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Review

A systematic review on materials, design, and manufacturing of swabs

Vedant Vashist[a,b,1], Neil Banthia[a,b,1], Swapnil Kumar[a,c], Prajwal Agrawal[a,*]

[a] AMM Engineering Laboratory, NewEra Hospital and Research Institute, Nagpur, Maharashtra 440008, India
[b] School of Mechanical Engineering, Department of Manufacturing, VIT Vellore, Vellore, Tamil Nadu 632014, India
[c] Department of Aeronautics, Imperial College London, London, SW7 2AZ, United Kingdom

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ABSTRACT

From simple cleaning to metagenomic studies and now the detection of the SARS-2 virus, swabs are absorbent pads with handles that hold significant promise in several applications and properties. Furthermore, the swab is now used for a wide range of medical purposes, such as the collection of bacteria and other pathogens such as influenza and H1N1. Various designs and materials used for the tip have led to a wide range of applications. In this review, we discuss the characteristics of essential tip materials such as rayon, polyester, nylon, and polyurethane in the context of specimen collection from various substrates. Further, this article reviews swab manufacturing techniques, including injection molding and calendar roll pressing, among others. In recent years, advances in additive manufacturing technology have made it possible to produce swabs in a fast and efficient manner. Furthermore, the design for additive manufacturing (DfAM) is given for the production of swabs. We also examine how 3-D printing of bio-resin swabs has revolutionized the manufacturing process, making it autonomous, quicker, more efficient, and environmentally friendly. Additionally, a shortage of medical devices for testing the SARS-2 virus has zealously motivated the medical industry to revolutionize through additive manufacturing of swabs, thus revolutionizing the medical industry. In conclusion, the limitations of the current techniques and future directions for swabs are discussed.

1. Introduction

Among the 5 primary senses, hearing is the most beneficial for communication. Our ears, however, have weaknesses, like earwax build-up and tinnitus, to name a couple. Because of earwax build-up, the ear is prone to infections and damage [1,2]. The ear cleaning problem has been a massive issue throughout history. This is mainly due to the damage to the eardrum while cleaning the canal for earwax. In the early centuries, 'Ear pickers' made of metal were used which was dangerous [3]. This practice continued until people realized that adding small fibers of cloth not only made them safer to use but also helped remove earwax more efficiently [5]. Cotton, a generic fabric used since prehistoric times, was the pre-dominant answer to put at the tips of the so-called ear pickers. This idea was derived from the mops that medieval sailors used for cleaning decks: Instead of sweeping the deck with a cloth, they attached fabric at the end of a stick to reduce the effort and maximize cleaning results. These deck-cleaning sailors were called 'Swabbers,' and hence through time, we adapted these absorbent pads for cleaning and sampling to be known as swabs [4].

Subsequently, since the first patent for swabs in 1874 was made by Moritz Leiner; the designs, manufacturing, materials, and applications have developed greatly. Swabs were initially made by twining wires and attaching a thread akin to a spoon at the end [5]. Soon, different materials like sponges, cotton, polyester, and rayon were attached at the ends of the wires, enhancing present-day applications. No longer for ear cleaning alone, swabs have been used to study the human genome. In the recent COVID-19 pandemic, nasopharyngeal swabs played an important role in testing in humans through the extraction of epithelial cells and membranes [6–8].

According to Verdon, Mitchell, and van Oorschot [9], present-day technology divides swabs into 3 significant designs: wound swabs, flocked swabs, and pad swabs. Each dominant design has specific applications. Their research describes each design in a detailed manner, summarized in the next few lines. A wound swab, as shown in Fig. 1a, consists of pure long fibers being wound up to the shaft, which is the antiquated design, [10]. Verdon described it to be extremely efficient under difficult situations of specimen collection when paired with the intended material. Fiber density and

List of abbreviations: AM, Additive Manufacturing; CAD, Computer-aided designing; PET, Polyethylene terephthalate; SEM, Scanning Electron Microscopy; DNA, Deoxyribonucleic acid; CFU, Colony-forming unit; IRB, Institutional Review Board; DiY, Do it yourself; FFF, Fused Filament Fabrication; SLA, Stereolithography Apparatus; MJF, Multi Jet Fusion; NP, Nasopharyngeal swabs; PETG, Polyethylene terephthalate glycol

* Corresponding author at: AMM Engineering Laboratory, NewEra Hospital and Research Institute, Nagpur, Maharashtra 440008, India.
E-mail address: pprajwal@ethz.ch (P. Agrawal).
[1] These authors contributed equally to this work

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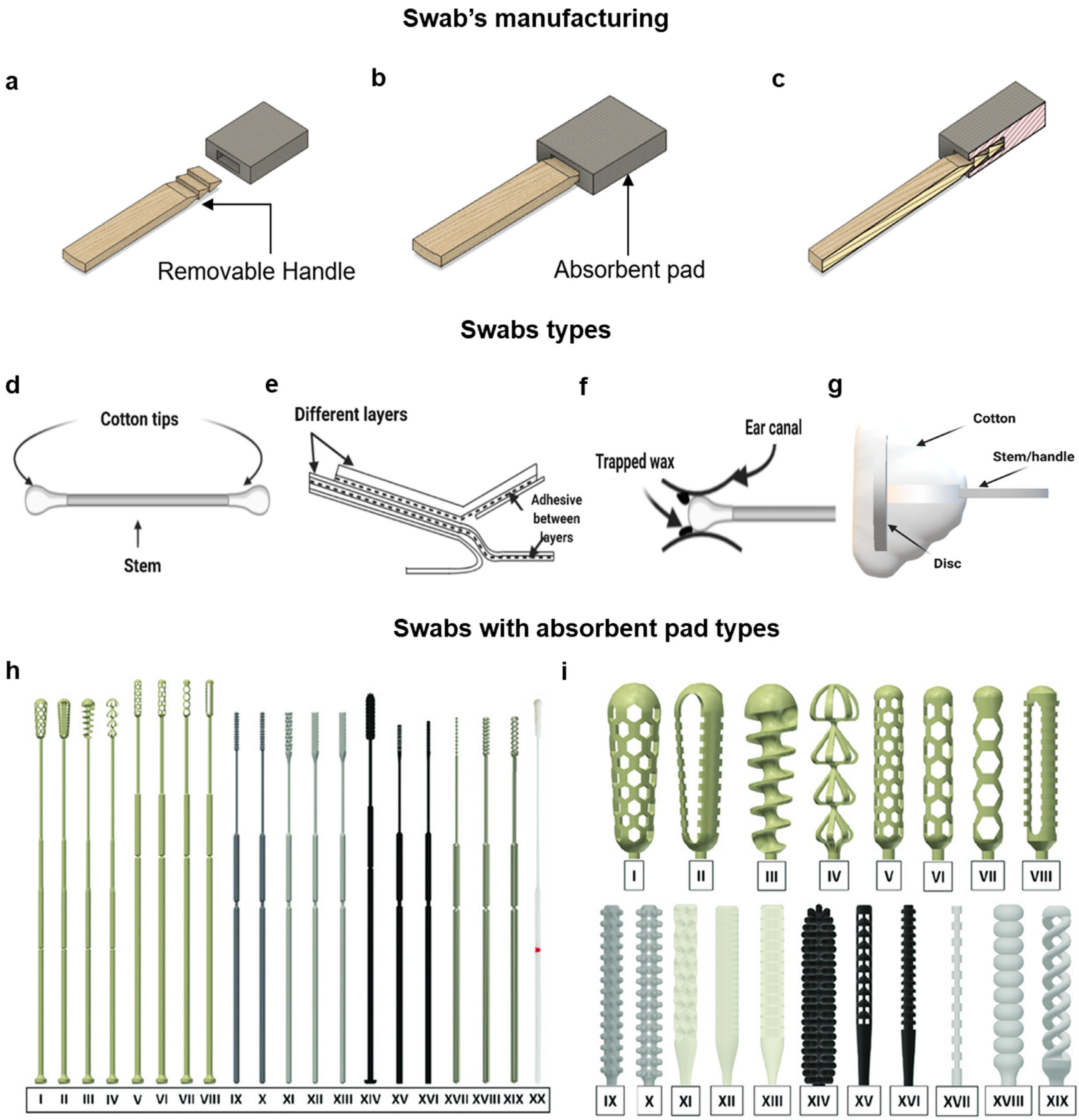

Fig. 1. Overview of differing types of swabs and their manufacturing. a. Absorbent pad with a cavity for attaching the handle. b. Swab with a non-circular cross-section. c. The sectional view of the absorbed pad with barbed handle inserted.**d.** Side view of the common cotton swabs with elongated tips. **e.** Edge view of the design of nematodic swab (during the removal of the lower layer from the other two layers for trapping microorganisms). **f.** A working demonstration of the cotton swab that cannot clean trapped ear wax in the ear canal. **g.** Side view of a newly designed cotton swab with a disc inserted at the terminal. **h.** Prototyped swab computer-aided design for 3D-printed fabrication. (I–VIII) FAMES Lab designs. (IX–X) Abiogenic designs. (XI–XIII) Fathom designs. (XIV) USF Health design. (XV–XIX) Wyss designs. (XX) Copan ESwab 481C swab. **i.** The heads of the swab designs are shown in 1h. h, i: Reprinted with permission from [93].

absorption also play a vital role in sample extraction. The next innovation was the advent of pad swabs, inspired by foams and other sponge-like porous materials, such as those in Fig. 1b. These can extract samples from porous surfaces like wood due to their high absorptivity and ranges in porosity. The foam, being produced in sheets, allows different pore sizes, tip shapes, and sizes for specific applications in various environments. Lastly, flocked swabs consist of fibers attached perpendicularly at the end of the swab stem similar to spines on porcupines, which allow a plethora of contact points and hence enhance the surface area for specimen collection [9]. Originally derived from the shape of hydrophilic plants, flocked swabs revolutionized the industry [11]. While wound swabs were originally produced by hand, now all three dominant designs can be produced by machines, mostly 3D printed, in much higher quantities.

The manufacturing technology of swabs has progressed from original hand-made products to automated manufacturing [12]. For the production of elongated swabs, specific parameters were set for the sheet material of the tip to be cut out from, which were then roll-pressed onto the shaft. In 1999, fully automated systems were developed for the fabrication of foam swabs. The process involved molding and then cutting pads, which were later attached to the stems through hot electrodes. The automated machines were subdivided into five stations for the processes discussed above. Lastly, oval-shaped swab tips were formed by calendar roll presses, which were set at a high temperature for molding of thermoplastic material, by deformation [13]. This economical process is currently used for making cotton earbuds. The motorized system for manufacturing involves five stations. However, current manufacturing systems are much more efficient and safer, thanks to many technological advancements in automated production techniques. For example, additively manufactured swabs are much safer to manufacture and are more durable than hand-made produce [14].

Since the beginning of the 21st century, the pace of technological development has surged [15]. One such impact has been through 'Additive Manufacturing (AM). Other equivalent names for this process are 3D Printing, Solid Freeform Fabrication, Layered Manufacturing, and Rapid Prototyping. It is a procedure through which virtual 3-D models on software, based on computer-aided designing (CAD) data are constructed. Currently, it encompasses major industries such as aerospace, defense, medicine, sports, automobiles, and many more. The name additive manufacturing" comes from the way it constructs the 3-D model, layer by layer. This makes the fabrication of products easier and faster even when complex shapes are designed. Furthermore, dimensional accuracy is high, and custom user-based models of complex geometries are also possible. This technological feat has been exploited for several purposes, but perhaps the most important is the advancement of healthcare. A good example would be medical equipment production. 2022's COVID-19 pandemic has taught us well that the production of medical equipment can be much faster, more efficient, accurate, and safer for all users when compared to current manufacturing techniques. Within additive manufacturing, there are not one but several processes through which objects can be fabricated [16,17]. Inventions of different materials used in 3D printing have allowed us to expand our horizons [18]. 3D printed swabs used for nasopharyngeal testing for COVID-19 are made from autoclavable biocompatible resins, which are non-toxic and very safe to use. Here, not only did swabs become safe, but also their mechanical properties were enhanced. For example, nasopharyngeal testing swabs 3D printed by Abiogenix displayed excellent torsional properties and were flexible enough to sustain the pressure put by the nasalis muscle in the upper parts of the nose [19]. Also, the usage of additive manufacturing makes things simple in the supply chain as all the required parts and designs can be manufactured using a single machine, and printing the products in bulk or single will cost the same thus also reducing the risk of huge logistics.

Among many additive manufacturing techniques, the occurrence of biological materials has become a growing trend due to the immense amount of resources spent to gain knowledge in this area. Like this, an emerging field in the medical expertise for surgical equipment and internal body structures, the predictions, results, and products need to be very safe and usable as ethical and moral issues in studies come into the picture. The arena of additive manufacturing has recently been able to achieve the use of biocompatible polymers and metals in coronary angioplasty and organ-on-chip designs [20]. Given these advancements in medical technology, this paper is intended to invigorate the role of additive manufacturing in the once-primitive tool known as the 'swab' [21].

As the importance of the swabs grew throughout history, many standard procedures were established to investigate and detect microbial samples through extractions performed on them. Processing sampled swabs, and testing for pathogens is a long and painstaking process. After a plethora of research, scientists formed a standard procedure for testing swab samples in labs, which has now become rudimentary for research in all fields. Here is one example [22]: Firstly, the swab is sterilized and then prepared for sample extraction from the given region. After extraction, it is stored in vials with enrichment media and transported under freezing conditions without antibiotics. Samples are then re-extracted from the swab into a prepared culture where it is incubated for the pathogen to grow as it will be easy to detect further. All of these processes are done carefully and the swabs are isolated in small medical storage chambers. A vortex mixer or a centrifuge is used, depending on what is needed, are used to take out the pathogen, and check under microscopic conditions [23].

After observing all the data given above, a perceptible analysis for each series of materials, manufacture, and design is required. Since swabs are of paramount importance for testing patients during the Covid-19 pandemic, it would be valuable to be well-informed about existing swabs types and the designs of swabs available. This includes the fact that most swabs would be fabricated through additive manufacturing techniques due to avoid health risks posed by a coronavirus and also for faster results. This review paper discusses the various designs, their drawbacks, and how additive manufacturing has aided in a new solution. Additionally, various material tips and manufacturing techniques for swabs are discussed with their application in various fields. Furthermore, due to the rise of additive manufacturing technologies, the current scenarios and the future of swabs are also discussed.

The main objectives of this review paper are to understand the various improvements made in designs and materials for swab manufacturing and to report on the functioning of suitable materials among cotton, rayon, polyester, nylon, and polyurethane by examining their clinical performance. Because of the Covid-19 pandemic, we have seen a shift in the paradigm towards 3D printed/ Additive Manufactured swabs due to their rapid manufacturability. In this manuscript, the spectrum of opportunities and challenges for the future of additive-manufactured swabs and their application is discussed.

2. Materials and Methods

Since swabs have so many applications in the medical industry, the effectiveness of materials in the tips has always played a significant role in specimen sampling. Scientists and researchers require achieving accurate results during experimentation through swab sampling. Knowing that the proximity of location for specimen extraction and data inspection is distant, swabs have to go through the storage and transportation phase where specimens extracted from the workplace have to be isolated. So, it would be no use to select swabs that degrade, lose, or lose inspection samples during storage, transportation, and experimentation. The evolution from ear-cleaning tools to DNA and pathogen detectors constitutes a major leap, as shown in the materials used. Swab materials have augmented their properties over time. Beginning with naturally-found products like cotton, researchers have shifted the paradigm to a more synthetic, human-made material usage. Most of these materials now can be 3D printed and are eco-friendly. Thus, the absorption capacity and sample collection properties of swabs in various environments have become more efficient, depending on the material used [24]. The science behind water absorption of swabs depends on factors like chemical composition, microstructure, and surface polarity. The chemical nature of the tips of swabs exerts polar forces that attract the hydrophilic or any other groups that are present in samples [25]. Furthermore, 3D printing allows swabs to easily be designed to include more surface area to augment properties.

Furthermore, capillary action also influences this property [26]. Hence, pre-moistening with water or a binder allows the hydrophilic groups to latch onto the tips as the attraction forces increase [27]. With many advancements taking place in materials, the development of diverse materials continued and even enhanced these properties depending on the uses, as the difference in chemical properties of fibers influences the efficiency of sample recovery (Different materials used for swab manufacturing are shown in Table 1. Even though there may be many swab products of the same material in the market, each swab type is generally backed by specific scientific evidence or literature. All the primary materials used for making the tips of swabs are discussed as follows:

2.1. Cotton

It is one of the oldest materials cultivated since ancient civilizations. It has been used throughout history for several medical and commercial purposes [27]. It consists of repeating units of cellulose that contain hydroxyl groups, giving excellent absorption through hydrogen bonding [28]. The scanning electron microscope image from Fig. 2a depicts thin, long, and tightly wound fibers, which enhance absorption. During cellular testing in body parts, like nasopharyngeal tests, the hydroxyl groups between cotton and carbohydrates in cell membranes form bonds [28]. The forensics industry has done significant testing with cotton and also compared it to several other materials. Cotton swabs have excelled in DNA testing, and major swab manufacturing industries have always started with cotton due to its inexpensive and efficient nature. Bacillus anthracis spore recovery from steel surfaces for cotton was the highest with a mean of 93.9% [29]. Furthermore, bacterium like Escherichia coli and Staphylococcus aureus found in the environment have shown high amounts of DNA, and colony-forming units (ability to multiply under controlled conditions), which have been easily sampled by cotton swabs with accurate results obtained [30]. For other sample recoveries, scientists/researchers have found that pre-moistening the swab with water or chemicals, depending on the use, will aid [29]. The overall efficiency of pre-moistened cotton swabs was better than standard cotton swabs. Nonetheless, employing cotton swabs to this date has been scarce due to environmental issues involved; however, newer materials and designs that clients quickly manufactured while providing similar or even better results are now dominating this industry [31].

2.2. Rayon

It is made from cellulose (wood pulp) and heavily processed and hence classified as a manufactured fiber [32]. It can imitate the tactile nature of cotton, silk, wool, and linen [33]. Many researchers from the early 1800s tried to find the perfect way to fabricate a safe, suitable yarn. By 1913, Camille Dreyfus used acetate to make a seamless sample of a continuous yarn, which revolutionized the fabric industry. Electron micrograph images of rayon (given in Fig. 2b), reveal it, as a long, thin, and less dense fiber, which explains the high liquid absorption and retention capacity. The difference between using cotton and rayon swabs is that cotton contains growth inhibitors for a few bacteria due to the diffusion of fatty acids in liquid presence, and also because they leave cotton fibers on the extraction site due to being tightly wound. Whereas, rayon, on the other hand, is softer, more economical, and doesn't leave fibers on the substrate giving it an added benefit [34]. Having cellulose in its chemical matrix allows a higher rate of water absorption and surfactant, although it doesn't make it better than cotton but is just widespread in use. In an experiment conducted by Kathryn Harry et al. [25] in 2013, where water and protein absorption by swabs were compared, the mean absorption of rayon-flocked swabs was 17.1% for water and 16.1% for protein. In all tests (including culture studies of test organisms), the rayon swab was not a paragon swab material, but it was conventional enough to give legitimate results [25]. However, according to Comte et al. [35], in a comparison between flocked nylon swabs and rayon swabs, they both show no significant difference in the recovery of common respiratory bacteria [36]. On the development side, the Cell swab, a new type of rayon swab, was examined by Esposito et al. [34], which showed absorption and release of the sample liquid up to 1.3 and 3.5 times more than dacron swabs. There are many rayon swab kits available with different designs, which include desiccants or ventilation holes to dry the swab promptly, hence evaporating the extra water/liquid collected by the rayon swabs [37].

2.3. Polyester

It is a synthetic fiber made through non-renewable sources like petroleum, which comes from a chemical type called polyethylene terephthalate (PET) and contains esters (functional group). It comes in different grades, which are used to make products including relatively inexpensive clothes and bottles [38]. Polyester swabs were tested for biological material samples from different substrates by the forensic crime department, and it is quite efficient in collecting and releasing specimens. Also, the scanning electron microscopy (SEM) images (Fig. 2c and d) depict polyester with long and irregularly-formed fibers that leave fewer open spaces than cotton and rayon. Therefore, it is less efficient for extraction [29]. Additionally, pre-moistened polyester swabs show no difference from the same dry swabs in Bacillus anthracis spore recovery from non-porous surfaces. However, Mulligan et al. [28] noted that cotton and polyester

Table 1
Different materials used for swabs and their properties.

TIP MATERIAL	PROPERTIES	PURPOSE	Feasibility of Materials in 'AM'
Cotton	Absorptive, No quick-drying, Leaves fiber residue on most surfaces, Poor chemical resistance, and compatibility, Contains growth inhibitors for bacteria due to fatty acid presence, Inefficient in specimen release, Inexpensive	B, C	Has to be wound externally
Rayon	Highly absorptive, No quick-drying, No abrasion of fibers, Excellent chemical resistance and compatibility (except strong acids and bases), Mediocre in specimen release, Cost-efficient	B, C, F	Difficult to use in machines, typically wound externally
Polyester	Reasonably absorptive, quickly dries, No abrasion of fibers, Excellent chemical resistance, and compatibility (except strong bases), Good efficiency in specimen release, Cost-efficient	B, F	Can be incorporated into machines
Nylon	Reasonably absorptive, quickly dries, No abrasion of fibers (used as flocked) but leaves a residue on rough surfaces, Excellent chemical resistance, and compatibility (except acids and bases), Very efficient in specimen release, Expensive	B, F	Can be incorporated into machines
Polyurethane	Highly absorptive, quickly dries, No abrasion (foam-based), Excellent chemical resistance and compatibility, Efficient in specimen release, Expensive	B, C, F	Difficult to use as foam structure in machines, typically foam is attached externally

[B – Biological, C – Cleaning, and F – Forensic]

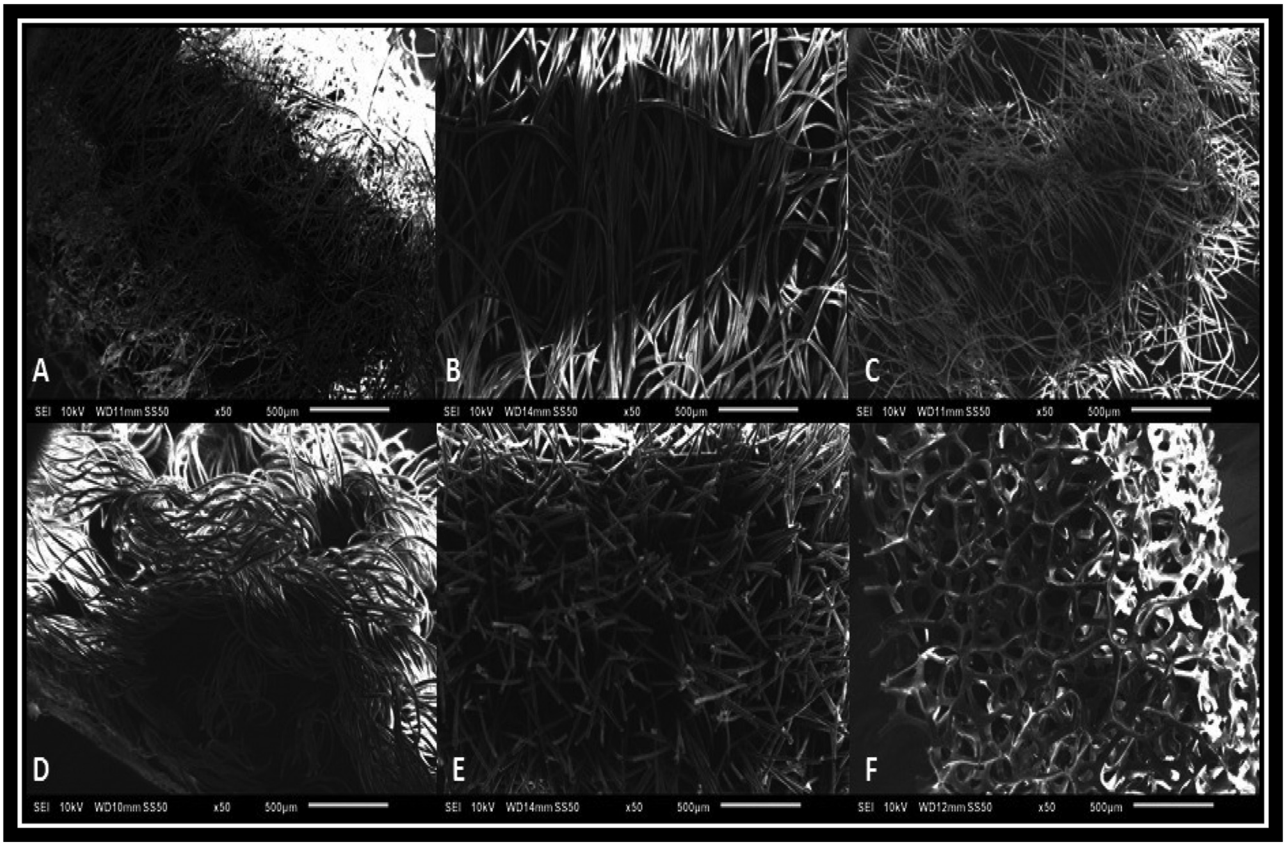

Fig. 2. SEM images **of different swab material tip portions.** a. SEM Analysis for cotton swab tip at 50 × 10KV and 500μm, b. SEM Analysis for rayon swab tip at 50 × 10KV and 500μm, c and d. SEM Analysis for polyester swab tip at 50 × 10KV and 500μm, e. SEM Analysis for nylon flocked swab tip at 50 × 10KV and 500μm, f. SEM Analysis for polyurethane foam swab tip at 50 × 10KV and 500μm. Reprinted with permission [38]. Copyright 2018, the Authors.

showed no significant difference in data collection for membranes. However, other studies from the same group suggest bonds formed in cotton and rayon are more robust than in polyester and acrylic, due to chemical compositions as seen with a 23% difference in range while Deoxyribonucleic acid (DNA) swabbing with water as a solvent [28]. Hence, proving DNA profiling is slightly better with cotton than polyester. Young et al. [9] found that the polyester swab was ranked 2nd in the collection and release for neat blood samples from surfaces like glass, pitted, brick, and wood with a range of 110 to 140 nanograms. Furthermore, biological specimen collection from rough, non-porous surfaces and touch DNA from smooth, non-porous surfaces were recommended for polyester swabs [9].

2.4. Nylon

It is the world's most commercially produced synthetic fiber. Being made from amide linkages, this thermoplastic has the most extensive variety of products in the market [39]. Nylon swabs were produced beginning in 2003 when the organization COPAN released flocked nylon swabs. Its advancement is such that in scanning electron microscopy (SEM) imagery (Fig. 2e), short fibers of nylon have split perpendicular ends, which provide improved surface area, surface tension, and microchannels for increased absorption and extraction, and recovery efficiency up to 48.4% [40]. Flocked nylon swabs absorb and release both cellular and cell-free material more effectively than comparator swabs after analyzing the sample recovery of infected cells [41]. For touch DNA, Hansson et al. [42] found flock nylon gave decent partial DNA profiles. CopanFLOQ swabs exhibited an active uptake and discharge of viruses and cells, which were additionally augmented in an Amies transport medium [15]. Furthermore, the high sensitivity factor for flocked nylon swabs proves them to be an excellent prospect as oral swabs for detecting pathogens and antibodies and storing them for further testing [15,39,41]. However, the main drawback of these tips is that swab material is left on the substrate of rough surfaces limiting its usability [9].

2.5. Polyurethane

It is an elastomer made by the condensation reaction of isocyanates with polyols. It was invented by Otto Bayer and Dieter Dieterich in Germany during World War II [43]. Due to its frequent use in foams and sponges, it was incorporated into swabs. As a natural sponge, these foam swabs allow the accessible collection and release of specimens. The SEM image (Fig. 2f) of polyurethane fibers displays a uniform open structure with a light density that corroborates its suitable absorption property. Spore recovery from the vortex and sonication extraction method gave it the highest percentage of 22.5% [29]. Young et al. [9] found that the Puritan foam swabs ranked 2nd in the absorption and extraction efficiencies of biological fluids and highest for the collection of 1.6 to 155 nanograms of biological materials from wood/porous surfaces. Furthermore, recovery of S. epidermidis bacteria and colony-forming unit (CFU)s were highest for foam swabs under close-to-reality conditions' [15,44]. Amongst different flocked swabs, polyurethane macrofoam again ranked 2nd giving 62% for protein, bacteria, and water absorption, whereas Puritan's Hydraflock was first [25]. However, the popularity of foam swabs was drastically reduced due to an incident in Wales, where the tips of the swab got detached from the stem and created significant safety issues for people [45].

3. Design

Swab design has evolved through the centuries, starting from the very basic stick-and-cotton type, all the way to a multi-layered synthetic swab. Each design had a purpose and need, discussed below (Different designs for swabs are shown in Table 2). The new design of swabs consisted of only a stick or tube usually made of wood with the absorbent covering at one of the ends or sometimes on both ends (As depicted in Fig. 1d). The handle part is called the stem of a swab.

The design was simple and very useful during the early days because back then, swabs were only used for cleaning ears, nose, or other sensitive tissues of the body. However, this simple design had its flaws. One such flaw was the potential damage to the eardrum, in response to counter this, some suggested installing flat discs under the absorbent covering at the ends. The size of the disc prevented the swab from entering the ear canal and therefore protected the eardrums [46]. Another problem was how to protect the tissue/inner ear skin from the stem in case it protrudes through the soft covering, which was resolved when a cushion was placed in between the stem end and soft covering to give some protection to the tissue [47,48]. But applying this solution proved to be difficult, because inserting a flat disc (As depicted in Fig. 1g) and cushion made the swab harder to manufacture, difficult to use, and inefficient.

Design formation using software like Solidworks, AutoCAD, and evaluation using the finite element method are the key parameters for the development of complex systems on a product level [94–98], and design for additive manufacturing serves as a foundation for developing lightweight products. Design for additive manufacturing (DfAM) is mainly dependent on the speed of the material deposition, optimization for shape and manufacturing process, and minimization of volume faction, and volume fraction is dependent on the voxel mesh optimization, and this produces optimized design and reduces the production time [96].

Nasal and nasopharyngeal swab testing are the two most widely used specimen-collecting methods for the SARS-2 virus. Swabs used for nasal testing are relatively smaller handles made of polystyrene and medium-sized tip made of flocked fibers. The process of collecting the specimen involves the insertion of anterior nare swabs into the nostril at least a centimeter deep with the tip touching the side walls of the nostril, the swab is rotated for about 10–15 s [86]. The process is then repeated for the second nostril.

Nasopharyngeal swab testing uses swabs that have a small miniature tip with ultrafine flocked fibers and a thin long flexible handle, breakable in the middle to make it easy to store/transport the collected specimen. Whereas for the nasal test the swab is inserted up to the nasal membrane. In nasopharyngeal swab testing the sample is collected from the upper part of the throat behind the nose, also called the nasopharynx [87]. The swab is inserted into the nostril parallel to the chin up to the point where resistance is felt. This testing requires precision and is only done by professionals. Although both testing methods give similar accuracy, they differ in their applications. Patients that felt easier to collect their samples by themselves and then deposit them for testing used AN swab and the testing method, as it was more comfortable and can be done without a professional [86].

Currently, the design of swabs could be complex and difficult to fabricate. However, 3D printing has allowed swab design to be complex, intricate, and specialized for suitable applications. Some of the different possible designs can be depicted in Fig. 1h and i.

3.1. Swabs with elongated tips

The next design introduced was called the cotton tip swab also known as the elongated tip swab (Depicted in Fig. 1d). In this design, the swabs were made with an elongated stem with a conical, outwardly flared hollow end. These ends made the tips softer and reduced the amount of material used, thereby reducing manufacturing costs. In this design, the stem is made of a flat cellulosic sheet [47]. Another essential feature of this design is that it was manufactured using die-cut paper, and hence less material was used for making the swab. These types of swabs found their use in the cleaning of ears, nose, baby care, and also for cleaning wounds.

Another enhancement to the expanded tips swab was to use a non-circular external cross-section configuration for the swab ends. The main reason for this improvement was that circular swabs could push the wax further into the ear canal rather than pull it out (As shown in Fig. 1f).

Thermoplastic material is usually preferred for manufacturing the stem. For the absorbent covering materials like cotton, or any other synthetic form material which can be made into the desired shape by pressurized heat treatment. To increase the rigidness of the wad

Table 2
Different designs used for swabs.

NAME OF THE DESIGN	INVENTOR	FUNCTIONAL FEATURES	APPLICATIONS	YEAR
Swabs with expanded tips	Bennet	Elongated ends, were outwardly flared and conical in shape. Softer, with less material required	Very helpful in the cleaning of ears, nose, or other sensitive tissues.	1998
Swab with an inserted disc	Schmerse, Jr.	A disc was inserted under the absorbent coverings to prevent the swab from damaging the ear canal. Much more difficult to manufacture.	Was used mostly for cleaning the ears and noses of children.	1992
Tip with a non-circular external cross-sectional configuration	Can	The shape of the tip was changed from a conventional round shape to a non-circular shape. This helped in removing the ear wax properly.	Used for cleaning ears and nose.	1987
Flocked design		Absorbent material flocked rather than attached directly to the stem or could be 3D printed as a whole. More absorbent than the default design.	Used for collecting cells for specimens.	
Nematodic swabs	V.P. Simmons	Swabs with multiple layers.	Used for collecting repeat specimens.	1961
NP and OP swabs		NP swabs are used for taking samples from the nasopharyngeal cavity and OP swab is used for taking the sample from the oropharyngeal cavity.	Used for detecting various viruses and diseases.	
Swab with an absorbent pad	Melcher & Speichert	Swab with a barbed removal stem attached to an absorbent pad or could be 3D printed as a whole.	Used for applying medication on wounds, cleaning wounds, or applying makeup.	1999

(absorbent covering found at the end of the stem), a stiffener-like starch is coated over the wad [13].

Besides cleaning, swabs found an application in metagenomic studies where they were mainly used for collecting biological and environmental samples [30]. This design consists of a cylindrical rod where one end is covered with a hydrophilic wad of fibers such as rayon or cotton. A hydrophilic material is preferred to increase the absorption of the specimens [49]. Adhesives were used to wrap absorbent material around the ends of the swab, thus creating the wad.

In this design, the cylindrical rod is manufactured using injection molding or 3D printing, with mostly plastic as a material. Due to this method, a sharp truncating cut was formed at the ends of the stem, which caused discomfort when inserting swabs into cavities [49]. To counter this issue, more absorbent material is glued to the truncated cut; this serves to reduce the discomfort for patients. For these reasons, the absorbent material is given a circular shape, which gradually becomes thicker towards the end. This design, due to increased thickness, provides comfort to patients but has its limitations. One such limitation is the oversaturation of liquid in the hydrophilic material of the wad which may cause inefficiencies in data sampling.

After the sample is collected, it is released from the swab for analysis. This is done simply by placing a petri dish and then gently spreading the swab over it. Even if this process is done carefully or repeatedly, it is not possible to extract the sample completely [49]. Additional problems regarding this design were the discomfort experienced by patients when the sample was taken from urethral or ocular cavities.

3.2. Flocked swabs

In response to the association with expanded swabs, flocked swabs were introduced. The significant difference between these and previous swabs was the method of attaching the absorbent material to the truncated cut, a process known as flocking, hence the name. In flocking, the fibers are placed perpendicular to the adhesive-coated surface of the tip in an electrostatic field [49]. The materials which can be used as an absorbent for flocked swabs are rayon, polyester, nylon, polyamide, carbon fiber, alginate, cotton, and silk. This design proved beneficial in the case of collecting samples of respiratory epithelial cells. Studies showed a two to three-fold increase in the cell yield during observation using the flocked design [41]. Furthermore, flocked designs can be easily 3D printed and are most commonly used for the testing of the SARS-2 virus.

3.3. Nematodic swabs

Another essential type of swab is a nematode swab. These swabs consist of three-layer short-length tape with each layer possessing slightly different physical characteristics (as depicted in Fig. 1e). As the inventor Vaughan P. Simmons [50] described in his patent, this swab worked well in samples taken for invasive parasites such as pinworms. These parasites tend to lay microscopic eggs around the anus of their host. For the best treatment to occur, a medical professional must take samples from that sensitive region daily.

Before this swab's invention, many unprofessional methods were attempted for sampling, including using cellophane tape wrapped around a caretaker's finger. This method was poor for collecting samples with integrity [50]. Thankfully, these days a multi-layered swab can be used for taking samples; in this nematodes swab, each layer uses different materials. The materials which can be used for making the top layer are cloth, vinyl, or any pliant sheet material. The essential requirement for choosing the material is cleanliness and resistance to fingerprints. The second layer is made of transparent pliant sheets; usually, cellulose acetate. The last layer is made of ethylene terephthalate, which serves to protect the adhesives applied to the middle layer. The layers are glued together using an adhesive such as polyisobutylene or any other rubber-based adhesive [6].

3.4. Swabs with absorbent pads

Absorbent pads in swabs served the purpose of applying makeup and medication. This type of swab usually came with an absorbent pad that was inserted into the stem part or handles. One of the prominent advantages of these swabs is the ability to go through autoclaving (a process used for making swabs sterile for medical uses). They are also cheaper to manufacture and more durable compared to other swabs. It consists of a rigid stem partially inserted into a removable pad (As shown in Fig. 1a). The pad can be made up of any material for retaining substances on its surface.

The stem has two ends, one in the user's hand, and the other inserted into the pad, as shown above. The end meant for insertion into the pad has barbed ends to stay (See Fig. 1c). These barbs can be made while molding or by using a cutting die [55].

The tips or wads underwent various changes in design, starting with the basic spherical form. However, the design was improved to prevent damage to the eardrum: A disc was inserted under the absorbent covering, changing the shape of the tip to resemble the letter D (See Fig. 1g).

A significant improvement in swabs tips came when one inventor suggested the use of a non-circular cross-section for tips. This solved the issue of wax being pushed deeper into the ear canal while cleaning. Swabs used for applying medicine or makeup tend to have a more cuboidal shape for the tip, usually called an absorbent.

4. Traditional swab manufacturing

Manufacturing is a more significant challenge than designing a product as it should be done cost-effectively and efficiently. In traditional swab manufacturing, the main parts consist of two processes: The first one is the manufacturing of the stem, and the other one is placing the absorbent tip onto the stem. Over the years, scientists and engineers have tried to make a fully automatic machine with different workstations for manufacturing swabs rapidly and on a large scale. The process of mass-producing swabs began in the late 1980s when an inventor suggested manufacturing swabs with a non-circular exterior configuration [13]. So, this swab is made with a non-circular external configuration, which helps it to overcome problems like pushing ear wax deeper into the ear canal rather than clearing it out (Fig. 1f).

4.1. First process: pressurized hot rolling

The basic idea behind manufacturing this type of swab is to give an oval shape to the cotton wad and then compress it under heat in a specific mold, to make it into the desired shape. The stem of the swab is usually made of thermoplastic material, and particular temperatures are set on these rolls for the softening of the thermoplastic material. Additionally, for applying the pressure to deform the stem and wad assembly, calendaring rolls are used. After the application of pressure under heated conditions, permanent deformation is observed in the shape of the stem-wad assembly. For making different shapes, different calendaring rolls with different cavities or openings are used [13].

4.2. Second process: die-cutting

In the year 1998, inventor Robert Bennet provided improvements in elongated cotton swabs, which were manufactured by only using a single flat cellulosic sheet. Fig. 3a shows the process in which the die-cut paper is used for the manufacturing of the stem and tapered ends of the swab. After preparing the sheet, as shown in Fig. 3a it is rolled

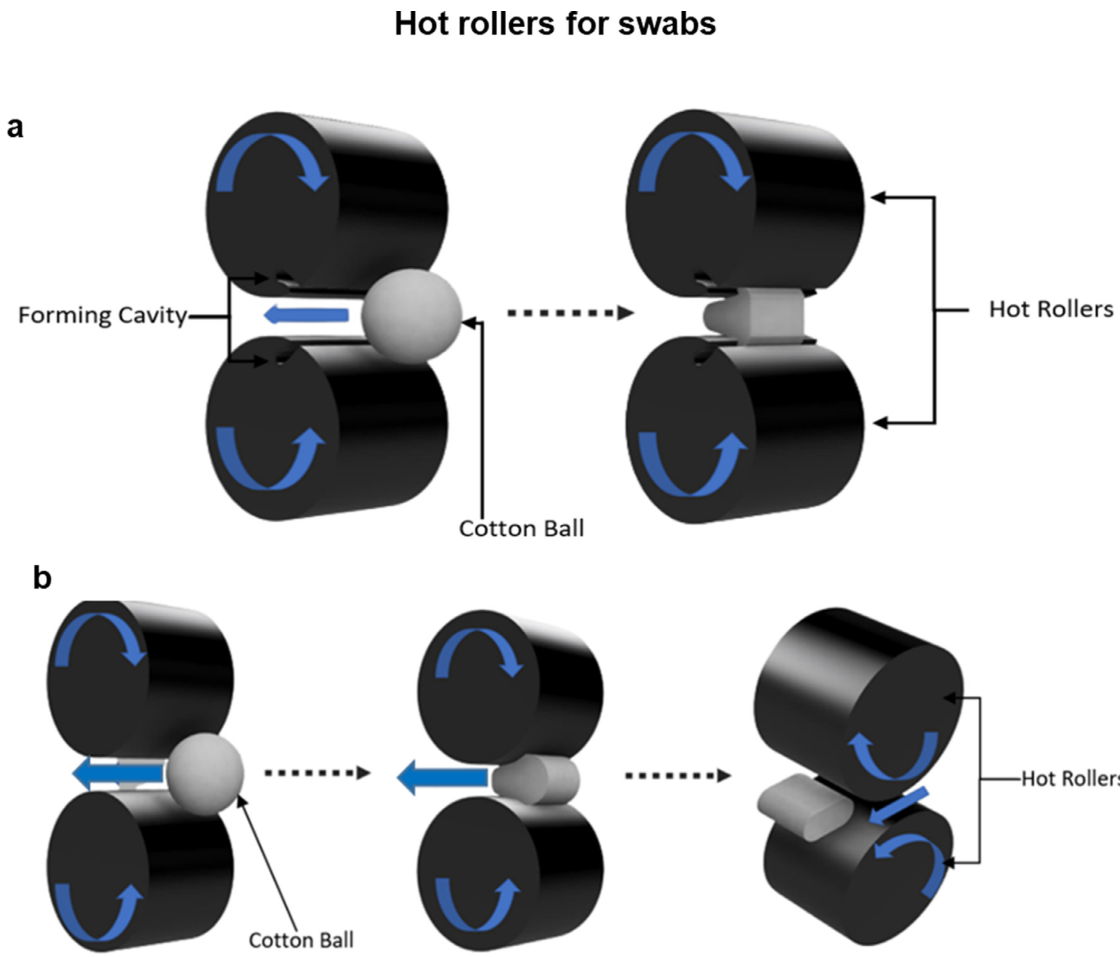

Fig 3. Hot rollers for swab manufacturing. a. For non-circular shape to the swab's tip. b. An advanced version of the hot roller process where different shapes with cavities are made.

to give a stick shape to the swab. During this process, adhesives can be used to maintain the shape. In the last step, a spinning mandrel is used to provide the outward projection to the end [47].

4.3. *Third process: a fully automatic multi-station system*

With the increased use of swabs in the sampling of specimens and clinical studies, it became a necessity to sterilize swabs before usage. To fulfill this need, a highly durable swab that can also be autoclaved was invented [55]. This swab consisted of a stem or rigid holder and an absorbent pad with a hole in it so that the barbed end of the stem can be fitted inside the pad. The barbs can be made by die-cutting or molding, and the pad is usually made by molding. Tips are made from foam plastics like polyurethane. The manufacturer decides to make a mold with or without slits in the pad that are used for attaching the stem. If done without the slits, then it can be formed later by burning hot electrodes or by cutting using a knife. A fully automatic method for making swabs is also shown in Fig. 3b.

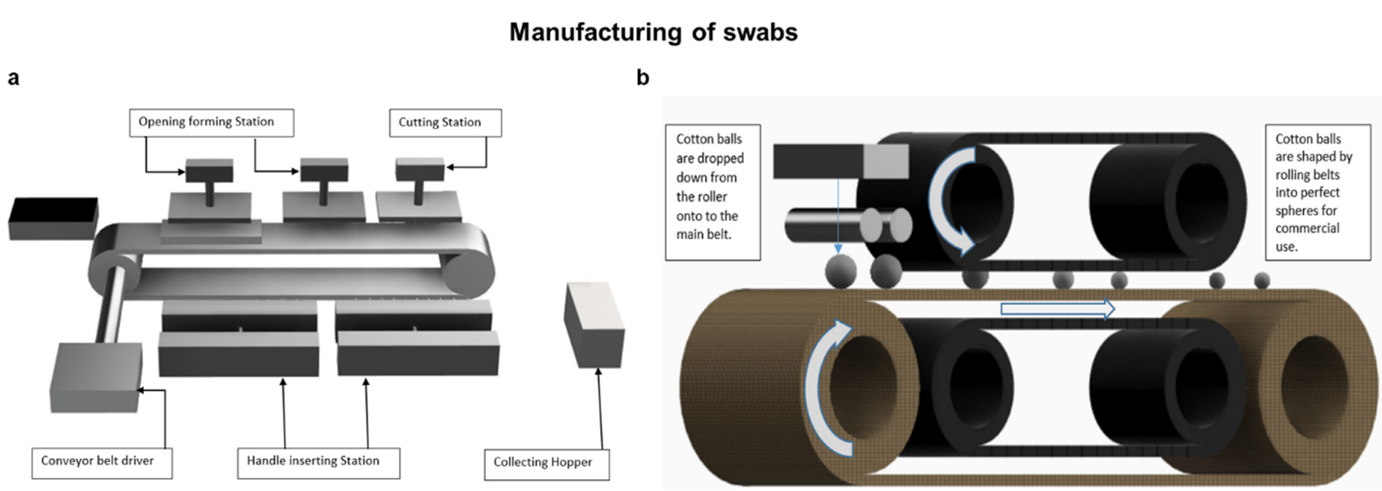

Fig. 4. Manufacturing machines for Swabs. a The diagrammatic view of a high-speed system for manufacturing swabs. **b.** Schematic of Murray's process for manufacturing swabs by using a cotton dispenser and 2 shaping bars.

The depicted machine consists of 4 regions: a pad-forming station, an opening-forming station, a handle-inserting station, and a cutting station, all attached to a conveyor belt. During the first step at the pad-forming station, a pad with the desired dimensions is used. However, the length is decided according to the plurality of the number of swabs being made. This is then passed onto the opening-forming station through a conveyor belt, where the pad (formed in the previous step) is automatically stopped and held in its place by using a flat clamp powered by a hydraulic actuator. While being held at the clamp, hot electrodes are moved into the pad using a piston mechanism, and the slits are formed in the pad to make a pathway for the handles. After this step, the pad is moved to the handle-inserting station, which uses a similar mechanism as the previous station. Here, the handles are inserted into the slits, and the pad is transferred to the cutting station. At the last station, multiple knives are placed to cut the pad into individual swabs using pistons. The obtained swabs are then packed and shipped as required.

4.4. Fourth process

In the year 2005, inventor Liam Anthony Murray [56] patented a fully automatic machine used for mass manufacturing swabs. This machine consists of 5 stations and a conveyor belt [56]. At the first station, individual stems are placed on the conveyor belt and clipped into place. At the next station, an adhesive is applied to the ends of the stems. At the third station, buds of the desired material (typically cotton) are applied to the stem. A coil of cotton is also obtained from the bale and is looped adhesively onto the coated ends of the sticks. At the next station, the cotton buds are given a proper shape using 2 shaping bars. The shaping bars travel faster than the conveyor belt, as it helps in reducing the tailing associated with a drag of cotton strands from the buds. Lastly, at the fifth station, defective swabs are removed, and the rest is forwarded to the packing assembly [56].

4.5. Injection molding

This pandemic has made it evident to the public, how fragile global supply chains can be in these crises. A shortage of important clinical supplies used for the detection and treatment of covid like nasopharyngeal swabs was observed [88]. A study by [89] put forth a new design manufactured using injection molding for nasopharyngeal swabs.

The paper [89] describes the development of a single component of the nasopharyngeal swabs also mentioned as Grooveswab, composed of medical grade polypropylene, mass manufactured using injection molding techniques. These swabs consisted of a non-absorbent stacked-ring structure which was inspired by cat tongue papillae that allowed it for efficient and comfortable collection of viscous mucus samples and faster release into the collection medium compared to traditional swabs [89].

Along with the absorbent pad, the swab also has a handle and a flexible neck. These nasopharyngeal swabs can get difficult to design due to their specific design and geometry based on the mold design, tolerances, and undercuts. The shortage led to various attempts to develop nasopharyngeal swabs solutions using 3D printing swabs [8−11,90−92] as it doesn't require complex multistep manufacturing as compared to other methods.

This is a relatively recent way of production of swabs and is sometimes preferred over 3D printing as it allows higher scalability for mass production purposes. In this process, the swab handles (shaft) are injection molded vertically into a mold, and a simple and efficient tip design is utilized. Injection molding has already been used for manufacturing medical devices; it offers the lowest cost per part for mass production. And with most of the infrastructure already available globally to produce low-cost nasopharyngeal swabs which will provide better availability and versatility in the clinics but also use a simpler manufacturing process for the masses.

5. Clinical applications

The usage of swabs has evolved within the past few decades [57] from being used just for cleaning, they now have an abundance of applications, including DNA testing [9,37,58]. The rise of the additive manufacturing industry has increased the manufacture and application of swabs.

This development led to increased application for cleaning wounds and applying medicine [55]. Additionally, researchers from various disciplines began to notice the swab's ability to collect samples and specimens [50]. For example, they can be used to take samples of pinworm eggs for the study and monitoring of the parasite [50]. A study from McMaster University showed that swabs are very effective in taking specimens for acute respiratory infections, mostly flocked and rayon swabs, which are used for this particular purpose, but flocked swabs have been proven more effective when compared with rayon swabs [41]. In the early 21st century, the use of swabs increased for taking specimens that were used as a replacement for nasopharyngeal swab aspirates because, in regular day-to-day clinical practice, it is a less harmful, more feasible, and inexpensive method to take samples [59]. Swabs are now widely used for the detection of viruses and bacteria [60]. The reason for using swabs is that they are cost-effective, easy to use, and effective in adhesion quality.

Mentioned below are some of the viruses, bacteria, and other tests in which sterilized swabs have been proven very useful:

- For determining the presence of candida Albicans in vaginal infection
- For identifying alpha and beta-hemolytic streptococci and staphylococci
- For detecting bacterial growth in urine
- For identifying staphylococci [61]
- For identifying proteus [62]

For the following viruses, nasopharyngeal swabs (NP) are used.

- Detection for influenza B [63]
- Detection for parainfluenza virus 2[51,52]
- Detection for parainfluenza virus 3 [53,54]

For the following viruses, oropharyngeal swabs (OP) are used

- Detection for influenza A [64]
- Detection for 2009 H1N1 [65]
- Detection for adenovirus [54]

There are many more viruses that can be detected using swabs, but the viruses, as mentioned earlier, have shown better detection probability using specified swabs. Recent studies have shown the use of swabs for forensics studies and in detecting traces of explosives in fingerprints. For this, the routine cotton swab is converted into a surface-enhanced Raman scattering (SERS) substrate [66].

In the COVID-19 pandemic, swabs made using additive manufacturing are used for the detection of the SARS-2 virus [64]. This application has helped the testing process for COVID-19, as it is cost-effective, easy, and fast [67].

6. Present technologies: manufacturing swabs using additive manufacturing

In the last few months, additive manufacturing has emerged as an effective manufacturing technique in the current COVID-19 pandemic. As testing for the virus (Fig. 7) is conducted around the world, it resulted in a shortage of test swabs (Also different additive manufacturing techniques used for swabs are shown in Table 3) [68]. So, the fabrication of swabs using additive manufacturing has proven beneficial, due to it requiring fewer laborers. Additive manufacturing processes like Stereolithography apparatus (SLA) printers are used widely for this purpose, and they are used to produce the stem part of the swab on which absorbent coverings are applied later. The material used for the stem is usually an autoclavable biocompatible resin [69,99], as seen in Figs. 5 and 6. The advantage of using the additive manufacturing process rather than the other process is both quantitative and qualitative [70]. Additive manufacturing involves the following process after the design is finalized, (a) conversion of the design file into an STL file (b) import of the STL file for manufacturing (c) Material selection (d) Setting of the AM parameters for manufacturing.

The technologies that additive manufacturing hold for us, in the future, are purely dependent on the extent of our imagination. Even the way that swabs are manufactured during this pandemic has been revolutionary. Many organizations like Form labs, Origin, Envision Tech, HP, and others have helped ameliorate this technology and have helped in developing different machinery [70,71]. Currently, these are some of the largest producers of 3D-printed swabs that were approved by the National Institutes of Health organization [72]. Even more biocompatible materials are being made for non-toxic, durable, and flexible swabs, Fig. 6**.** One such example is surgical guide resin, a biocompatible and autoclavable resin used to fabricate dental guides and surgical implants. These swabs are now being made through select carbon digital light synthesis printers, and HP's multi-jet fusion technology printers [73], Fig. 5.

Additionally, a partnership between Mark Forged (manufacturers of 3D printing systems) and Neurophotometrics (a fiber photometry company) has produced a Fiberflex Rayon material and additively manufactured a nasopharyngeal swab. This swab is beneficial for gathering viral particles and may diminish the number of incorrect swab tests [71]. The swab is fabricated using a nylon base with rayon fibers wrapped around the tips for efficient absorption at the given area for sampling. Validation of these swabs has been done by the Institutional Review Board (IRB) at the University of California, San Diego, and Rady's Children hospitals. (The top portion of the shaft is exposed to rayon fibers which are flocked onto the thin stem of the swab shaft) [74].

New technical innovations like HP's multi-jet fusion printers have allowed a revolutionary design for nasopharyngeal swabs through companies like Fathom and Abiogenix. This design and specific material allow the swab to be extraordinarily flexible and sustain torsion during testing [19], Fig. 6f–h. It also has a break-point area that allows easy storage in mediums for further testing. The design is nothing like flocked swabs but a twisted protruded spiral that traps the epithelial cells between the crests and troughs [19]. The same collaboration has been done with 3D printing companies Origin and Stratasys, which have produced over a million NP O1 Swabs with similar properties and quality as the Fiberflex but a different design [69].

The principal reason for this paradigm shift to additive manufacturing is based on the fact that this process is automatic and doesn't require much manpower, hence adhering to the government restrictions/protocols and safety from the SARS-2 virus. When compared to mass production techniques, which require immense skilled labor, this process has provided an alternative to production directly from design with brief delivery time and complex designs.

6. Experimental testing

The mechanical test is designed for the clinical use of the nasopharyngeal swabs and to evaluate the potential failure modes. The mechanical analysis includes testing the swabs in tension, torsion, and flexure to evaluate the following conditions respectively, pulling out of the nasopharyngeal space; catching an obstruction when being rotated within the nasopharyngeal space, and bending when inserted into a nasal cavity [92].

7. Future perspective

The inventions mentioned above provide extensive scope for the future of swab usage. Swabs are being applied in new ways all the time, like the SERS Q-tip being used to detect traces of explosives on fingerprints. Traces of explosive materials on fingerprints up to a femtogram was detected by recently developed SERS Q-tip swabs. This application could prevent acts of terror and extremism [66]. Additive manufactured swabs could acquire new built-in analogous technology, like in pregnancy test kits, which immediately detect viruses or other samples for which they are being tested. After reviewing a variety of swabs, their designs, materials, and manufacturing, we have found that flocked designs manufactured using additive manufacturing among swabs have a significant influence on studies and in the market.

The COVID era has brought a great progression in the evolution of technology, especially manufacturing. With more than a million cases a day, swab testing requirements had been increasing rapidly. On top of that, existing technologies for manufacturing swabs had become less feasible to use due to safety concerns of individuals and the spreading of Covid cases. This brought immense pressure on the medical professionals as swabs were getting scarcer and testing had become expensive. From the business perspective, this was a disaster as the supply chains had disrupted due to less manpower and a shortage as working professionals were bound by government regulations of safety issues of COVID protocols.

The additive manufacturing industry bridged the gap between researchers, designers, and industry workers as it allowed production to be safer, faster, and more qualitative. This allowed more and more on-time deliveries of swabs to hospitals, stores, and government testing sites.

Table 3
Additive manufacturing technologies used for COVID-19 swabs.

Additive Manufacturing type	Manufacturer	Swabs Material and Type	Refs.
FFF	AMIST and the University of Louisville	NP swab made of Pliable resin material	[68]
SLA	Stratasys and Origin	NP swab made of Biocompatible Photocurable Resin	[69]
SLA	Formlabs	NP swab made of Surgical Guide Resin	[73]
FFF	Markforged and Neurophotometrics	NP swab made of Fiberflex Rayon	[71]
MJF	Abiogenic and FATHOM	NP swabs made of biocompatible, flexible plastic	[74]
SLA	Michigan Technical University	NP swab made of PETG	[75]
FFF	Carbon	NP swan made of a biocompatible material, KeySplint Soft Clear	[76]
SLA	EnvisionTEC	NP swab made of E-Guide Soft C-29C resin Non-cytotoxic, not a sensitizer, non-irritating	[43]
MJF or Inkjet Printing	HP	NP swabs made of nylon-based material	[77]

FFF- Fused Filament Fabrication, SLA- Stereolithography Apparatus, MJF - Multi Jet Fusion, NP- Nasopharyngeal swabs, PETG- Polyethylene terephthalate glycol

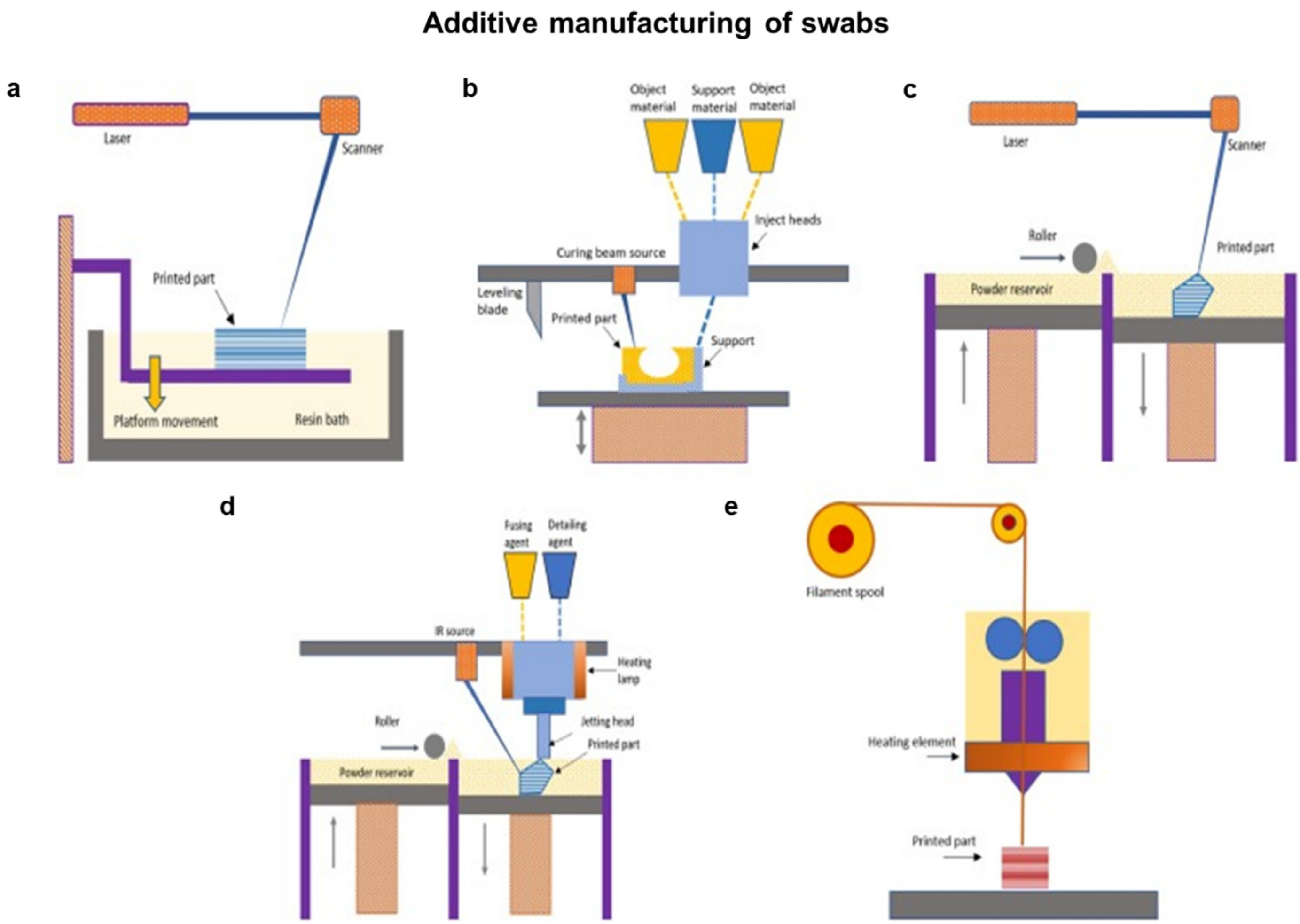

Fig. 5. Five major Additive manufacturing techniques used for making 3D printed products during COVID-19: a. SLA: Stereolithography Apparatus, b. MultiJet (or PolyJet) Printing, c. SLS: Selective Laser Sintering, d. MJF: Multi Jet Fusion, e. FDM/FFF: Fused Deposition Modelling/Fused Filament Fabrication. Reprinted with permission from [100].

Implementation of AM technology allows easy fabrication of prototypes and manufacturing models. This bridges the accuracy gap between prototypes and production models. This is an incredible achievement for manufacturers and customers as they'll be able to experience the product as it was prototyped [78]. Furthermore, the cost of materials and production significantly decreases in the long term, even though the initial investment in machines would be high [69]. Recently, due to the development of the do-it-yourself (DIY) community in the additive manufacturing field, the applications in the field of additive manufacturing have increased significantly. One example is the production of organic material for medical testing.

Furthermore, the research on the additively-manufactured heart was unveiled by Professor Tal Dvir from Israel, in 2019, and the material used is called "bio-ink. Though the size is that of a rabbit's heart, further research is being conducted to make a fully functional 3-D printed human heart (fully biocompatible with the body) [79]. This speaks to the current impact of AM in the manufacturing world and applies to our discussion of swabs. There is a vast amount of potential for AM in the world today [80,81]. There could also be a plethora of biomedical applications that revolutionize organ donation and replacement [82–86].

8. Conclusions

The studied swabs among cotton, rayon, polyester, nylon, and polyurethane depict distinctive results based on their performance in various situations and extraction from different substrate surfaces. SEM images gave good detail to the fiber descriptions, which provided information about the absorption properties of materials. Swab materials like rayon and nylon have superior absorption and release properties, which enables their usage in wide-ranged applications Furthermore, these materials can be used in 3D printers which makes them useful for fabrication by additive manufacturing. The flocked design invented in the 21st century has not only made sampling efficiency better but also has become a polymath in all sampling scenarios due to its enhanced surface area design. The operations of these swabs in several situations as nasopharyngeal swabs, oropharyngeal swabs, and even buccal swabs allow good specimen collection and accurate result determination. These swabs are now mostly 3D printed due to their complex design as traditional manufacturing techniques are expensive and inaccurate. Aggregating the statistics from the manufacturing of swabs, the sudden rise in Additive Manufacturing/3D printing technologies has augmented product quality, as discussed in the present technologies. Design for additive manufacturing (DfAM) is dependent on the speed of the material deposition, optimization for shape and manufacturing process, and minimization of volume faction, and volume fraction is dependent on the voxel mesh optimization, and it helps in reducing the production cost, furthermore, optimizes the overall design configuration. The COVID-19 pandemic has aided to achieve better and more efficient swabs, like Fiberflex Rayon utilizing additive manufacturing. 3D printing could bring many revolutions to medicine and the environment due to its functionality, lesser production time, and accurate design of the intended product.

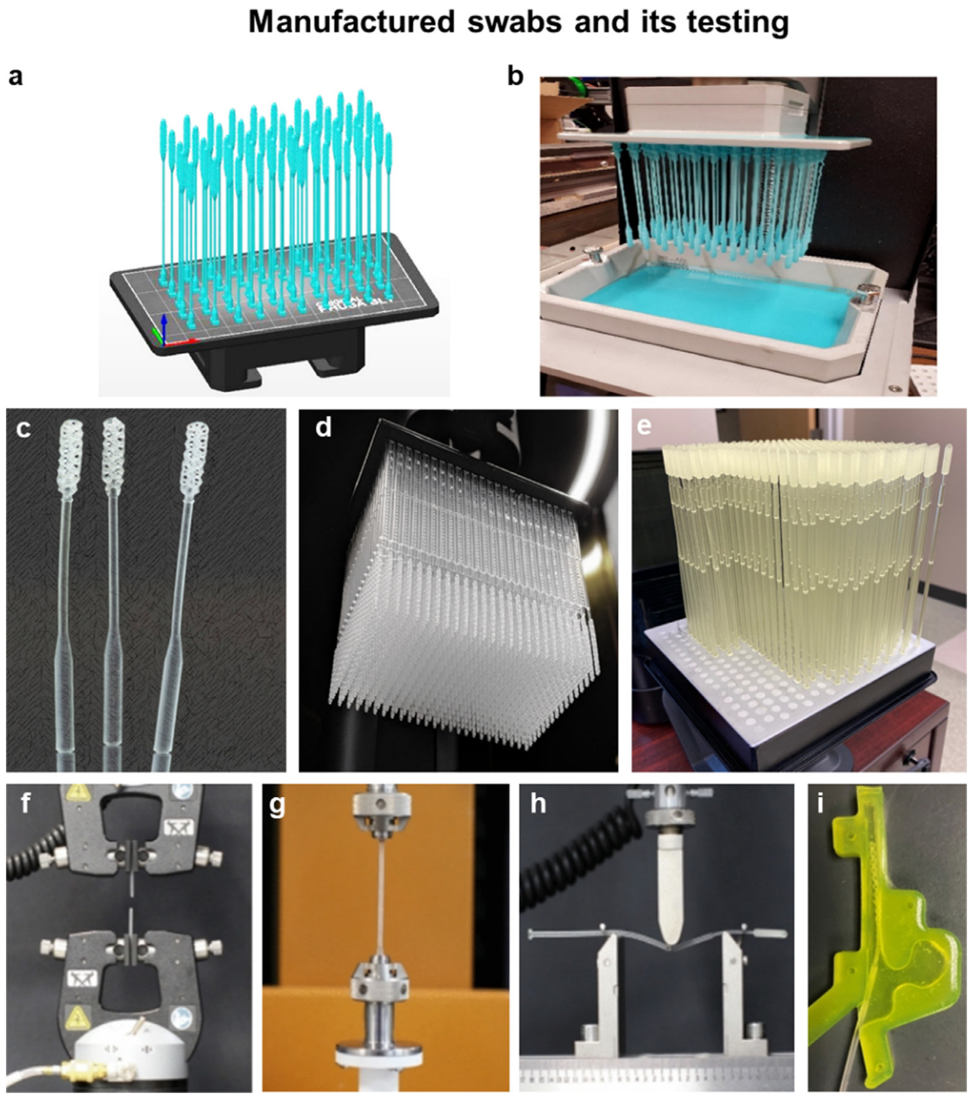

Fig. 6. Manufactured swabs and their testing. a and b. Swabs design and manufactured swabs, respectively. Reprinted with permission from [99]. **c.** a closeup of three NP sticks that depict the intricate geometries of the instrument. **d.** a batch of the NP swabs printed by Carbon3D's DLS technology. **e.** Formlabs manufactured a variety of NP swabs with the SLA technique of vat polymerization. Reprinted with permission from [100]. The images of the swabs in the different test setups. **f.** Tensile. **g.** Torsion. **h.** Break and **i.** Abrasion. A similar nasal cavity mold as that shown in i was 3D printed and used for the combined torsion and flexure test. Reprinted with permission from [92].

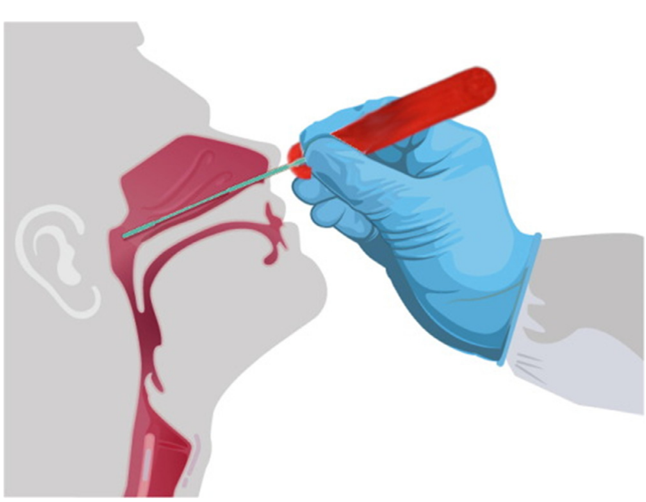

Fig. 7. The usage of the open-source nasopharyngeal swab and press-fit handle. Reprinted with permission from [99].

Compliance with ethical standards

Research involving human participants and/or animals

This research did not involve the participation of any humans or animals.

Consent for publication

All authors consent to the publication.

Availability of data and material

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CRediT authorship contribution statement

Vedant Vashist: Data curation, Methodology, Validation, Writing – original draft. **Neil Banthia:** Data curation, Formal analysis, Methodology, Writing – original draft. **Swapnil Kumar:** Formal analysis, Writing – original draft, Writing – review & editing. **Prajwal Agrawal:** Conceptualization, Funding acquisition, Resources, Supervision, Writing – review & editing.

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