spores entering and building up in the alveolar spaces of the lungs. A cross-section of an alveoli showing spores inside was illustrated in Adobe Photoshop *(Fig. 20.4)*, also with some simple elaboration similar to how the lungs were visualized to maintain consistency and additionally to depict the anatomy in a clear and easily understandable way.

Fig. 20.1

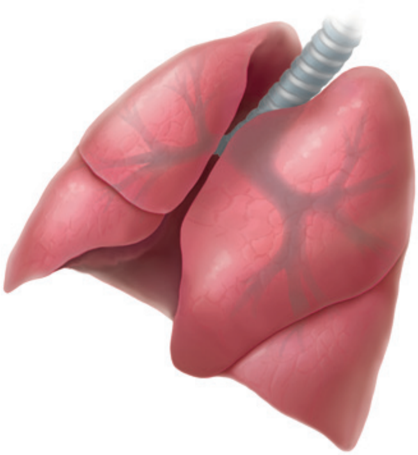


Fig. 20.2

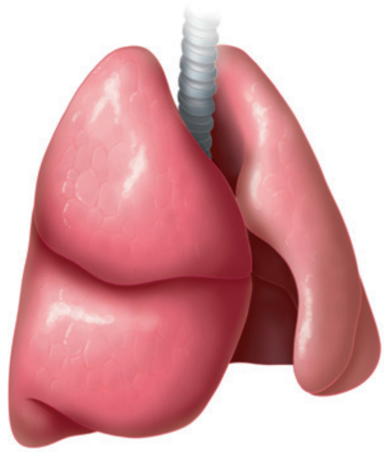


Fig. 20.3

Fig. 20.4

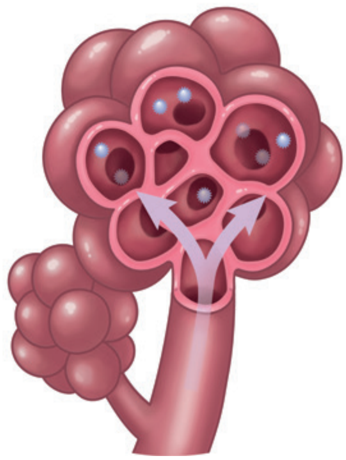
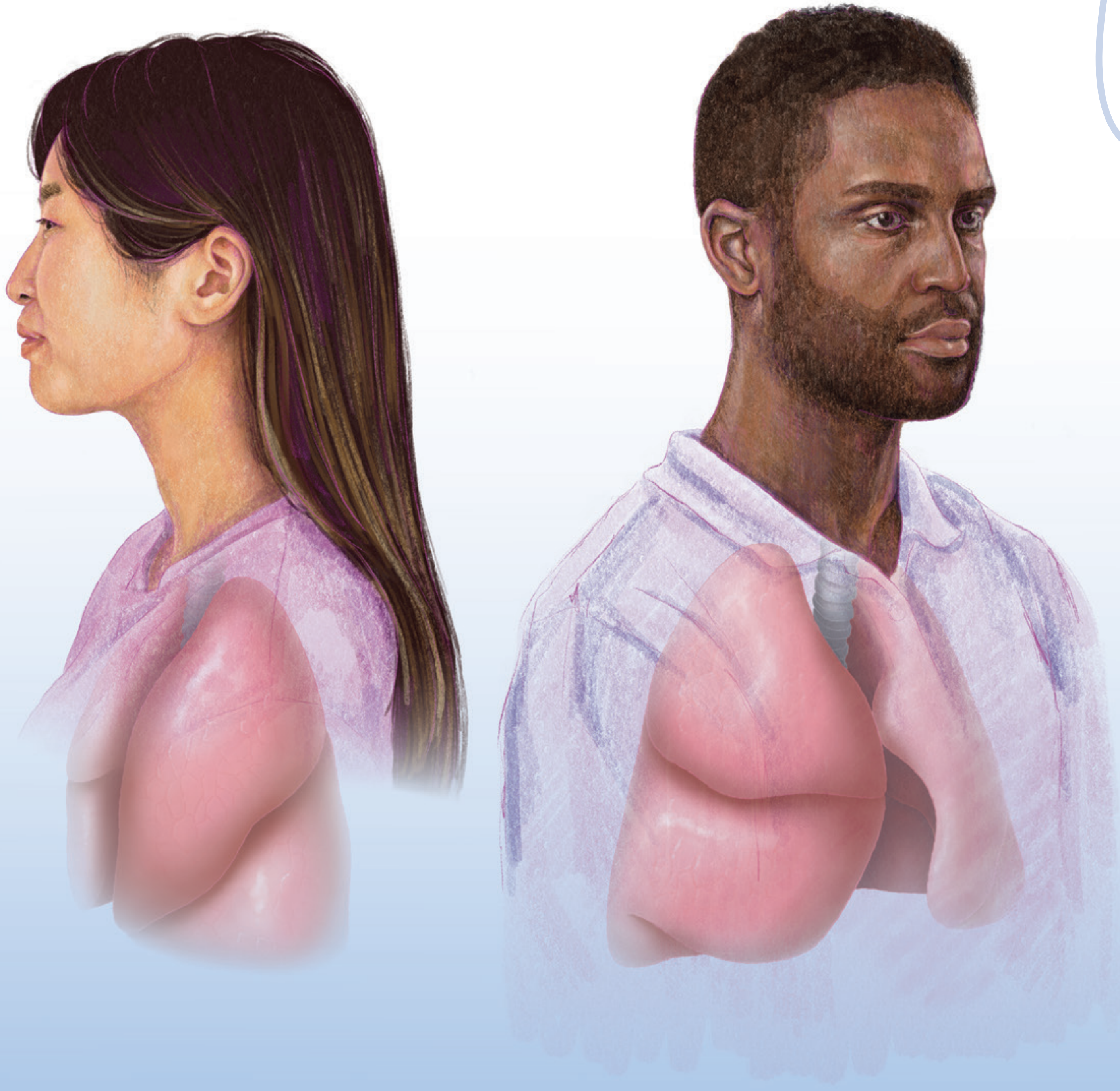


Fig. 20: Lung illustrations in various orientations to fit the patients (***20.1:*** *Aspergillus* infographic, ***20.2:*** *Cryptococcus* infographic, ***20.3:*** *Mucorales* infographic, ***20.4:*** Illustration of alveoli cross-section showing spore entry).

Fig. 21: Series of patient illustrations depicting the inlaid lung anatomy. (From left to right: *Aspergillus* patient, *Mucorales* patient, *Cryptococcus* patient.)



MANIFESTATION OF INVASIVE FUNGAL DISEASES

Cryptococcus

The main associated danger of cryptococcal infection is that in severe cases it can disseminate from the pulmonary system and travel to the central nervous system *(Fig. 24.2)* where it can cause cryptococcal meningitis and cause fungal growths within the brain parenchyma known as cryptococcoma (WHO, 2022).

To visualize this pathology, first the brain needs to be illustrated *(Fig. 23)* and placed within the patient. An insert showing the anatomy involved in cryptococcal meningitis such as the cerebral cortex and the various meningeal layers is also an important addition. The first concept for this insert showed an exterior view of the brain, but it was difficult to effectively depict the meningeal layers in this way of visualization. The solution was to create a cross-section of the brain along with the meningeal layers and spaces to effectively show the layers in context to each other and to also show exactly where the fungus can be detected.

The first cross-section created *(Fig. 22)* was a very graphical representation and depicted the layers as solid bands with bright highlights. This created the illusion that the layers were bulging out instead of a clean cross-section. In revisions, instead of bands with hard highlights and drop shadows between each layer, smaller highlights were created only on the edges of each layer to emphasize the way light catches only those areas of the cross-section cut. The web-like nature of the arachnoid mater was also illustrated to also better visualize the subarachnoid space beneath. The color of the dura mater was changed from red to purple to deter confusion of the sheath layer for a layer of muscle which is conventionally depicted as red in scientific illustration. Inflammation is still shown but with more subtlety to not take away from the anatomical information being presented.

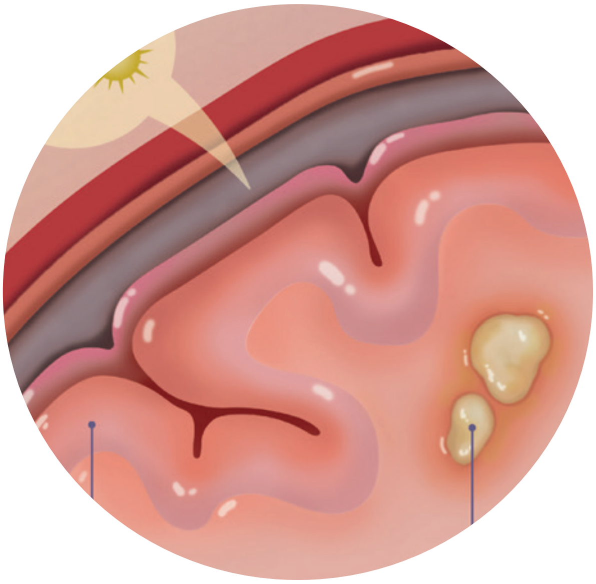


Fig. 22: (Above) Early illustration of the brain and meningeal layers with cryptococcal meningitis.

The final version *(Fig. 24.1)* of the cross-section provides an educational view on the meningeal layers affected in cryptococcal meningitis with a modest view of the pathology to shy away from disturbing patients.

Fig. 23: (Above) Illustration of the brain, in an orientation that fits the *Cryptococcus* patient illustration.

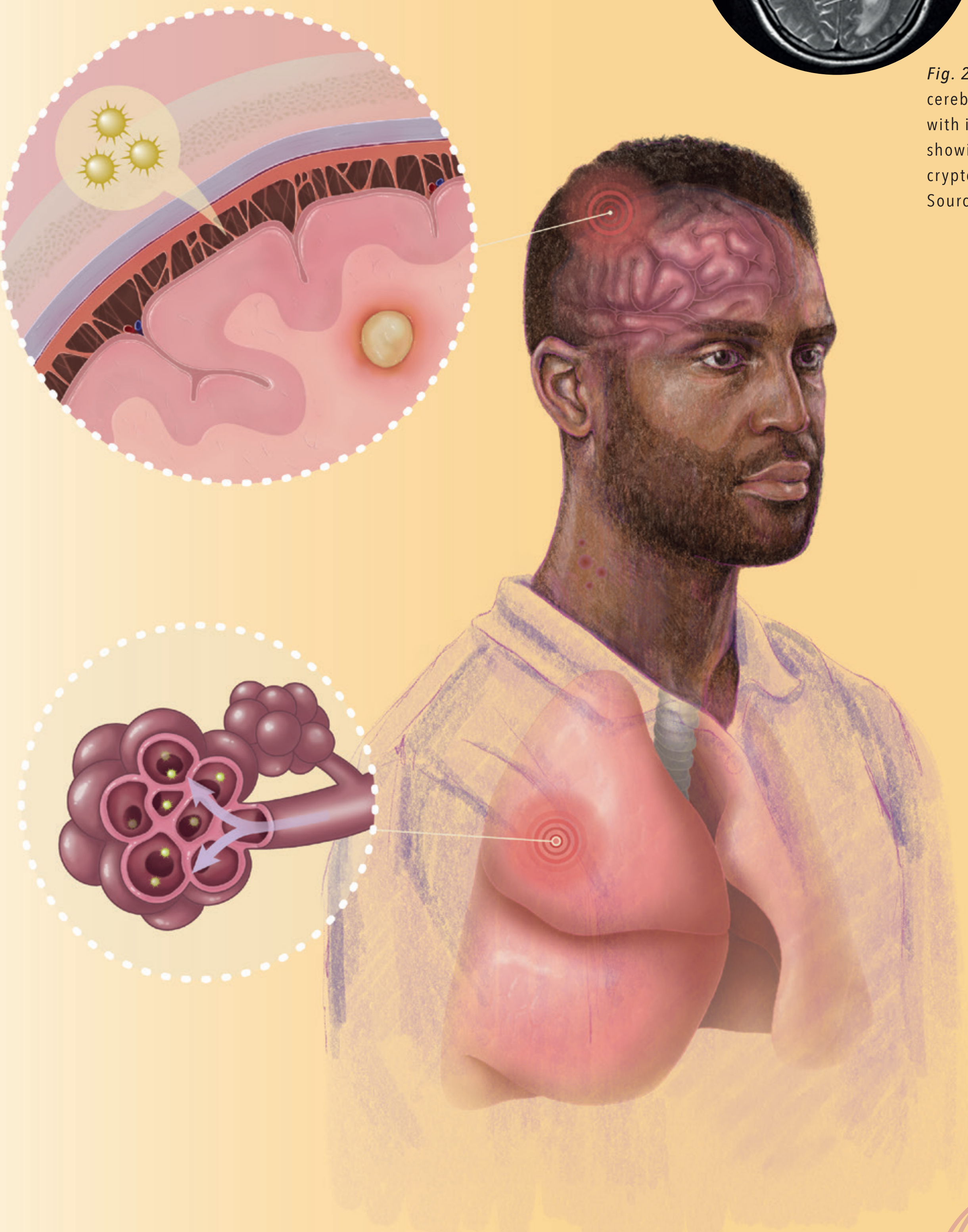


Fig. 24.1: Illustration of patient presenting with several key clinical manifestations of cryptococcosis.

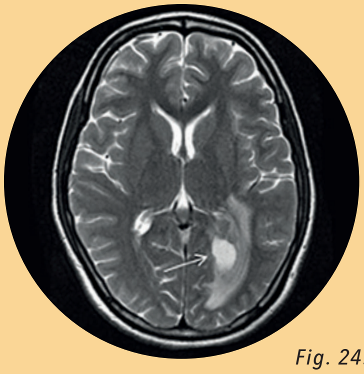


Fig. 24.2: MRI finding of cerebral cryptococcosis, with indicator showing location of a cryptococcoma. Source: Shaoqiong Chen.

Fig. 25: Illustration of patient indicating key modes of entry for *Candida* to cause invasive candidiasis.

Candida

Candida auris is a yeast known to cause yeast infections in the mouth, ear, and vagina when overgrowths occur. These growths can be managed and often do not transpire into more serious symptoms in healthy individuals. But in immunocompromised patients, *Candida* can result in more threatening manifestations such as invasive candidiasis.

Outbreaks have been recorded of *C. auris* in healthcare environments as it can enter the body through catheters inserted into the bloodstream. This mode of entry is a point I intended to highlight on this infographic, as once *C. auris* enters the bloodstream, it can easily travel to various parts of the body and cause infection *(Fig. 25)*.

In the first iterations of this illustration, the vessel was colorized red which in scientific illustration conventionally represents arteries. After discussions with my mentors, the vessel was changed to blue as most IVs and catheters enter veins, which conventionally are colored blue. Originally, the vessel was intended to appear as if it were dynamically coming from the patient's arm towards the viewer to show an enlarged view inside of the vein. However, through several experiments with layout design, the final spread shows the zoomed in vessel as an insert, with an additional zoom in of the *Candida* cells in greater magnification.

Fig. 26: Series of icons depicting anatomical areas where candidiasis can manifest.

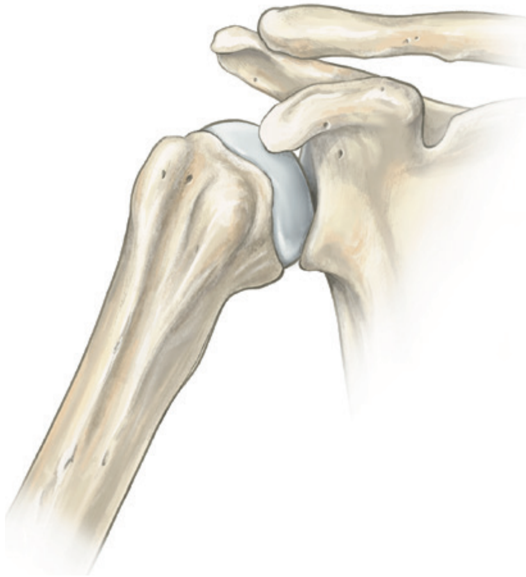


Fig. 27: Illustration of the glenohumeral joint.

For early versions of the infographic, I intended to highlight some additional areas of the body that the fungus can spread to and cause infection. The idea was to make elaborated digital illustrations of the brain, the glenohumeral joint *(Fig. 27)*, and the lungs to inlay into the patient and to pinpoint the secondary infections possible in the central nervous system, in bones, and in the lungs. Following discussions with Dr. Kontoyiannis, we decided that it is more informative to place emphasis on the intestines, as overgrowth of *Candida* in the gut is another cause of fungal invasion of the bloodstream (Kumamoto, 2020), which can spread infection to other parts of the body. With time in mind, I decided to repurpose my previous illustration of the Somso model abdominal cavity *(Fig. 28)* to fit within the *Candida* patient.

For the areas of the body susceptible to secondary infections of Candidiasis, I made the artistic decision to create vector icons with Adobe Illustrator, which serve as identifiable representative glyphs that can be easily fit into the page *(Fig. 26)*. It also made sense to display these icons in a column, so the viewer can quickly identify points of the body and read about the associated symptoms the fungal infection can cause for that anatomical part. As manifestation of infection in these areas is less common than in the blood and intestines, depicting them in a less elaborate style also places less emphasis on these areas. I also found creating icons to be an enjoyable diversion from making more realistic elaborated drawings as it felt like solving a puzzle while exploring what is the best way to design straightforward symbols that are immediately distinguishable.

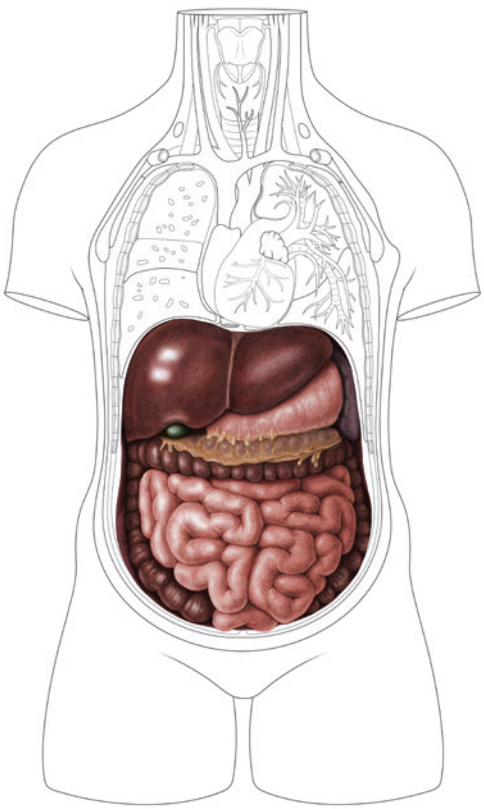


Fig. 28: (Left) Somso model illustration showing the abdominal cavity, repurposed and adjusted to fit within the *Candida* patient.

Aspergillus

Aspergillus has pathogenic potential and can cause severe illness such as aspergillosis, a term used to describe the range of infections that arise from this fungus. *A. fumigatus* predominantly causes pulmonary disease (with increasingly severe symptoms in patients with previous lung conditions), but can also disseminate from the lungs to other areas of the body as described in the WHO FPPL report.

Fungal growth in the lungs can cause inflammation of the bronchi (Kousha, 2011), which I chose to illustrate as a cross-section *(Fig. 30.1)* slicing through a bronchus to show the redness and irritation in the airway.

Another cross-section was utilized in the insert on aspergilloma, which are fungal balls that can accumulate in pre-existing cavities or *(Fig. 30.2)* scarring in the lung from previous conditions (Lee et al., 2004). Since aspergilloma forms within the lobes, and not the surface, I wanted to show it wedged within the lung as viewed as a cross-section through the lobe *(Fig. 30.1)*.

To illustrate this pathology accurately, I used chest x-rays and CT scans of infected patients *(Fig. 29)* as well as photograph references of the pathology from cadavers. When educating patients or laymen, these images would be overwhelming to look at and are not easily understandable without background knowledge in anatomy or knowledge on how to read CT scans, for example. With scientific illustration, extraneous information can be eliminated to direct the viewer's attention to what is of importance without distracting background "noise". Visualizations also make anatomical structures more recognizable and can be simplified from reality to be better distinguishable and understood by people with different educational backgrounds, which is difficult to achieve with photographs. In my illustration for the manifestations of aspergillosis, I aimed to simplify and make structures readable.

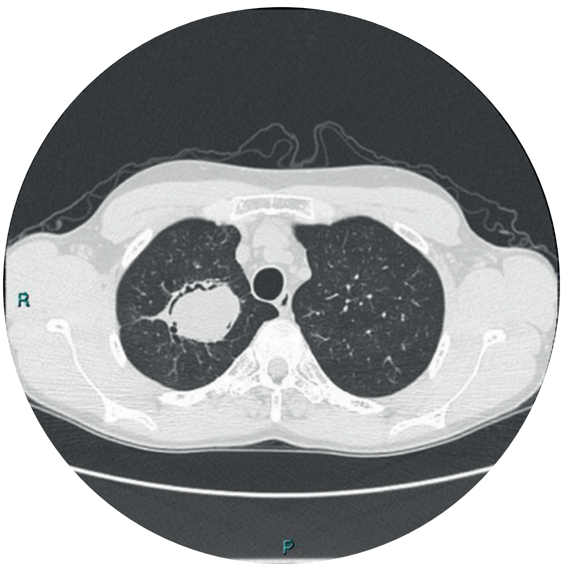


Fig. 29: (Left) CT scan showing a transverse cross-section of the thoracic cavity of a patient with pulmonary aspergillosis.
Source: Domenico Nicolettti, University of Bologna.

Fig. 30.1: (Right) Illustration of patient presenting with several key clinical manifestations of aspergillosis.

Fig. 30.2: (Right) Surgical removal of aspergilloma from lung. Source: Watchmen Lynch

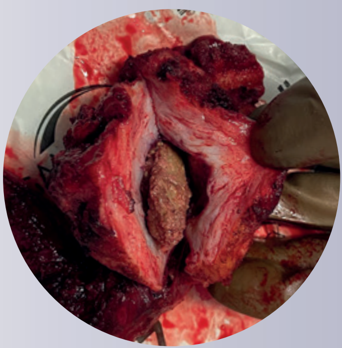


Fig. 30.2

Fig. 30.1

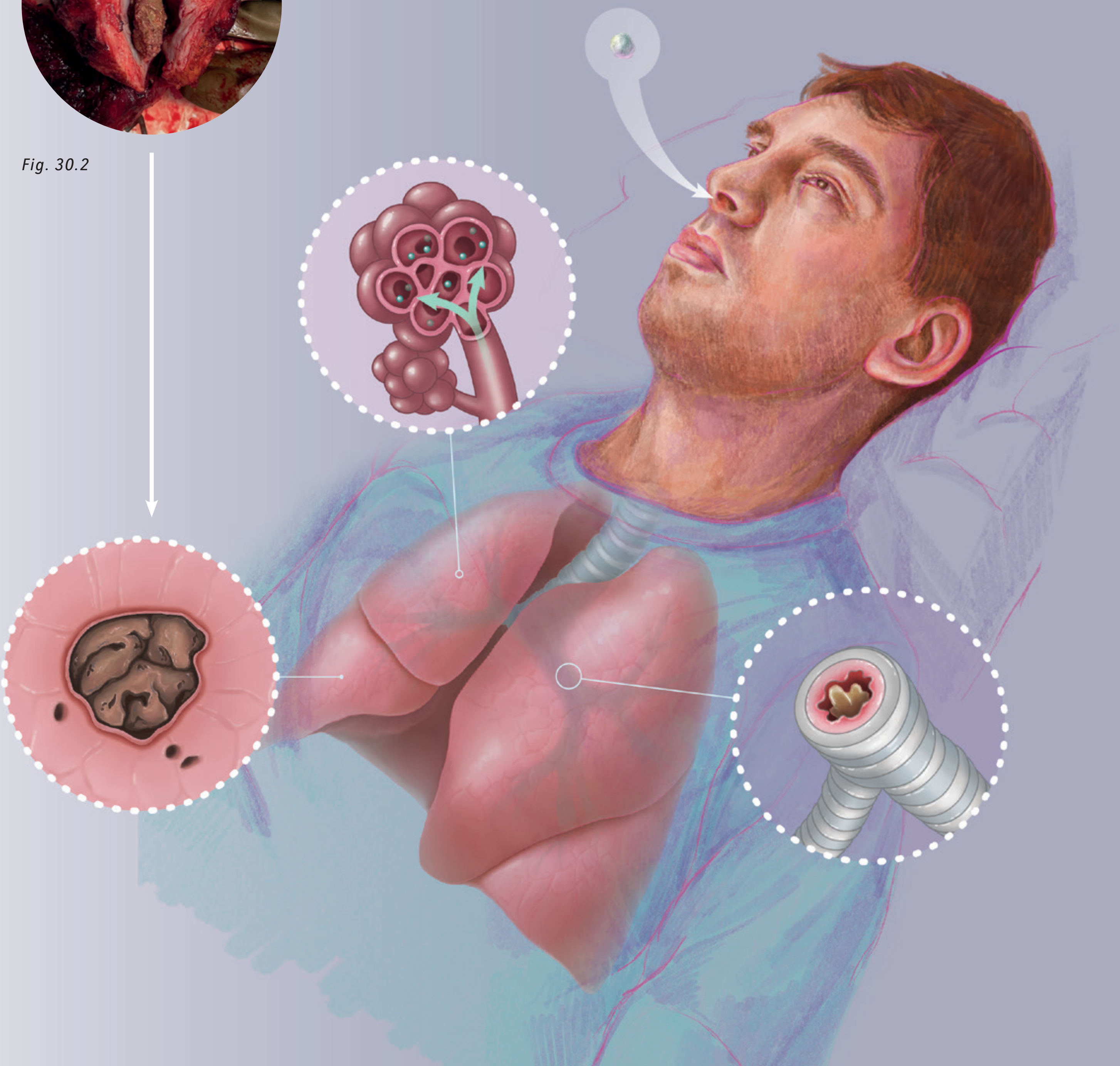


Fig. 31.1

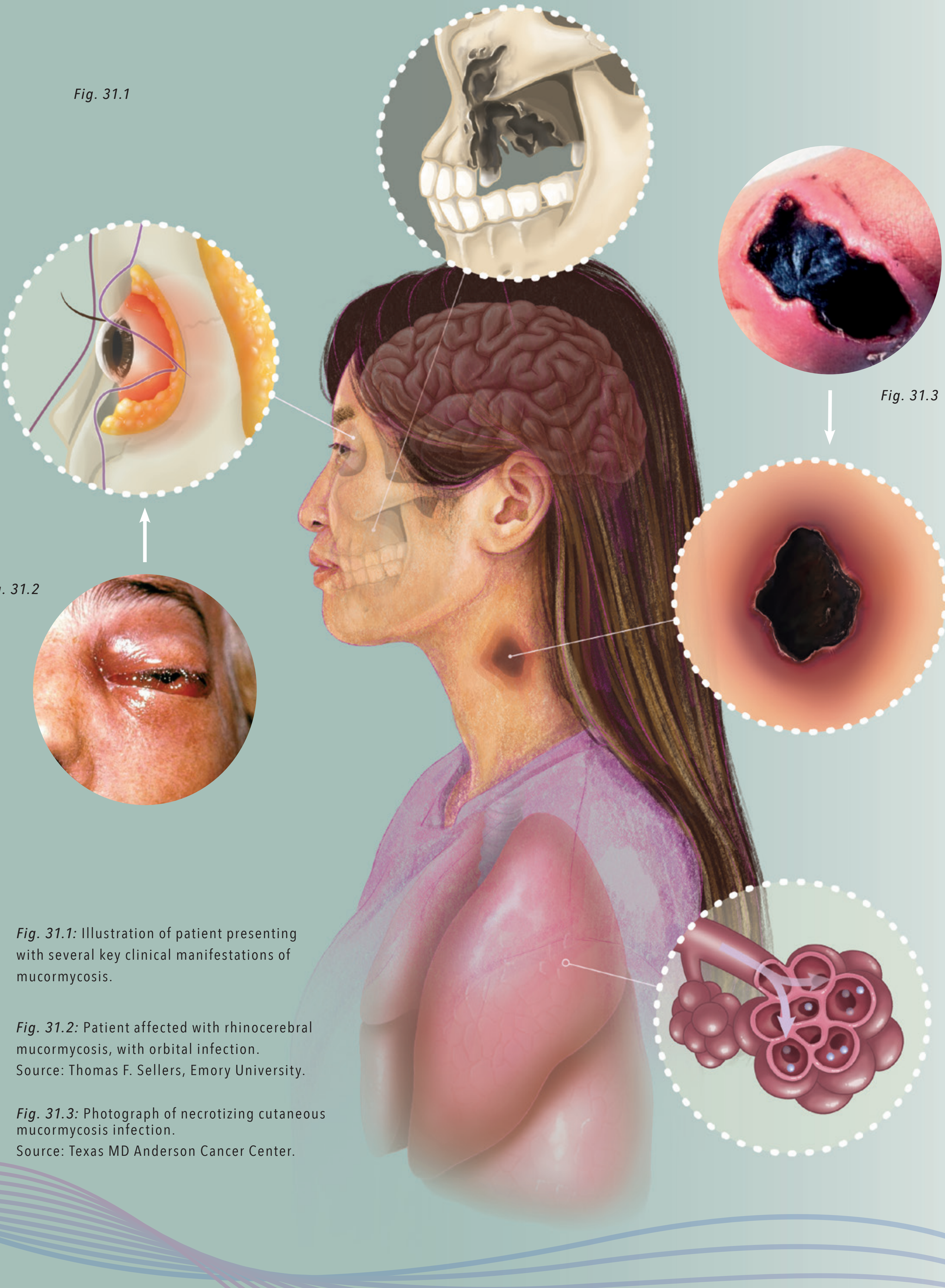


Fig. 31.2

Fig. 31.3

Fig. 31.1: Illustration of patient presenting with several key clinical manifestations of mucormycosis.

Fig. 31.2: Patient affected with rhinocerebral mucormycosis, with orbital infection.
Source: Thomas F. Sellers, Emory University.

Fig. 31.3: Photograph of necrotizing cutaneous mucormycosis infection.
Source: Texas MD Anderson Cancer Center.

Mucorales

As *Mucorales* primarily enters the body through spore inhalation, mucormycosis often affects the lungs and sinuses of immunocompromised patients who are at highest risk. However, patients with poorly controlled diabetes mellitus are also at risk of mucormycosis that targets the rhino-occipital region *(Fig. 31.2)* (Gupta and Honavar, 2022). The WHO FPPL overview on *Mucorales* additionally states that the fungus can also enter through skin breaks in patients that have experienced trauma such as burns or other soft-tissue injuries, *Mucorales* in this case can create those necrotizing skin lesions *(Fig. 31.3)* that give it the nickname "black fungus".

Reviewing photographic references of the ruthless tissue-eating pathologies caused by this fungus provided evidence of the value and necessity of scientific illustrations. Disfigured faces, gaping black holes of decay (not only through skin and muscle tissue but also bones), and bloody surgical reconstructions are only a few examples of what can be found of the endless disturbing photos of those inflicted by this devastating fungus. These images are far from pleasant and can be too graphic for patients, which can be solved with the use of scientific illustrations.

Armed with the arduous task of visually communicating these manifestations, my goal as a scientific illustrator was to erase as much of the unsettling and frightening aspects from my visualizations. Choosing to only show the pathology elaborated through inserts is a way to create some distance between the patient and the macabre results of infection. The elimination of blood and use of lighter colors also helps reduce anxiety in the viewer, despite the heavy content being illustrated. The resulting scientific illustrations created through the use of these methods certainly have an upper hand in clearly telling the story of these infections over photographs that are often unusable and difficult to understand. In side-by-side comparisons of the clinical photos and my illustrations *(Fig. 31.1)*, the difference between the two is undeniable, with my interpretations being far more palatable and friendly.

Fig. 32: Skull illustrated in a lateral view, used as a base for the insert showing *Mucorales'* ability to eat away at bone.

The brain illustrated originally for the *Candida* infographic *(Fig. 33)*, was then repurposed for the *Mucorales* infographic as Dr. Kontoyiannis indicated that mucormycosis of the sinuses can spread into the brain, which is common in patients with uncontrolled diabetes. Since both patients were illustrated with lateral views of their heads, by reflecting the brain horizontally, and with minute revisions to the lighting, the illustration was able to be adjusted for use within this infographic.

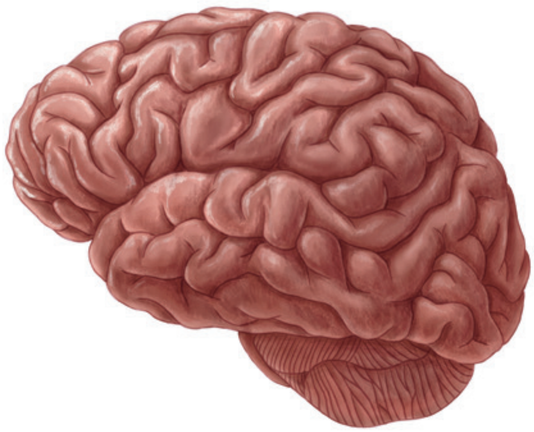


Fig. 33: Brain illustration, placed within the *Mucorales* patient to represent the possibility of infection spreading to the brain and nervous system.

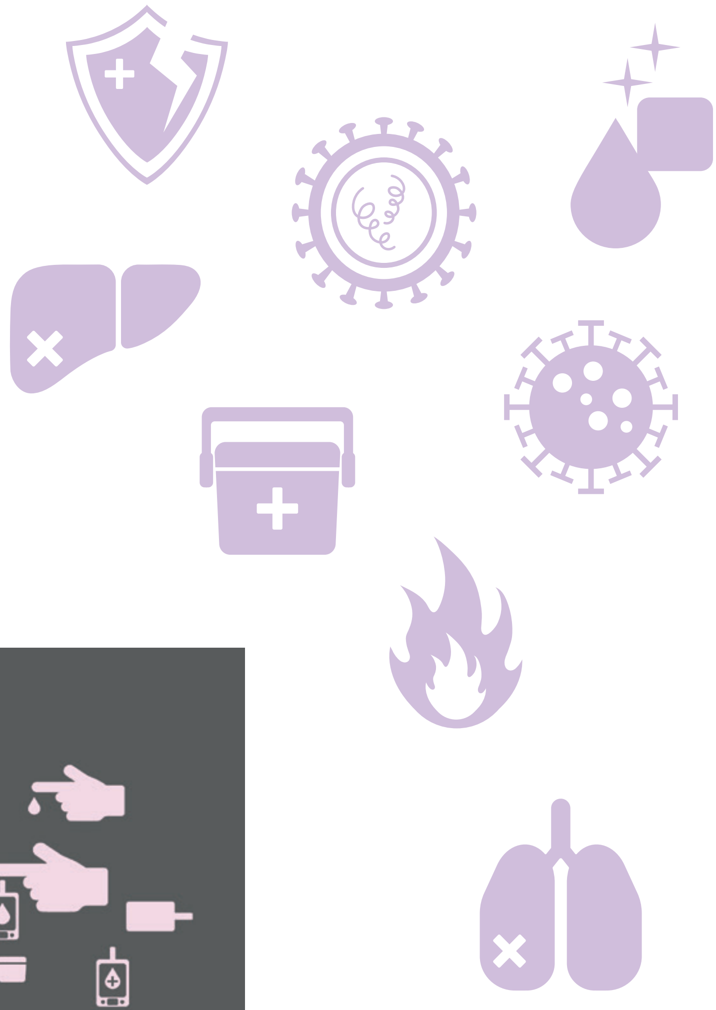
III. PUTTING IT ALL TOGETHER

Use of Icons

To counterbalance the elaborated inserts of the various clinical manifestations of each invasive fungal disease, the risk factors for developing these diseases were depicted with clear, simple, and representative icons *(Fig. 34)*. The icons, created in Adobe Illustrator consisting of the manipulation of simple shapes *(Fig. 35)*, also give the elaborated pieces room to breathe and only work to supplement the storytelling instead of taking away from the main eye-catcher elements.

The collective of the fully elaborated fungi and the more loosely sketched illustrations of the patients, slightly more graphical illustrations of the relevant pathology, and the fully vector-based icons for the risk factors creates a technically diverse and engaging page without coming off as overwhelming or too crowded.

Fig. 34: Final versions of risk factor and clinical manifestation icons.



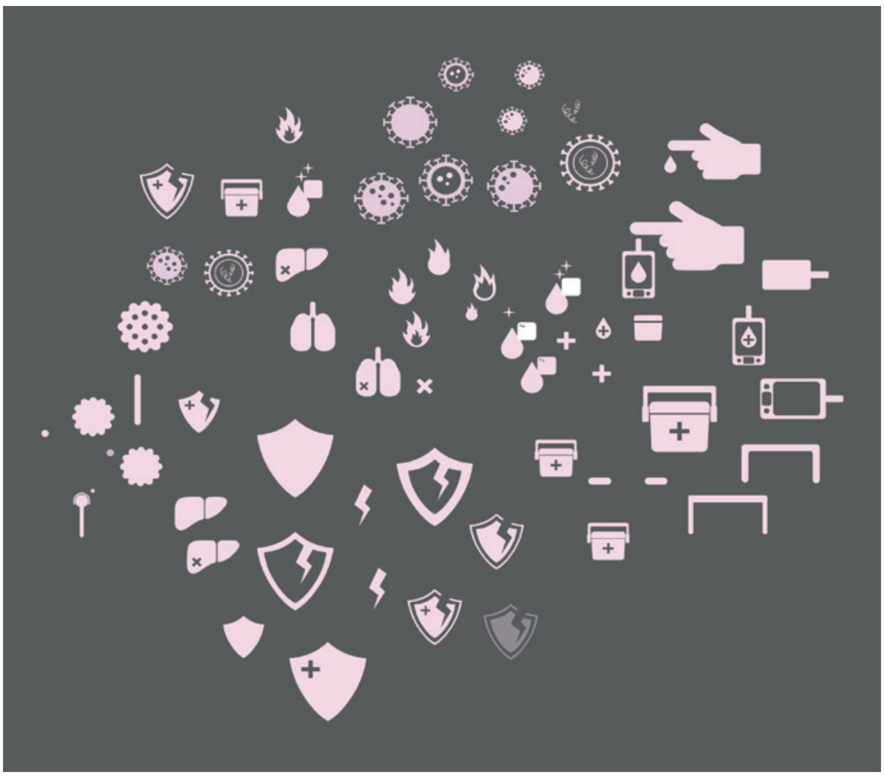


Fig. 35: Adobe Illustrator workspace during icon development.

INFOGRAPHIC STYLE AND COLOR THEORY

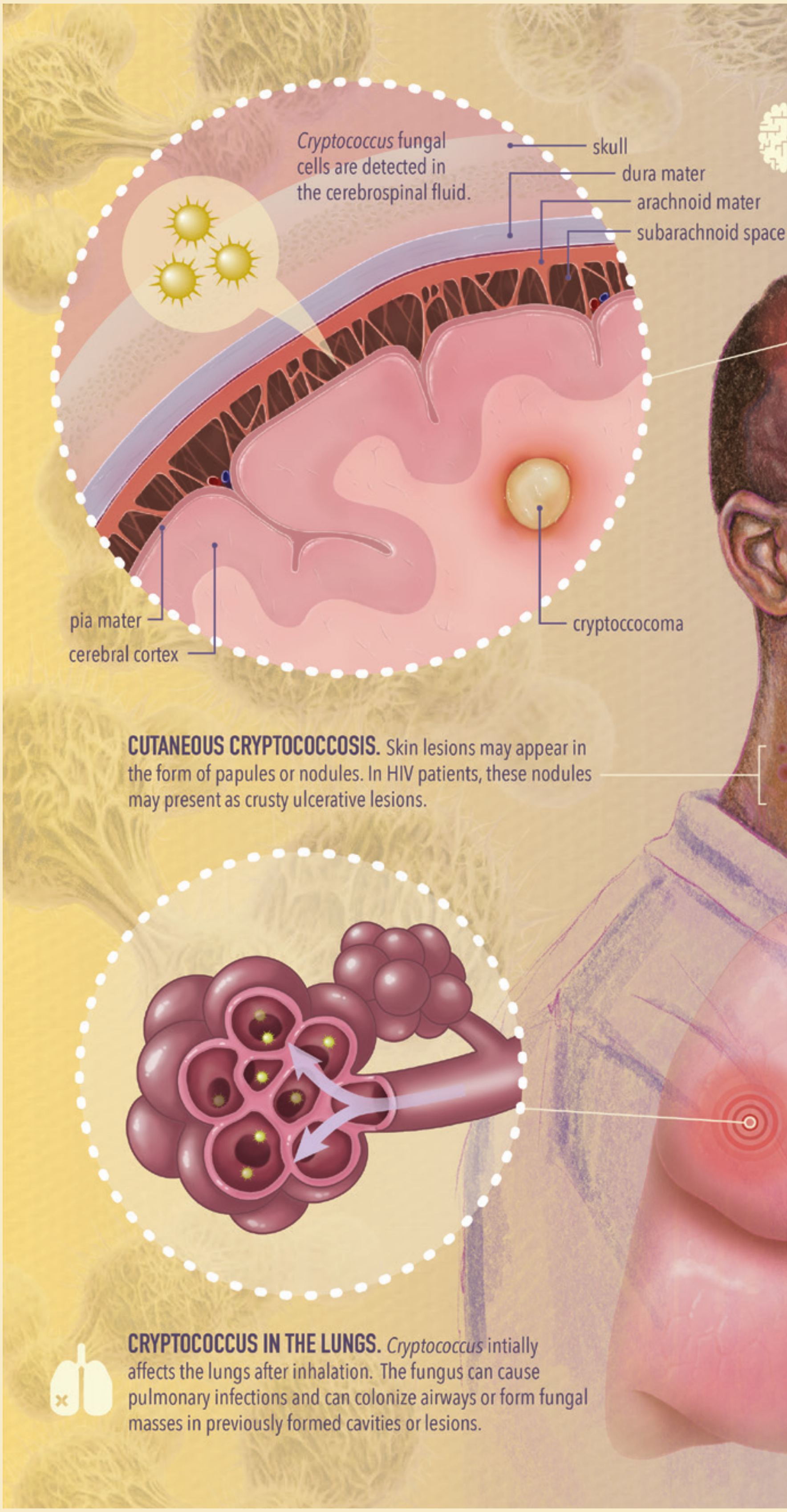
Purple is used as an unifying color to tie the separate infographics together, with muted hues throughout the backgrounds and in smaller instances on the patients as well as in reflection light on the illustrations of the fungi themselves.

The use of purple can be seen throughout healthcare settings, often used as the color for hospital walls or used in waiting room furniture. Purple, likewise with blues and greens, evokes a sense of calmness. Each infographic *(Fig. 36-39)* also uses another color to compliment the purple, to create a more engaging page that does not just disappear in all the other medical posters that use various shades of pastel purple. These color choices also allow for differentiation among the four fungi, while maintaining a cohesive style throughout the infographics. The colors selected for each spread reflects the color of the respective fungi colonies– for example, *Cryptococcus neoformans* colonies often appear yellow or brown, thus yellow was chosen as the thematic color for the *Cryptococcus* infographic.

A paper-like texture was used for the backgrounds of each infographic to complement the playful sketch-like elements. This was done to subtly push the spreads towards a more light-hearted and welcoming direction. White text juxtaposes the colorful backgrounds, which presents additional information to the page without distracting from the illustrations and it keeps the infographics clean.

Fig. 36: Completed *Cryptococcus* infographic.

pg. 34-35
Fig. 37: (Left) Completed *Aspergillus* infographic.
Fig. 38: (Right) Completed *Mucorales* infographic.



CRYPTOCOCCUS

A FUNGAL GLOBAL BURDEN ON HIV/AIDS PATIENTS

CRYPTOCOCCAL MENINGITIS. In severe cases, *Cryptococcus* can spread from the lungs to the brain causing inflammation of the meninges.

CRYPTOCOCCUS NEOFORMANS is an encapsulated yeast that causes infection known as cryptococcosis. This fungus primarily affects the pulmonary system. However, in severe cases it can spread to the central nervous system causing meningitis or fungal growths within the brain called cryptococcoma.
Most patients of *Cryptococcus* infections are immunocompromised, with HIV patients the most susceptible. Treatment often involves antifungal therapy with amphotericin B.

Mode of entry.
Cryptococcus is acquired when the fungi are inhaled from the environment.

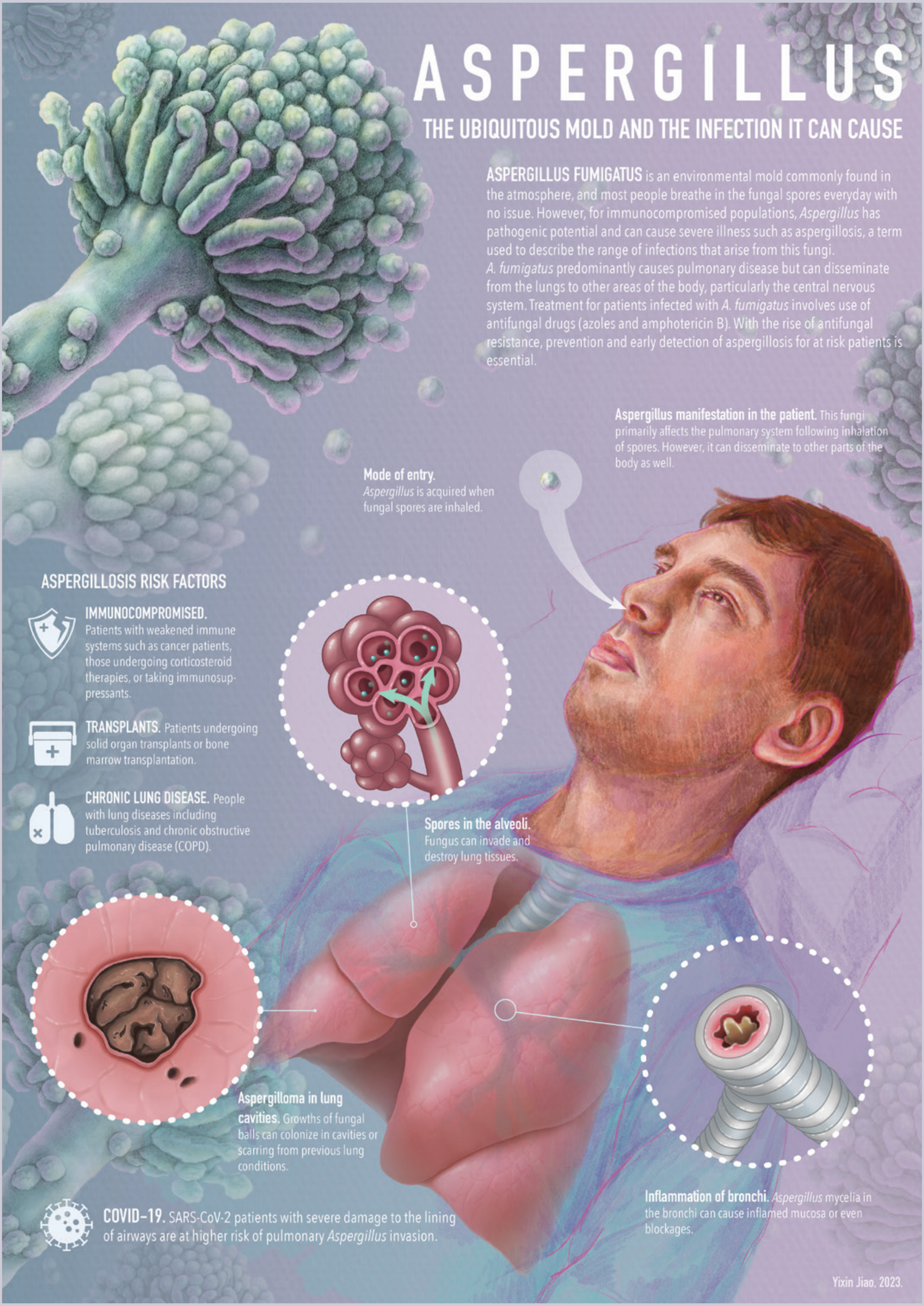
CRYPTOCOCCOSIS RISK FACTORS

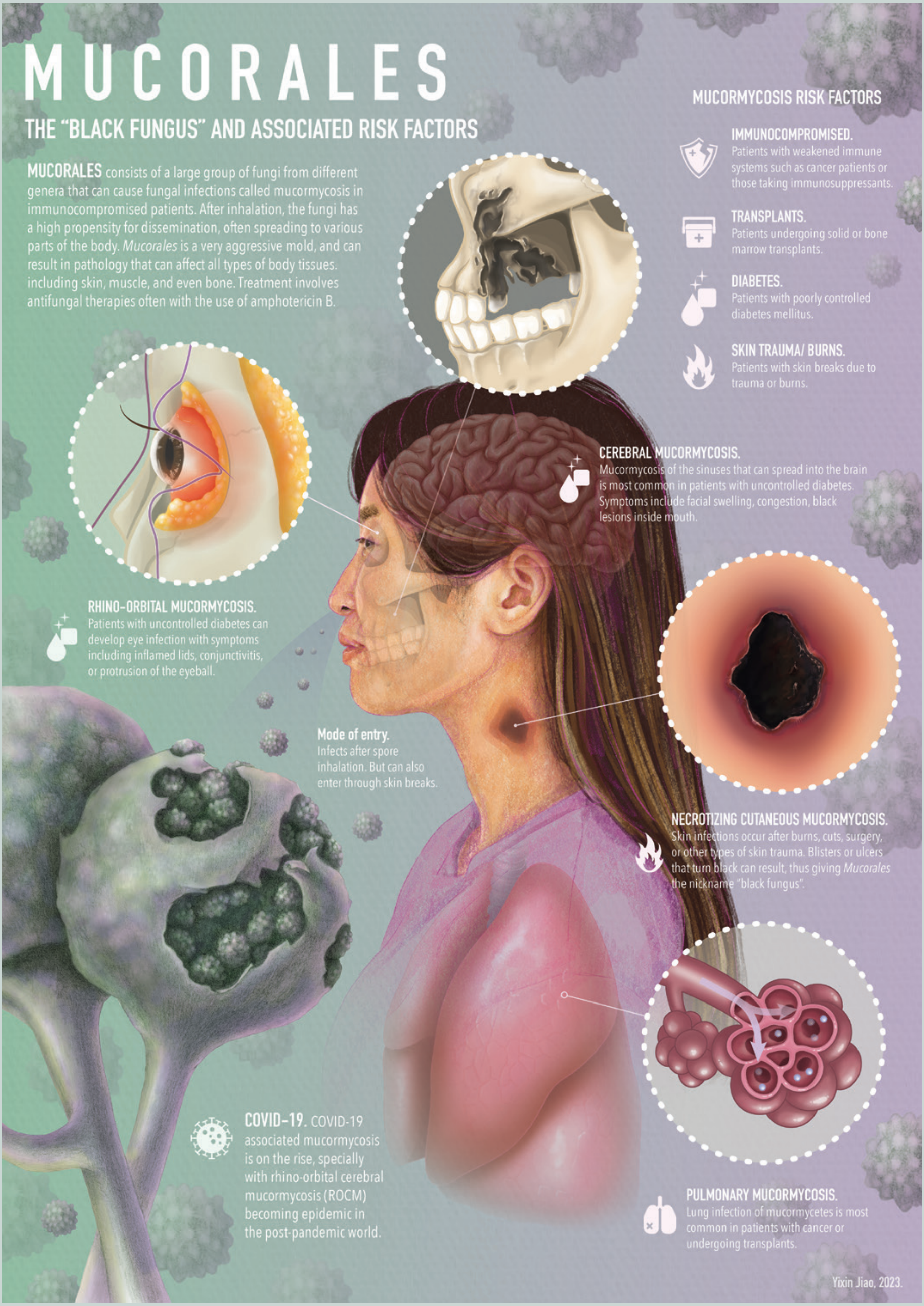
HIV/AIDS. The leading risk factor for cryptococcosis is HIV-infection. For these patients, cryptococcosis often disseminates to the central nervous system, presenting as meningitis with discernable meningeal symptoms such as fever, headache, neck stiffness. Skin lesions are another manifestation of disseminated cryptococcus for HIV patients.

IMMUNOCOMPROMISED. Patients with weakened immune systems such as cancer patients, those undergoing corticosteroid therapies, or taking immunosuppressants are at higher risk for invasive cryptococcosis.

TRANSPLANTS. Patients undergoing solid organ transplants or bone marrow transplantation are at risk for developing invasive crypotococcosis.

Yixin Jiao. 2023.


ASPERGILLUS
THE UBIQUITOUS MOLD AND THE INFECTION IT CAN CAUSE
ASPERGILLUS FUMIGATUS is an environmental mold commonly found in the atmosphere, and most people breathe in the fungal spores everyday with no issue. However, for immunocompromised populations, Aspergillus has pathogenic potential and can cause severe illness such as aspergillosis, a term used to describe the range of infections that arise from this fungi. A. fumigatus predominantly causes pulmonary disease but can disseminate from the lungs to other areas of the body, particularly the central nervous system. Treatment for patients infected with A. fumigatus involves use of antifungal drugs (azoles and amphotericin B). With the rise of antifungal resistance, prevention and early detection of aspergillosis for at risk patients is essential.
Aspergillus manifestation in the patient. This fungi primarily affects the pulmonary system following inhalation of spores. However, it can disseminate to other parts of the body as well.
Mode of entry. Aspergillus is acquired when fungal spores are inhaled.
ASPERGILLOSIS RISK FACTORS
IMMUNOCOMPROMISED. Patients with weakened immune systems such as cancer patients, those undergoing corticosteroid therapies, or taking immunosuppressants.
TRANSPLANTS. Patients undergoing solid organ transplants or bone marrow transplantation.
CHRONIC LUNG DISEASE. People with lung diseases including tuberculosis and chronic obstructive pulmonary disease (COPD).
Spores in the alveoli. Fungus can invade and destroy lung tissues.
Aspergilloma in lung cavities. Growths of fungal balls can colonize in cavities or scarring from previous lung conditions.
COVID-19. SARS-CoV-2 patients with severe damage to the lining of airways are at higher risk of pulmonary Aspergillus invasion.
Inflammation of bronchi. Aspergillus mycelia in the bronchi can cause inflamed mucosa or even blockages.
Yixin Jiao, 2023.


MUCORALES
THE "BLACK FUNGUS" AND ASSOCIATED RISK FACTORS
MUCORALES consists of a large group of fungi from different genera that can cause fungal infections called mucormycosis in immunocompromised patients. After inhalation, the fungi has a high propensity for dissemination, often spreading to various parts of the body. Mucorales is a very aggressive mold, and can result in pathology that can affect all types of body tissues. including skin, muscle, and even bone. Treatment involves antifungal therapies often with the use of amphotericin B.
MUCORMYCOSIS RISK FACTORS
IMMUNOCOMPROMISED. Patients with weakened immune systems such as cancer patients or those taking immunosuppressants.
TRANSPLANTS. Patients undergoing solid or bone marrow transplants.
DIABETES. Patients with poorly controlled diabetes mellitus.
SKIN TRAUMA/ BURNS. Patients with skin breaks due to trauma or burns.
CEREBRAL MUCORMYCOSIS. Mucormycosis of the sinuses that can spread into the brain is most common in patients with uncontrolled diabetes. Symptoms include facial swelling, congestion, black lesions inside mouth.
RHINO-ORBITAL MUCORMYCOSIS. Patients with uncontrolled diabetes can develop eye infection with symptoms including inflamed lids, conjunctivitis, or protrusion of the eyeball.
Mode of entry. Infects after spore inhalation. But can also enter through skin breaks.
NECROTIZING CUTANEOUS MUCORMYCOSIS. Skin infections occur after burns, cuts, surgery, or other types of skin trauma. Blisters or ulcers that turn black can result, thus giving Mucorales the nickname "black fungus".
COVID-19. COVID-19 associated mucormycosis is on the rise, specially with rhino-orbital cerebral mucormycosis (ROCM) becoming epidemic in the post-pandemic world.
PULMONARY MUCORMYCOSIS. Lung infection of mucormycetes is most common in patients with cancer or undergoing transplants.
Yixin Jiao, 2023.

Mode of entry.
C. auris can infect the bloodstream in hospitalized patients through medical equipment, such as catheters or other lines.
CANDIDIASIS RISK FACTORS
IMMUNOCOMPROMISED. Patients with weakened immune systems such as cancer patients, those undergoing corticosteroid therapies, or taking immunosuppressants.
TRANSPLANTS. Patients undergoing solid organ transplants or bone marrow transplantation.
COVID-19. Patients with COVID-19 are more predisposed to infections of candidiasis.

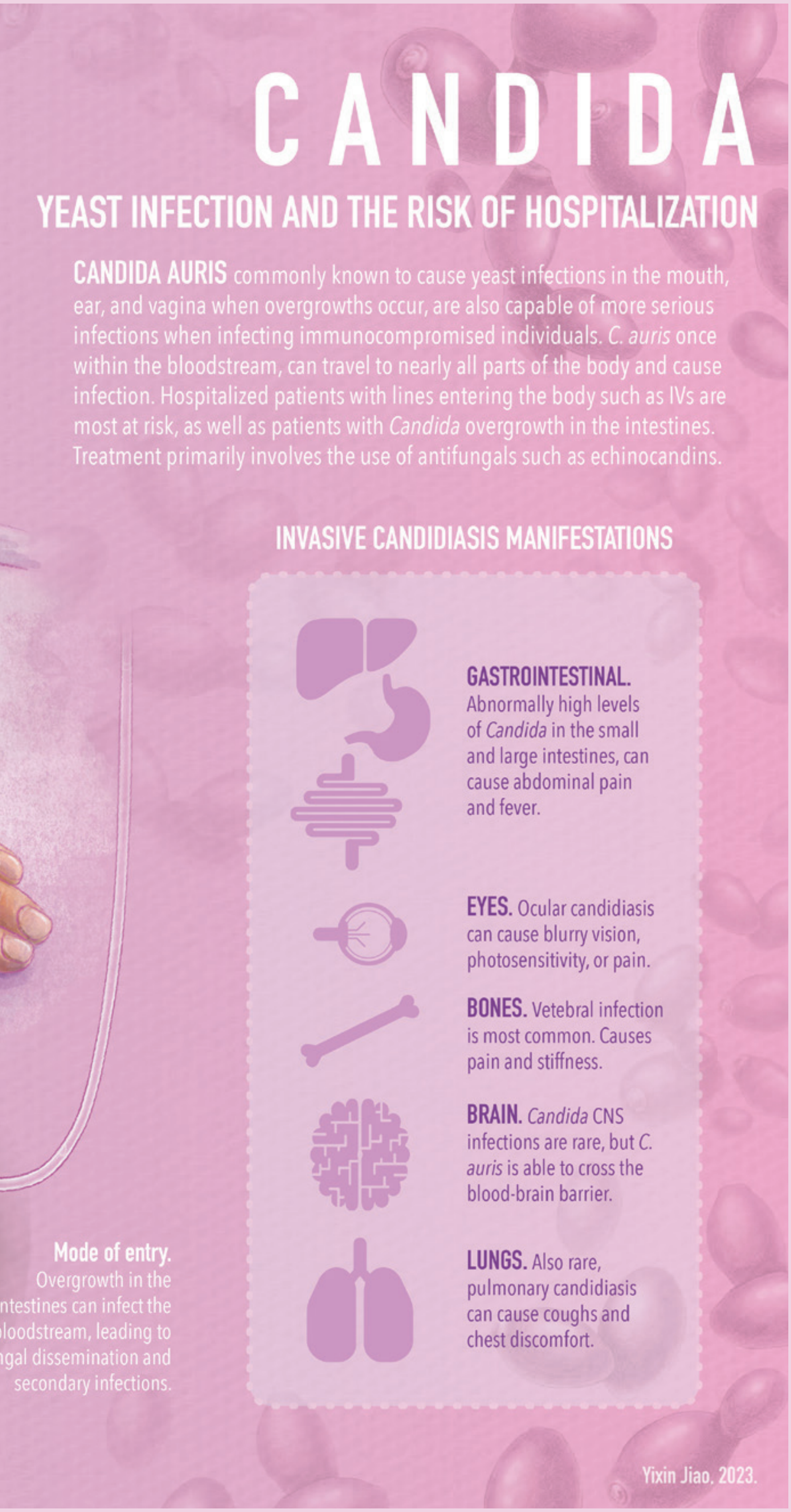


Fig. 39: Completed *Candida* infographic.

CONCLUSION

From the start, I knew I wanted to focus my thesis on something fungi related, as there are so many interesting aspects to these organisms and over the years, I've interacted with and viewed fungi through various lenses.

First off, I'm a huge proponent of putting mushrooms into any dish, and a true believer that if you don't like eating mushrooms, you just haven't had them cooked right. Stemming from this love of eating mushrooms, I took up the hobby of growing them myself (highly recommend for those with a green-thumb, but are too impatient to wait for plants to grow, because mushrooms almost double in size overnight!). I then had my first run-in with the dangerous side of fungi a few years ago, when a friend of the family had a close call with eating toxic mushrooms which they misidentified while foraging. As a biologist, I've enjoyed working with molds and yeasts under the microscope and I found interest in learning more about the pathological capabilities these organisms have on the human body.

Now as a scientific illustrator, I'm able to look at fungi and fungal disease from both scientific and artistic perspectives to reach the goal of visually communicating them. Scientific illustrators are, in a way, translators; we work to transform the language of the scientific community into forms that can be understood by various other audiences. Through the endless revisions, double checking– then triple checking anatomy, and indecision about which layout version is the best, I sought to bridge the gap in understanding of these fungi with my illustrations. The use of illustrations in science allows for information to reach greater audiences, and greater understandability, across various education levels.

With the task of transforming invasive fungal infections for patients, I found it challenging to view the graphic photographs and read papers that reveal the severity of disease and to then be able to shield others from this reality. Exposure to this material provided me with first-hand experience on the value of scientific illustration, where you can present the truth in an informative way while excluding explicit imagery. I found that the best way to achieve this is to step into the shoes of the patient, and make artistic decisions through the their eyes– carefully considering their possible emotions and reactions when viewing the illustrations. In doing so, I was able to work towards the goal that Dr. Kontoyiannis and I set out to achieve, to help educate patients and the general public in a much more pleasing way than if they were to receive this information straight from the World Health Organizations' report.

I started this course after a long hiatus with art, and completing this thesis seemed so daunting and unattainable in the beginning. Throughout the past two years, I've not only been able to grow my technical skills, but also gain confidence in my work. Now, as a more refined illustrator, I feel well equipped and harnessed with all the right tools and outlook to tackle future projects. Working towards this thesis has refreshed my traditional art skills, and significantly developed my previously minimal experience with digital media. I also find myself settling into a better workflow, and I am communicating and developing feedback loops with ease. I can't wait to see how scientific illustration continues to evolve in the future and I hope this is only the beginning of my contribution to the field, and I'm looking forward to continuing to learn better methods of presenting science and medicine to others. I am grateful to be part of this field where I can serve as a liaison between science and the general public, while existing in this sweet spot between science and art.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my mentor Arno, for his invaluable guidance, inexhaustible knowledge, and support throughout my thesis process. A big thank you to Dirk, Rogier, and Alex for their insight, motivation, and for being the best instructors. I'm forever grateful for all they've taught me.

Dr. Kontoyiannis, his eagerness to be involved despite his busy schedule and his expertise were instrumental in guiding me in the right direction. I thoroughly enjoyed our collaboration, which went without a hitch. Thank you for providing me with all the resources I needed and more. I've learned so much.

I would also like to thank my friends and family for providing an endless source of inspiration and motivation. To my MSI cohort, I'm so proud of how far we've come. It's been a wild 2 years and I cherish every bit of it. This is the best group I could have asked for.

Finally, I'd like to thank Ricky, for his constant encouragement and love, which kept me going even during the most challenging times. Thank you for watching videos of cute otters with me and for all those much-needed boba runs (we really should have asked for a new stamp card).

Truly grateful for the support of all those who helped me along the way, I could not have completed this project without their help.

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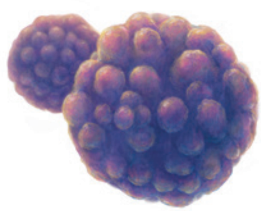

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