From Vision to Reality in Face of the Pandemic – The Transformation of the Israel Defense Forces Forensic Lab into a COVID–19 Detection Lab

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ABSTRACT

The COVID-19 pandemic reached the Israel Defense Forces in the beginning of March 2020, and an urgent need to detect cases arose. Within a week, the IDF's Medical Corps retrofitted its forensic laboratory to perform SARS-CoV-2 rt-PCR tests. Multiple sites were deployed to perform the tests, including a mobile unit that performed them at the bedside of non-ambulatory soldiers. This report will describethe process of this unique effort.

Introduction

COVID-19 was first identified on December 31st, 2019, in the city of Wuhan in central China. The patients most notably presented with clinical symptoms of dry cough, dyspnea, fever, and bilateral lung infiltrates on imaging [1].

The causative agent was identified from throat swab samples collected by the Chinese Center for Disease Control (CCDC) and was named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The disease was named COVID-19 by the World Health Organization (WHO) [2,3].

On the 30th of January 2020, the WHO declared this outbreak a public health emergency of international concern which poses a high risk to countries with vulnerable health systems. The spread of the COVID-19 pandemic may have been delayed by early detection, isolation, proper treatment and contact tracing [4, 5].

In the midst of the COVID-19 pandemic in Israel (March 1st, 2020), the first case was discovered in the IDF. Dealing with infected military personnel requires different measures and resources in order to avoid the risk of compromising national security. Standard army life, where soldiers are in close contact with each other and train with multiple units, is naturally a platform for infectious diseases to spread easily. The harmful potential of a pandemic spreading within the ranks of the IDF must not be underestimated. In order to avoid such an outbreak, it was clear that the IDF needed to develop the autonomous capability to perform the entire testing process – a call center to approve tests, sampling capabilities, a detection lab and a results delivery system.

The extremely high infectivity of the virus called for quick identification and isolation of infected personnel in order to limit the outbreak [4, 5].

This entire process needed to be operational as well as validated and approved by the Ministry of Health, creating an functional IDF SARS-CoV-2 lab, within 7

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days. The limited time and resources resulted in the formulation of a unique solution.

Within a time frame of 48 hours, the following process needed to be possible in entirety: a call is received at the call center, a sampling unit is sent to the soldier's home or army base (alternatively the soldier is referred to one of our stationary sampling stations), the sample is sent to the lab, both extraction and PCR are performed, and the results are delivered.

Method of Detection

The nonspecific nature of the clinical presentation of the disease required an alternative method of detection that is accurate and efficient. Detection became essential in order to prevent the rapid spread of the virus and thus the danger of harming Israel's defense capabilities.

Given both the specificity and the early appearance of viral extractions, molecular (genetic) methods used on respiratory specimen are the gold standard for detection of the virus.

In the analytical stage, real time reverse transcription-PCR (rt-PCR) assay is considered the molecular test of choice for the diagnosis of SARS-CoV-2 [6]. In the post-analytical stage, test results should be carefully interpreted using molecular and clinical findings [7].

Nucleic acid tests for infectious diseases are primarily based on amplification methods that use primers and probes designed to detect specific organisms. Because prior knowledge of nucleic acid sequence information is required to develop these tests, they are not able to identify unanticipated, newly emergent, or previously unknown infectious organisms. Broad-range polymerase chain reaction (PCR) methods provide an alternative to single-agent tests. By amplifying gene targets conserved across groups of organisms, broad-range PCR has the potential to generate amplification products across entire viral families, including COVID-19 [8].

Sampling

The laboratory isolation sequela begins with the pre-analytical stage, collecting the proper respiratory tract specimen at the right time from the right anatomic site (oropharynx, nasopharynx or both). As part of the IDF's full pandemic-related strategy, medics were trained for the mission of sampling. At the beginning of the pandemic, the sampling process was based on mobile teams, with the sampling performed in the patients' units or homes and all samples delivered to one central lab. Later on, in order to deal with the growing demand for sampling, the IDF deployed stationary sampling points, working in the form of drive-ins and walk-ins. Medics, whether operating in patients' homes or in drive-ins, utilized protective personal equipment (PPE). In this procedure, the sample is taken from 2 anatomic regions (oropharynx and nasopharynx) using two different swabs. After collection, swabs are placed in a viral (universal) transport medium and inside protective packaging for rapid transportation to the clinical virology laboratory, under refrigerated conditions.

Analytical Phase

The IDF COVID-19 laboratory was created in one week, on the foundations of a DNA forensic laboratory established in 2015.

Since the beginning of the pandemic, it has been a necessity to develop autonomous military capabilities for SARS-CoV-2 detection. Relying on the civilian laboratories would have led to a lack of control of the number of tests performed for the army, as well as a natural conflict between civilian health protection and the needs of the army. Prioritizing military test results over civilian ones for operational reasons would have become impossible. Waiting time was speculated to be prolonged, costs higher, and data analysis absent [9].

In order to transform the DNA forensic laboratory into a SARS-CoV-2 detection laboratory, the following procedures took place:

> Reversing the cleanroom pressures
>
> Reprogramming of the STARlet Hamilton Robot
>
> Identifying a compatible PCR
>
> Choosing chemical reagents (for extraction and PCR set-up)

Cleanrooms used for DNA identification are categorized as positive pressure cleanrooms. Positive air pressure means the cleanroom is "pumped up" with more filtered air than the surrounding space. The air escaping the room prevents contaminating particles from harming the DNA sample processing. It is important to note that the air escaping from doors, ceilings, or walls is not a hazard for safety and does not cause any health concerns.

Considering the danger of spreading the coronavirus,

it was essential to flip the direction of the airflow. Within 48 hours of the start of the operation, the cleanroom was redesigned and transformed into a BSL P-3 bio-hazard containment lab, with specific negative air pressure levels and automatic pressure control with 100% exhaust through a HEPA filter system.

Anticipating the exponential increase in the need for coronavirus tests, it was clear that the IDF coronavirus detection lab should rely on automatic liquid handling workstations. The fact that there was already a Hamilton STARlet available in the DNA lab, combined with the prolonged waiting period for any other liquid handling system on the market, dictated the course of action: redesigning and reprogramming the existing Hamilton robot to execute the extraction and PCR Prep stages of the sample processing. Proving more complicated than expected, this most critical process, including the verification and validation of the results, extended into the 72-hour range. In the weeks that followed, more robots were purchased, tripling the capacity of the lab.

According to the Israeli Ministry of Health guidelines, The Allplex 2019-nCoV Assay (Seegene, Seoul, South Korea) was the kit of choice (for both extraction and PCR preparation), and for ease of use and compatibility, the PCR of choice was the Bio-Rad CFX 96 with the complementary Seegene software.

The Allplex 2019-nCoV Assay (Seegene, Seoul, South Korea) was designed for amplifying three viral targets: the E gene (specific of the subgenus Sarbecovirus) and the N and the RdRP genes (both specifics of SARS-CoV-2). The first assessment of its performance by the manufacturer demonstrates a specificity of 100% and a detection limit of 100 RNA copies/PCR reactions [10].

After the completion of all four steps, the facility and all working protocols and personnel were examined by the Ministry of Health. Upon receiving the state's approval, a validation process was carried out using pre-analyzed samples from the Ministry of Health central laboratory. After completing this process, which took exactly one week from beginning to end, the IDF's COVID lab became one of the first operational labs in the state of Israel.

The IDF developed an independent route of supply of chemicals, to avoid being a burden on the public health system and enable a quick response in times of supply shortage.

For the first few weeks, this workflow processed about 400 samples a day. Afterwards, when the new equipment arrived, it was cloned (creating two separate lines of sample handling), doubling the lab's capacity. The lab operated until March 23rd, 2021, and processed almost 140,000 samples in total. The working hours varied between 18 and 24 hours a day, according to demand. In times of peaking demand, the lab operated through the weekends. In a 12-hour shift, up to 11 staff members occupied the different stations of the lab. Additional personnel were needed for logistics and maintenance.

Having no medical advantage over the cheaper and quicker PCR detection, no sequencing was performed "in-house". As part of a large-scale study intended to identify the different variants of SARS-CoV-2, samples were sent both to the Shaare Zedek Medical Center and to the Ministry of Health's central lab – both identifying, among other strains, a unique "Israeli army variant".

During the first few weeks of operating the lab, solutions such as the GeneXpert were not available. At a later stage, when GeneXpert-like systems became available, there was no real excuse for using such a system in a lab that produces results within 2 hours and 40 minutes via conventional systems. Nevertheless, wanting to expand the capabilities of the lab, quick PCR systems were used, albeit mainly in situations when the number of samples was too low to operate the Hamilton.

Concluding Remarks

It was Hippocrates who claimed, "Drastic times call for drastic measures" (paraphrase). The decision to transform the IDF DNA laboratory to a SARS-CoV-2 detection lab was creativity at its best. This ambitious project was planned, executed and validated within a week, in the same manner that the army carries out operational missions. Alternative solutions would have probably been more time-consuming, expensive or ungainly. To the best of our knowledge, no other forensic DNA lab in the world was utilized in this way during the COVID-19 outbreak. As we gained more experience in dealing with this pandemic, the decision proved itself to be right; thanks to the IDF SARS-CoV-2 detection lab, more than 30,000 samples from all security organizations in the state of Israel were analyzed from March 2020 until סיוון-תמוז ה'תשפ"א

2020, which makes it one of the most efficient labs in Israel.

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