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HIGH TECH IN LOW-RESOURCE SETTINGS

CONTENT

HIGH TECH IN LOW-RESOURCE SETTINGS AND VICE VERSA

Technology is changing fast, and many of the innovations developed and applied in other sectors have found their way to the field of medicine. Some examples include the use of m- and e-health in healthcare prevention and treatment, such as the application of mobile technology in the promotion of medication adherence, and 'e-Estonia' where in 2009 the country decided to fast track the use of electronic solutions in many sectors, most notably in the health sector. The Estonian nationwide Health Information System (EHIS) now contains all health data of every Estonian resident from birth to death, allowing each citizen and health provider to access an e-patient portal containing medical data, prescriptions and medical images. Besides the obvious direct practical uses, these data form the basis of many of the country's health policies.

Many of these technological advances enable more accurate diagnosis, including imaging. Though perhaps not novel, they may include redefining its original application, such as the use of ultrasound. Here, developments in high-income countries (HICs) and low- and middle-income countries (LMICs) run in parallel; simple protocols enable clinicians to do bedside ultrasound leaving the more difficult imaging to the radiologists, thus saving cost and time.[1] Another example of technology transfer is the use of 3-dimensional scanning and printing as a diagnostic tool or for replacing amputated limbs. On a similar note, laparoscopic surgery, which replaced open surgery in many surgical procedures in HICs, is being introduced in LMICs with obvious advantages such as speedy recovery, less blood loss and reduced need for anaesthesia. The list of technologies continues, including virtual reality labs, drone delivery of medical supplies, and the use of artificial intelligence to spot tumours.[2]

The actual and potential use of such technologies is enormous; so are its (ethical) implications. As with non-technological solutions, there is the question of *equitable access* to these devices and techniques. According to the World Health Organization, the need for medical devices is the highest in LMICs, as they account for three quarters of premature deaths largely due to a lack of testing and monitoring equipment needed to screen for, diagnose and treat noncommunicable diseases.[3]

Introducing new technologies is not only a matter of transferring knowledge. In drug development, for example, it requires creating a more diverse global bio bank – as less than 2% of genomic data represented in research is from African populations[4,5] – and developing business models that also work for LMICs. The latter requires removing financial hurdles to accessing biologicals (engineered monoclonal antibodies that target key steps in inflammation or cancer biology) for the treatment of infections and degenerative and auto-immune diseases. New initiatives are underway to make these expensive drugs available in LMICs.

In this issue of MT*b*, we present some of these technologies. If you had thought the direction of these new developments is a one-way street from North to South, you are wrong. Tropical fruits such as pineapple and papaya contain enzymes that clean wounds and promote healing of e.g. burn wounds, providing a cheap, effective and safe solution. This technology has now successfully been transferred to HICs, where it has revolutionised burn care – reducing costs, blood transfusions and healing time.

The potential of high tech for resource-low settings is beyond imagination, overcoming difficulties in communication, long-distance travel, and expensive laboratory tests. Is it always by definition progress? It may well be(come), but only if we are willing to take the 'white elephant' lessons truly to heart.

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Esther Jurgens

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Imaging in low-resource settings: old and new techniques

In everyday clinical practice, in high-income countries (HICs) as well as low- and middle-income countries (LMICs), medical imaging is important in making a diagnosis. Particularly in LMICs, in most settings, patient assessment in internal medicine is done through carrying out a thorough clinical assessment, laboratory tests and imaging. In most peripheral settings, this would be limited to a chest x-ray, an abdominal x-ray and ultrasound examination. At the central level, a CT scan or an MRI scan may be available. A differential diagnosis is then made against the background of knowledge of the local epidemiology of most common conditions. Obviously, in LMICs, this differs between, say, Sudan, Papua New Guinea and Peru.
Clearly, other specialties have different priorities in imaging, as in orthopaedics and obstetrics and gynaecology (O&G), but the available tools are basically the same. Ultrasound is well integrated in daily practice for example in O&G and in urology.
In recent years new imaging tools have become available, and old tools have been adapted to be used in a LMIC setting. In this paper, an overview is given of two such important developments: portable ultrasound performed by the clinician and 3-dimensional scanning.

ULTRASOUND

Ultrasound is widely available in LMICs and is often performed by a radiographer, but there are few trained radiologists. The quality and interpretation of the scan depends on the radiographer's skills acquired by training and experience as well as continuing education and supervision; the latter two factors are often not sufficiently addressed. Portable ultrasound machines are widely available and can be used at the bedside or in the field.

Point-of-care ultrasound (POCUS) refers to the use of ultrasound by the clinician and is performed at the bedside for diagnostic and therapeutic purposes. It helps to narrow the differential diagnosis. It is non-comprehensive in the sense that it only focuses on specific clinical questions, such as the presence of pleural fluid or post-renal obstruction as the cause of renal failure. Wider, unbiased screening e.g. the cause of abdominal pain of unknown origin is still in the domain of the diagnostic ultrasound performed by the radiology department. POCUS is increasingly used in the emergency department, clinical departments, and in the out-patient clinics in HICs.

Studies are ongoing on the evaluation of the quality of the point-of-care use by a clinician vs. regular ultrasound scanning by a radiologist. Good sensitivity (90%) and specificity (100%) were found in the evaluation of acute kidney failure in ultrasound scans performed with POCUS in an emergency department compared with ultrasound at the radiology department. In addition, the negative predictive value of 99% suggested that POCUS can serve as a tool to reduce the need for regular ultrasound scanning.[1] Recently, the use of portable ultrasound at the bedside was demonstrated in the diagnosis of Covid-19 pneumonia and daily follow-up. It was emphasised that imaging of the lung should be combined with scanning of surrounding structures such as the heart for the purpose of the differential diagnosis, and that the findings should be interpreted in combination with clinical features.[2]

As portable ultrasound machines are becoming increasingly available, POCUS should be integrated in the curriculum of clinicians who prepare to work in LMICs.[3] POCUS courses have been introduced in LMICs, for example at the level of registrars in internal medicine in Malawi (EE Zijlstra, personal communication). In this POCUS course, clinicians are trained in a two-weeks hands-on training course on the wards. Following the course, half

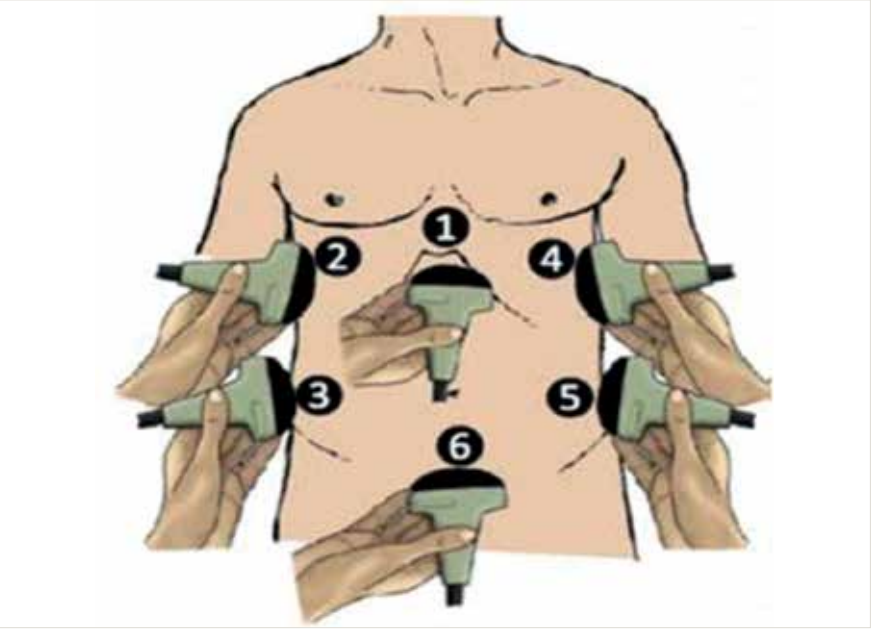

Figure 1. Ultrasound transducer positions in a FASH examination reproduced with permission from ref. 6.

of the departmental ultrasounds were done as POCUS.[4] It aims to enable the clinician to assess the following:

- free fluid – pleural, pericardial, ascitic
- heart function
- pneumothorax
- kidney size and brightness (points to chronic kidney disease); hydronephrosis
- deep vein thrombosis
- signs of disseminated tuberculosis

The POCUS course in Malawi is adapted to the local pathology and addresses, for example, issues in the diagnosis of tuberculosis and heart failure. There are disease-specific protocols such as FASH (focused assessment by sonography of HIV-associated extrapulmonary tuberculosis) (Figure 1).[5]

- Cardiac (subxiphoid or parasternal long-axis), aortic and upper abdominal view to assess for pericardial effusion and abdominal lymph nodes in the upper abdominal peri-aortic region
- Right lung base to assess for pleural effusion
- Right upper quadrant (RUQ) view to assess the liver, right kidney and the space between Morison's pouch for free fluid
- Left lung base to assess for pleural effusion
- Left upper quadrant (LUQ) view to assess the left kidney, spleen, subphrenic and splenorenal space
- Pelvic view to assess the suprapubic region, urinary bladder and rectouterine/retrovesical pouch

The FASH protocol helps to identify diagnostic options, e.g. an aspirate of pleural or ascitic fluid may be examined for protein, glucose and LDH levels; white blood cell count and Gram stain and stain for acid-fast bacilli, to support the diagnosis of extra-pulmonary tuberculosis.

Another protocol is CURLS (cardiac ultrasound in resource-limited settings). Here the aim is also to enable the clinician in a LMIC setting to diagnose the most important conditions that may underlie common clinical presentations such as heart failure and cardiomegaly.[7]

- pericardial effusion
- dilated cardiomyopathy
- cor pulmonale
- mitral valve disease
- left ventricular hypertrophy

There are also disease-specific protocols such as FASE (focused assessment with sonography for echinococcosis) that may be used in diagnosis and monitoring of treatment.[3]

3-DIMENSIONAL SCANNING

3-Dimensional scanning is a novel diagnostic tool that allows assessment of abnormalities that are in or above the level of the skin. This technique has been developed in detail in oral and maxillofacial surgery for patients in whom large parts of facial structures have been removed because of (surgery for) cancer or trauma. The technique helps to construct a facial prosthesis with great accuracy that can then be printed by a 3D printer and implanted surgically with optimal fit.[8]

The scanning can be done by a mobile scanning device; only limited training is needed. The scan is imported into a laptop computer and with specific software a computerised image is constructed

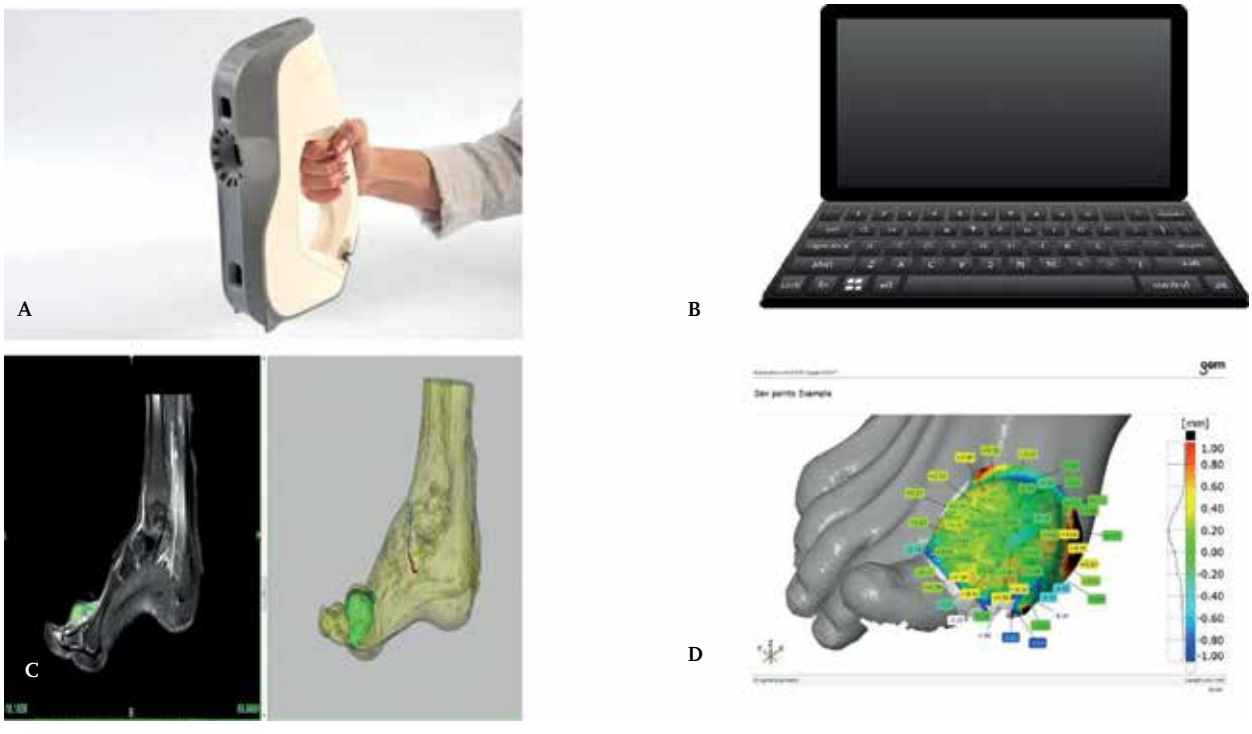

Figure 2. Panel A. Hand-held scanner. Panel B. Image is transferred to a laptop. Panel C (left). MRI scan of the foot. Panel C (right). Computerised image of mycetoma lesion on the big toe. Panel D. Colour codes correspond to elevation above the skin with measurements in mm. Reproduced from ref. 9.

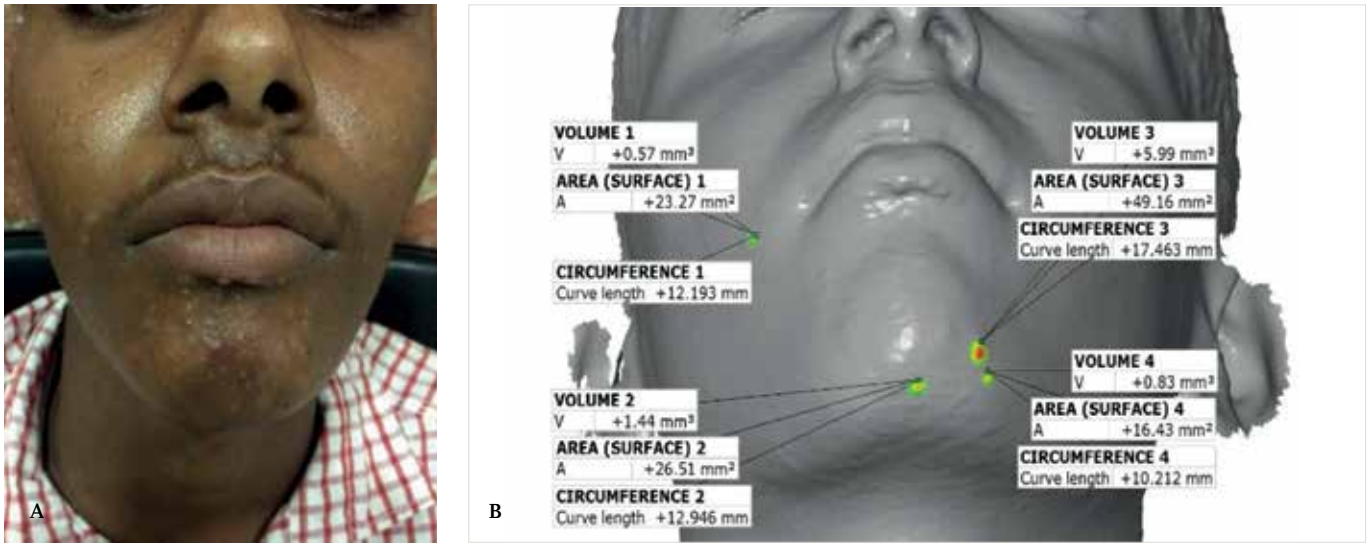

Figure 3. A patient with post-kala-azar dermal leishmaniasis (PKDL). Panel A. Papular rash, mainly on the chin. Panel B. Computerised image from the 3D scan, showing circumference, surface area and volume of each lesion. Reproduced from ref. 10.

that allows measuring the circumference, surface, and volume of the lesion, including changes in skin colour. The latter is done by an engineer/technician and requires some more training.

This imaging modality is under investigation in tropical medicine. So far, it is being studied in mycetoma and post-kala-azar dermal leishmaniasis (PKDL), but this modality may be useful in other (infectious) conditions that affect the skin. Its main value may lie in the unrestricted, safe and inexpensive monitoring of these skin lesions in response to treatment as a biomarker, even under field conditions.

In mycetoma, the lesion is above and under the level of the skin, and an MRI scan is the gold standard. Obviously, an MRI scan requires a patient to travel to a central facility and has cost implications. Currently, research is ongoing to see if the lesion size above the level of the skin lesion may prove to be a proxy for the whole lesion, at diagnosis and during treatment (Figure 2). The 3D scan is therefore an ideal biomarker, as it can be done repeatedly, and it is safe; only patients who suffer from epileptic fits may be excluded as the flashes of light may trigger a seizure.

In PKDL *Leishmania* parasites persist in the skin after successful treatment of visceral leishmaniasis; the increasing immune response causes a maculopapular or nodular rash surrounding the parasites. All lesions are above the skin surface, even the smallest lesions, can be measured. Subsequent computer images can be subtracted from one another making it possible to objectively record the difference between measurements with an accuracy of 0.1 mm (Figure 2, 3); this provides better accuracy than reporting via sequential (2-dimensional) photography, which is inevitably subjective.[10]

CONCLUSION

In summary, new applications of ultrasound imaging and innovative imaging tools such as 3D scanning are increasingly available and affordable for LMIC settings. Bedside diagnostics by the attending clinician saves time, helps to quickly narrow the differential diagnosis, and may be used in monitoring treatment. Integration in the medical curriculum should be considered also for those who are in training or who prepare to work in a resource-limited setting

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3D Printed prostheses in Sierra Leone

There is a global need for affordable prostheses. An estimated 0.5% of the global population in low- and middle-income countries (LMICs) requires prostheses or orthotics according to the World Health Organization and the International Society for Prosthetics and Orthotics.[1] The workflow of the International Committee of the Red Cross (ICRC) has long been considered as the standard to produce prostheses for LMICs.[2-4] Traditional plaster methods are used to perform stump measurements and production of the prostheses socket. These plastered socket shapes are highly dependent on the experience and skills of the prosthetic specialist and this implies difficulty in quality assurance regarding fit and durability.[5,6]

There is an increasing interest in implementing 3D printing technology for health-related problems.[7] A relatively new way to design and produce prosthetic sockets is using computer-aided design (CAD) and computer-aided manufacturing (CAM) systems.[8] Using this technique, the production process could be more consistent and faster. Because, the entire process is automated, the socket fitting would become less dependent on the individual prosthetist's skills and experience. This could increase the rate of successful prosthetic fitting, especially in LMICs.

Several foundations have been set up to produce customised 3D printed medical aids in LMICs.[9,10] However, because of the limited research and follow-up performed on these projects, it is difficult to assess the quality of the medical aids and the extent to which the projects have been successful and are still ongoing. Scientific research on 3D printed arm prosthetics in LMICs is very limited, and no research has been done on 3D printed prosthetics for lower extremities. As a result, it remains unclear what the potential of these 3D printed prosthetics is and how much impact it has on the quality of life.[11] Below, we describe a 3D project in Sierra Leone in which we aim to provide scientific evidence for our approach in 3D printed prosthetics.

3D LAB SIERRA LEONE

The 3D lab was set up in the Masanga Hospital in Sierra Leone in collaboration with the 3D lab at the Radboud University Medical Centre. The project started in 2018 with a feasibility study to investigate the added value of a 3D printer in a resource-limited healthcare setting. Low-cost 3D printed arm prostheses and other medical aids, such as umbilical cord clamps, braces for patients with scoliosis, and splints to prevent burn contractions were produced.[12] Van der Stelt et al. concluded that aesthetic designs for arm prostheses were just as important as functional designs due to stigmatism of handicapped people. 3D Printed braces were helpful because of the patient-specific design and were produced without many extra costs. In 2020, a clinical study was conducted to test low-cost 3D printed transtibial prostheses. Technical studies were performed, and initial pilot designs were clinically tested on Dutch patients first.[13] Test results showed that the prostheses were sufficiently durable, and after ethical approval had been obtained in Sierra Leone, the prostheses were approved for testing in practical life in Sierra Leone. The short-term results were published in *EClinicalMedicine*.[14] Patients received several weeks of physical therapy after receiving the prosthesis, and local physiotherapists were trained to provide this training. After six weeks, all participants were still wearing the prosthesis and six out of eight participants reached their personal rehabilitation goals. All of the participants were no longer in need of using crutches thanks to the prosthesis.[14] These studies showed that the design of the socket and aesthetics were of added value regarding both functionality and restoring confidence. Long-term follow-up is required to prove the sustainability of the 3D printed prostheses and improved health related quality of life of patients. The uniqueness of this project is that we aim to provide scientific evidence for our approach. All our study results and clinical outcomes are published in international peer-reviewed scientific journals, which is not often the case with many other projects where prostheses are handed out and patients are not followed up. In addition, we believe it is very important to work together with the local population. Our main goal is to make the project fully independent and sustainable in the future.

COSTS AND MANUFACTURING TIME

First, the patient's stump is 3D scanned in approximately ten minutes. After this, the 3D design of the transtibial socket is created within twenty minutes. Last, it takes approximately twenty hours to 3D print the prosthetic socket. See Figure 1 and 2 for the optical scanning and 3D printing process.

Figure 1. Scanning of the stump with the EinScan Pro Plus.

The printing material of the socket costs around US$ 20. The other parts of the prosthesis do not have to be custom-made, standard prosthesis parts can be used for this. See Figure 3 for the prosthesis with 3D printed

Figure 2. 3D Print of the prosthetic socket with the Ultimaker S5.

Figure 3. 3D Printed prosthesis without aesthetic coverage.

Figure 4. 3D Printed prosthesis with aesthetic coverage.

socket. The prostheses were equipped with a 3D printed aesthetic coverage, so that they resembled a 'real' leg in the respective natural skin colour of the individual participant (Figure 4). We currently use imported prosthesis parts that cost a total of US$ 62. The local manufacturing of the prosthetic foot cost US$ 5. The entire material cost of the 3D printed prosthesis is around US$ 87. These costs are low compared to the regular prostheses, which would cost between US$ 100 and US$ 200.

After a two-week rehabilitation process, people can start walking again (see example in Figure 5).

SUSTAINABILITY

Within the framework of this project, we try to recruit and train as many local staff as possible. This is easy for most manual labour and physiotherapists. However, digitally designing and printing of the prosthesis is still a process that requires specific skills and knowledge, and developing these skills is difficult due to the lack of general IT knowledge. This results in a need for automation of the digital designing process and strategic investment into a structured training programme. The focus for the coming years is on making a simple software programme so that prostheses can be designed and produced in a standardised and automated way by local employees themselves. It is expected that this will make prosthetics less dependent on the skills of the individual prosthetist and enable more people to be trained in a short period of time.

There is a close collaboration with the National Physiotherapy and Rehabilitation Programme in Sierra Leone. In this way, we are trying to implement this technique as much as possible in cooperation with the local authorities. Our goal is to make the project completely independently run by the local population.

FUTURE PERSPECTIVE

Further research on standardisation of the 3D workflow will be performed. Our team has been expanded with several students from the University of Twente, Delft University of Technology and HAN University of Applied Sciences. In the future, we hope to include students from the University in Freetown, Sierra Leone.

Essential elements for sustainable approach are: easy-to-work with 3D software, training of local people, and replacement of the imported prosthetic parts by local products. This will lower the costs of a prosthesis and make the prostheses more financially accessible for the local population.

In the next few years, the foundation intends to provide complete workflow packages for each type of amputation. Each package will consist of a 3D scanner and 3D printer, electricity supply, and an automated software package. This will replace a large workshop to fabricate prostheses; and it would even be possible to create a mobile workshop, so that prosthesis facilities can be available everywhere.

Figure 5. This patient received a prosthesis and could walk again after many years of using crutches. He was also able to pick up his work as a tailor again, as he needs two legs to operate a sewing machine.

CONCLUSION

There is an unmet urgent need for prostheses in LMICs. Competitively priced, fully functional prostheses can be locally produced using 3D printing technology and improve the lives of amputees. Apart from helping patients, this project will include a locally driven manufacturing programme that will create qualified jobs.

See for more information and pictures: www.3dsierraleone.com

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In memoriam

Wouter Nolet

In 2017, Lars Brouwers drove an old car to Sierra Leone together with Wouter Nolet. Wouter assisted Lars with the start of the 3D printing project in Sierra Leone. Wouter passed away in 2019 (see MTb obituary, edition 2019-4). Without his ingenuity and determination, the project most likely would not have been successful. He will remain in our memory as best friend and adviser.

~ Whatever ends is remembered. What is remembered never ends ~

Laparoscopic surgery for all, and its development in rural India

Laparoscopic surgery (LS) has been one of the most revolutionising techniques in general surgery in the past decades. Starting in the 1930s as a diagnostic tool, it evolved into an operative procedure representing one of the first and most common forms of minimally invasive techniques. In Text box 1 the definition and procedures are summarised (from ref 2).

TEXT BOX 1

"Laparoscopy is a minimally invasive surgery in the abdomen and/or pelvis used diagnostically or therapeutically. Small incisions are used to insert the laparoscope (a camera), surgical instruments like a grasper, and a tube to insert gas (typically CO2) in the abdomen to provide a clear view. It is usually performed under general anaesthesia, requiring the presence of a trained anaesthetist with appropriate equipment and drugs. Due to advanced surgical equipment, insufflation equipment etc, additional costs are involved and specialized training is needed."[2]

Due to its proven positive effects and wide availability, laparoscopy is one of the most commonly used technique in surgery in developed countries. The technique has many advantages for the patient including reduced blood loss, reduced chance of surgical site infection, reduced length of admission and of post-operative analgesia, and quicker return to work compared to open surgery. In addition, more efficient use is made of scarce resources. These advantages may be even more pronounced in low-resource settings where clean water, sanitation, and blood banks are scarce, and follow-up to detect common complications of surgery is often complex.[3] Similarly, efficient use of beds can be very beneficial in low-resource settings considering the great surgical demand and limited inpatient capacity. Furthermore, laparoscopy can be adequately used as a diagnostic tool and is cheaper than investing in computed tomography (CT) or magnetic resonance imaging (MRI).[4] Despite the obvious advantages, laparoscopy remains unavailable to 80% of the world's population, mostly those living in low- and middle-income countries (LMICs).[5,6] In this article, we describe the feasibility and challenges of laparoscopic surgery in LMICs, illustrated with the experience in rural India.

FEASIBILITY AND ADAPTATIONS

Minimally invasive surgery, especially laparoscopic surgery, offers clinical and economic benefits compared to open surgery, and it is feasible in low-resource settings if adaptive measures are taken. A systematic review by Wilkinson et al. (2021) identified seven key barriers: funding, availability and maintenance of equipment, local access to experienced laparoscopic trainers, lack of knowledge/effective training curricula, practical opportunities for trainees, stakeholder dynamics, and surgical departmental structures.[7] Equipment is not always available because of costs and lack of funding, often relying on donations. The absence of companies producing and maintaining laparoscopic equipment in LMICs is another important barrier. In order to work around the limitations of laparoscopy in LMICs, adaptive strategies and measures can be followed, for example: approaching local soft drink manufacturers to supply affordable CO2, the re-usage of (disposable) instruments by sterilisation and repairs, the innovative use of cheaper instruments or substitutes for expensive equipment (e.g. sunlight used as a light source, cystoscope as a laparoscope) and gasless laparoscopy.[3] Also, the application of local or spinal anaesthesia is an alternative when general anaesthesia is resource-intensive. Laparoscopic training is often done in partnerships between surgical programmes in high-income countries (HICs) and LMICs, where the programmes from HICs facilitate training, equipment, and clinical guideline development. This model however is not sustainable, as often resources are exhausted when the training ends.[5] To overcome this barrier, innovative adaptations are implemented by developing training programmes with low-cost surgical simulations and skills labs, teleproctoring, internet based surgical videos, and training courses by local trainers. To enhance the feasibility of laparoscopy in LMICs, a collaboration between surgical societies and local and governmental institutions can provide policy, guidance, equipment, monitoring and incorporation of laparoscopic teaching in training curricula.[3,5,7]

THE EXAMPLE OF RURAL INDIA

Rural surgeons in India began in 2001 with laparoscopic surgical procedures with equipment that was already available: the cystoscope.[8] Initially, it was used for diagnostic laparoscopy and for biopsies and, building on experience, was later used for procedures such as tubal ligation and appendectomies with the addition of a cystoscopic grasper. The lessons learnt from these laparoscopic surgeries were applied to provide minimally invasive surgeries. With the start of conventional laparoscopic surgery in rural areas, lack of general anaesthesia was a main concern because of costs involved and absence of trained staff and resources. To overcome these barriers, several methods were used.[9] Ether and an EMO machine (Epstein, Macintosh, Oxford machine, a temperature-controlled vaporiser) were used. As bottled CO2 is logistically difficult to get to a rural surgical facility in India, dental compressors (a machine that compresses atmospheric air) were used as a substitute. Disposable instruments were reprocessed. Although these measures

led to an increase in laparoscopic surgeries, it did not prove to be sustainable as there were too many fluctuations in accessibility and affordable availability of gas and working equipment.

The Gas Insufflation Less Laparoscopic Surgeries (GILLS) proved to make a difference. Gasless laparoscopy is a form of mechanical lift laparoscopy, is relatively inexpensive in terms of equipment, and may be undertaken with spinal anaesthesia (Figure 1).[10] Spinal anaesthesia is three times less expensive than general anaesthesia and readily available. In addition, the learning curve for surgeons proved to be shorter compared to conventional laparoscopic surgeries, partly because long conventional instruments for open surgeries could be used without the risk of gas leakage. The International Federation of Rural Surgeons made teaching videos available, among others on low-cost technique for surgeries and GILLS cholecystectomies. The World Health Organization included the GILLS procedure in their compendium of innovative health care technologies for resource-poor settings[11] and steps were undertaken to further implement GILLS in rural India. The Association of Rural Surgeons of India organised workshops at medical colleges to promote and teach GILLS. The University of Leeds developed formal teaching for GILLS through the TARGET training programme. Finally, innovative proctorship programmes were established where faculty provides surgical training camps for rural surgeons at their local facility.

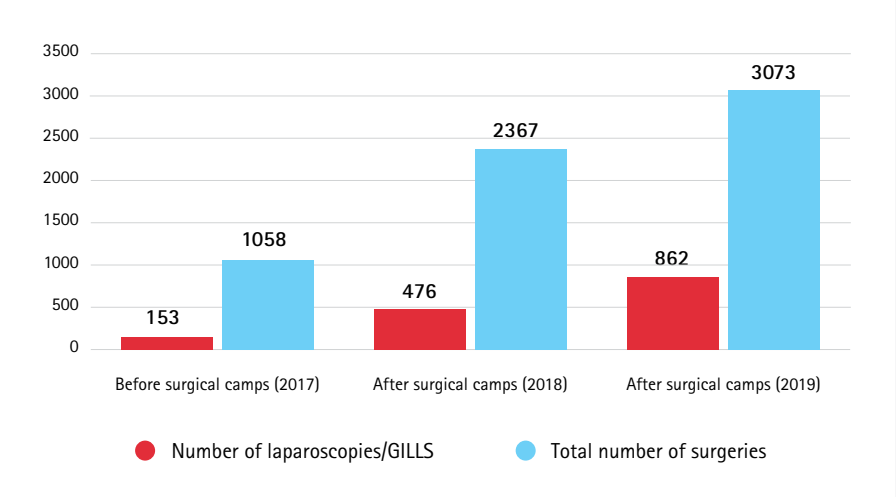

Figure 2. Total number of surgeries carried out (blue) of which laparoscopic surgeries or GILLS (red) carried out before and after surgical training camps in eight surgical facilities in rural India, representing a population of 82,187 people.

IMPACT

The proctorship programmes greatly improved surgical coverage. During the proctorship programme itself, 317 surgical procedures, mostly GILLS, per 100,000 people per year were carried out. Before the start of the programme, in 2017, the proportion of laparoscopic surgeries was 15%, which increased to 20% in 2018 and 28% in 2019 (Figure 2). Besides the surgical procedures done during the training, the total surgical volume increased between 2018 and 2019 from 2,880 to 3,739 per 100,000 people in the training target area. If this trend continues, 5,000 procedures per 100,000 population will be reached by 2030 – an important target set by *The Lancet* Commission on Global Surgery in 2015.[12]

In 2020 and 2021, the surgical training camps were affected by the Covid-19 pandemic. A positive side effect was the increase in digital consultations and supervised procedures through video calls, which are useful experiences for the future. Residents in surgery and rural surgeons are continuing to learn and perform laparoscopic surgeries, including GILLS, through proctorships including surgical training camps and training programmes at medical colleges.

CONCLUSION

With the increasing need for safe access to surgical care, minimally invasive surgeries including laparoscopic procedures play an important role, especially in rural settings. Implementing laparoscopy in LMICs, however, still faces great challenges. Overcoming those barriers is essential to gain clinical and economic benefits in surgical care. Therefore, innovative adaptive measures should be taken in infrastructure, equipment, technique and training. Training programmes (including local trainers and facilities) play a big role in safe implementation of laparoscopy but are still scarce and too reliant on HIC involvement, therefore not producing a sustainable

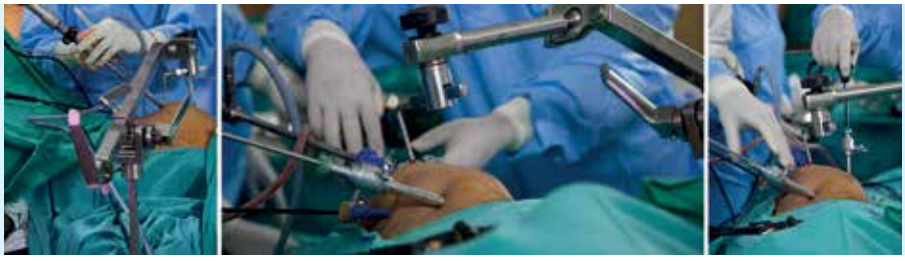

Figure 1. GILLS system: a fixed construction attached to the operation table with an adjustable arm to lift the abdominal wall, several trocars with a laparoscope and surgical instruments are inserted in the abdomen to perform gasless laparoscopy.

training model. GILLS is an example of a high-potential affordable and available solution as seen by the uptake in rural India. To achieve sustainability and overcome barriers, collaboration of all (local) stakeholders is needed.

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Reverse technology in the treatment of burns: the use of tropical fruits

Since the Second World War there has been a major improvement in the treatment of burn injuries and wound management. Burn casualties are treated with fluids for management of hypovolemic shock in the first 24 hours which saves many lives. Surgical interventions such as early and aggressive surgical excision of necrotic tissue (also called an eschar) helps to stop infection, and the application of silver dressings is also beneficial to reduce infection rates. On top of that, isolation and other environmental conditions such as specially designed airflow systems prevent cross infections.[1] Nowadays a huge variety of wound dressings enables patients to go home earlier or receive treatment at home. However, burn care and in particular wound dressings and topical agents are expensive.[2]

Burn care in low- and middle-income countries (LMICs) is a challenge because of the huge number of patients

Figure 1.
Panel A. A girl in a remote area of Mozambique presented with a deep partial thickness burn injury. Wound treatment was with honey. She developed hyper-granulation that interferes with wound healing.
Panel B. Papaya treatment was started instead. After four days the hyper-granulation tissue has considerably reduced.

and a lack of staff as well as expensive topical agents, silver dressings and gauzes. Often wound dressings and gauzes are not available or of poor quality. Infection is common, which further delays wound healing.[3] Many hospitals and burn centres switch to the use of less expensive topical agents such as tropical fruits like pineapple and papaya if there is necrotic tissue. Other wounds that do not have necrosis are normally treated with ointments such as honey, which has an anti-bacterial effect, or locally prepared Vaseline gauzes.[4,5] Vaseline (petroleum jelly) gauzes, the standard in burn care, create a moist environment which promotes wound healing. If no Vaseline or petroleum jelly is available, palm oil can be a good substitute.[6]

TREATMENT OF DEEP PARTIAL AND FULL THICKNESS BURN WOUNDS

Deep partial burns are also referred to as mixed burns. Some areas are partial thickness burns and heal within fourteen days. Areas that are deeper and not healing are assessed for surgical intervention. If wound healing is slow, hyper-granulation of the wound may occur. This will interfere even more with wound healing because deep wounds will only heal from the wound edges.[7] Therefore, hyper-granulation needs to be scraped off during surgery or can be treated with enzymatic debridement (Figure 1).

Full thickness burns form a necrotic crust (eschar) that feels leathery on touching and needs to be surgically removed. However, surgery may result in complications such as extensive blood loss.[7] Compared to high-income country (HIC) settings, ensuring good (post-)surgery conditions in LMICs is much more difficult (e.g. accessing a blood bank because of delays in donor blood identification). Also, wounds that need surgery are often infected, which also causes delays because the infection needs to be treated first. In such cases, another option is to start enzymatic debridement to loosen the crust and treat infection.[8]

Papaya treatment in burn management is not well known to health practitioners in LMICs. The fruit comes from the papaya tree (*Carica papaya*) and is always available throughout Africa and other continents.[9] The fruit contains the enzyme papain that is widely used as meat tenderiser in the food industry.[10] In wounds, it removes slough and necrotic tissue and does not interact with the normal skin. It also prevents infection, and after debridement healthy granulation tissue can develop. This results in reduced operating time and blood loss. It is also known to reduce hyper-granulation in wounds.[8, 9,11] Papaya mash flattens the hyper-granulation and increases wound healing. However, health staff in LMICs often need to be convinced about starting this treatment. "It is a fruit and you are supposed to eat it, so how can it benefit wound healing?" Once they see the improvement, they are enthusiastic.[12] Positive results with both unripe and ripe papaya have been published,[13] although ripe papaya mash is easier to apply and more comfortable for the patient (H Hofland, personal observation).[12]

There are other plants such as kiwi and pineapple that originate from LMICs that enable enzymatic debridement. Pineapple contains bromelain (a mix of enzymes) that is known to reduce inflammation and nasal swelling. In some areas, it is used, for example, in orthopaedics, obstetrics and dentistry as an oral anti-inflammatory treatment similar to non-steroidal inflammatory drugs (NSAIDs), and in wound management to remove slough and necrotic tissue.[14] Although it has the same results as papaya, it is not often used in African burn centres or hospitals, perhaps because it is more expensive and not available all year round, or because the treatment is more painful. The bromelain seems to be more aggressive in removing eschar and slough compared to using papaya.[14]

REVERSE TECHNOLOGY

Honey is one of the agents in wound treatment that has been more widely accepted and embraced by the pharmaceutical industry. In 1991 the first trials with honey dressing were published in HICs although it was already being used in LMICs. The use of honey was already described in ancient Greece and Egypt. Nowadays, impregnated honey gauzes and honey ointment are readily available in HICs.[15,16]

The experience in LMICs with papaya or pineapple has revolutionised the treatment in HICs of necrotic or full thickness burn wounds. MediWound Ltd (Yavne, Israel) developed a new

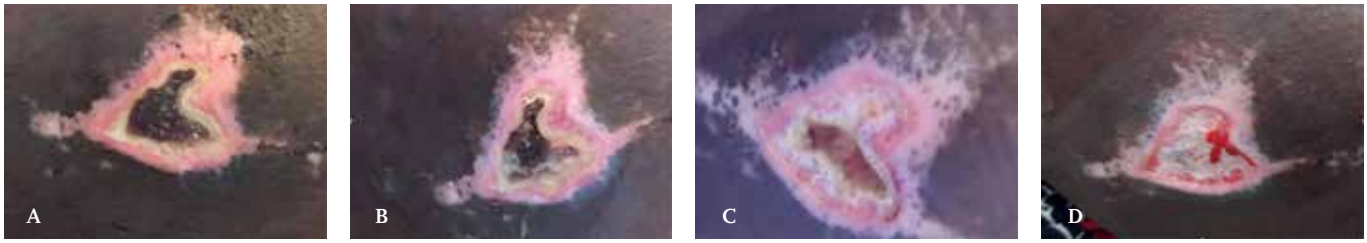

Figure 2.
A. A man with a pressure ulcer was admitted in a hospital in Rwanda waiting for surgical debridement. The crust was too difficult to remove by the nurses. Wound treatment was given with dry gauze; there was no infection. Surgery was delayed as priority was given to more severe cases.
B. After 2 days of papaya treatment, a change was observed; the crust became increasingly loose.
C. After 6 days, the necrosis has disappeared, leaving granulation tissue that was dressed with honey.
D. Within a week, patient was able to go home with a healed wound.

treatment to remove necrotic tissue, a bromelain-based enzymatic debridement (NexoBrid™) based on the enzymes of pineapple. This conservative treatment is likely to replace surgical interventions. NexoBrid™ is now in phase 3 multicentre studies and is used in more than fifteen countries worldwide.[17,18]

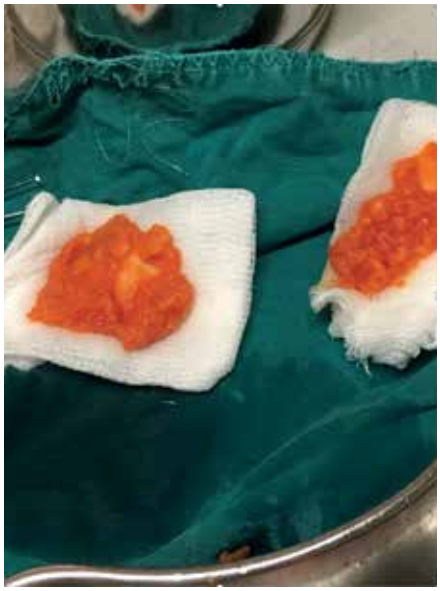

Figure 3. The mash from a ripe papaya is put on a dry gauze and left for 24 hours, after which the dressing is renewed. This treatment causes no discomfort.

Heitzmann (2020) reported that this enzymatic debridement has become an integral part of burn therapy and even the standard of care in specific burn centres, although it cannot replace surgical intervention altogether.[19] Increased experience showed that it cannot be used on burned feet, because it deepens the wound for unknown reasons. Also, its use on chemical and electrical burns requires further research. On large surfaces, the effects of the bromelain treatment have not been evaluated. One treatment takes four hours, after which the paste is removed. Because of the high enzyme concentration, bromelain treatment is painful; some patients need ICU treatment or anaesthetic nerve blocks. It is time consuming, and extra nursing staff is needed to properly apply and remove the NexoBrid™ paste and to monitor the patient. Furthermore, it is relatively expensive; treatment of a small to medium sized burn injury would cost around 4,000 euros. However, it is generally felt that the advantages heavily outweigh all these potential problems and costs. Overall, the advantages are faster removal of the eschar, reduced blood loss, and the reduced need for skin grafting especially in hand and facial burns. All this contributes to a faster cure and reduced burden on resources.[17-19] Research is ongoing to produce dressings with a combination of papaya and alginates (another promising wound dressing) and dressings with honey and papaya.[20-22]

CONCLUSION

That the use of enzyme-based therapy from fruits like papaya and pineapple have revolutionised the treatment of burns in HICs, based on experience in LMICs, is quite amazing.[8,9,11] In both settings, these treatments are favourable for promoting wound healing, particularly in case of necrosis or infection. In LMICs these treatments with papaya or pineapple are very cheap and almost universally available and can be applied repeatedly. As a result, the burden on the staff, the need for consumables, and the need for operating capacity are all considerably reduced.

Similar logistical advantages exist in HICs, where NexoBrid™ with a high concentration of enzymes may be used on large areas of burns, potentially with major advantages compared to standard management; this is the subject of ongoing randomised clinical trials. However, this comes at a cost in terms of the need for staff, adequate pain management, and other resources. It is therefore somewhat ironical that these new effective dressings using NexoBrid™ are unlikely to be ever used in the countries where the practice of enzymatic debridement first started.

PANEL 1

THE HEALING PROPERTIES OF HONEY

- anti-bacterial effect
- hyper-osmotic because of high sugar concentration
- low pH and capacity to absorb fluid helps to clean the wound

PREPARATION OF HONEY PASTE AND APPLICATION

1. Mix with Vaseline, cetomacrogol or 'ghee' (clarified butter) (1:2)
2. Vaseline should be sterile or sterilised
3. Apply paste on Vaseline impregnated gauze
4. Leave on the wound for 2-4 days

PANEL 2

PROPERTIES OF PAPAYA

- contains the enzyme papain, normally used as meat tenderiser
- beneficial for a variety of skin problems
- in burn care, the properties for enzymatic debridement are used
- removes thick necrosis and hyper-granulation and even dirty wounds can benefit from papaya treatment
- also has anti-bacterial properties that increase wound healing

PREPARATION AND APPLICATION

1. Make a mash from the ripe papaya (not the seeds)
2. Keep it refrigerated
3. Put the papaya mash on a dry gauze
4. Administer it to the wound
5. Change daily

PANEL 3

BROMELAIN-BASED ENZYMATIC DEBRIDEMENT (NEXOBRID™)

- licensed for total wound area of 15% total body surface area (TBSA)
- wound needs to be cleaned

including removal of blisters
- adequate analgesia needs to be given before, during and after the procedure
- treatment contains a powder that is mixed with a jelly

PREPARATION AND APPLICATION

1. Paste (1.5-3 mm thick) is applied on the wound and left for 4 hours
2. After 4 hours the paste is scraped off and wiped with a large sterile dry gauze followed by a normal saline dressing until the bleeding points are seen.
3. Then an antibacterial soaked dressing is applied and left for 2 hours.
4. After this treatment, the wound is dressed before a permanent or temporary skin substitute is in place.[17,18]

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ANNOUNCEMENT

Knowledge sharing on global health in the Netherlands

At the peak of the first wave of coronavirus infections, Global Health & Tropical Medicine (GH&TM) physicians assisted in several hospitals to deal with pandemic in the Netherlands. Their experience and knowledge was acknowledged, including taking a solution-oriented approach and improvising safely and effectively in critical situations. Dutch physicians with a background in GH&TM were also involved in the development of a guideline for a medical check-up of refugee children upon entry to the Netherlands.

These are just two illustrations of how global health knowledge acquired abroad, can be applied in the Netherlands. Facilitating this process of knowledge transfer on global health in a structured way is at the heart of the newly established Dutch organisation Knowledge Connectors Global Health (KCGH).

The initiative of the NVTG and OIGT – the training institute GH&TM – resulted in the establishment of KCGH, with financial support from the Ministry of Health, Welfare and Sport (VWS). In March 2021, the KCGH team started operations: Anke Tijtsma (Director), Fleur Nieuwland (Operations Officer), Nienke Freije (Jr. Communications Advisor) and Leontien Laterveer (Sn. Communications Advisor).

In recent months, we worked on KCGH's mission, vision and strategy, launched www.kcgh.nl, hosted a meeting with the NVTG working parties, and created a LinkedIn group. KCGH co-organised the NVTG symposium on mental global health and the Dutch Global Health Film Festival. Other activities are currently being developed, for which we are inviting you – students and young professionals in GH and TM, not limited to GH medical doctors – to share your ideas on how to act upon our mandate of supporting knowledge transfer from global health experience and skills acquired in low- and middle-income countries for the Dutch health (care) sector.

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Improving access to biological products in low- and middle-income countries: a Dutch initiative

THE NEED FOR AFFORDABLE MEDICINES

Globally nearly two billion people do not have adequate access to essential medicines (EM).[1] Especially in low- and middle-income countries (LMICs), medicines are often unavailable or unaffordable, even though these countries have adopted a national essential medicines list as part of their healthcare policy. There can be several causes for the poor availability of EM in these countries, including the lack of production and distribution infrastructure and the difficulties in obtaining market authorisation of such products.[2,3] Even more important for access are the costs of medicinal products, in particular of high-priced biological medicines*. As LMICs have often not yet (fully) embraced universal health coverage, medicines must be paid out of pocket by patients, which makes these products unaffordable.[4,5] The development and marketing of lower priced biosimilars** can help in increasing the accessibility of EM in LMICs.

Experiences in the field of vaccines have shown that empowering manufacturers in LMICs to manufacture locally can lead to considerable price reductions and increased access. However, industrial development alone is not sufficient to ensure that local production can lead to improved access to EM. The success of technology transfer depends on a multitude of factors, including product factors, regulatory expertise at LMICs, and the ability to generate profit for local manufacturers.

THE UTRECHT CENTRE FOR AFFORDABLE BIOTHERAPEUTICS

In 2014, the World Health Organization (WHO) and Utrecht University in the Netherlands entered into a memo of understanding (MOU) which emphasises that technical collaboration will contribute to the shared goals of both organisations in promoting the wide availability of safe, effective, and affordable biotherapeutics, in particular in the public sector of developing countries. Based on this MOU, Utrecht University established the Utrecht Centre for Affordable Biotherapeutics for Public Health (UCAB) as a central hub to facilitate the development of safe and affordable biotherapeutics for LMICs in a sustainable way. UCAB was founded in 2015 and combines the scientific knowledge and expertise of Utrecht University with the global targets of the WHO. Within UCAB, all the appropriate development, clinical and regulatory expertise has been brought together. As a non-profit organisation, UCAB has a unique position to facilitate affordability and accessibility by enabling successful local production of biotherapeutics.

UCAB's strategy is to initiate the formation of a business consortium with biotherapeutic manufacturers, consisting of a lead manufacturer, who will develop the biosimilar, and local manufacturers in LMICs for local production and/or distribution of the product. The business associates share the cost for the biosimilar development. The product development expertise of the lead manufacturer is shared with the consortium members in LMICs to build a dossier for marketing authorisation at the European Medicines Agency (EMA) and in their local regional territories. UCAB assists in the submission process to the EMA and to the local authorities by providing regulatory advice and assisting in the interactions with local authorities, but the lead manufacturer and local manufacturers are the market authorisation holders in their respective territories. This provides a sustainable situation after the product has been approved by local authorities. UCAB is the point of access for the formation of the business consortium, oversees the development activities, and facilitates the technology transfer to local manufacturers by providing advice, know-how, documentation and contractual services to manufacturers and regulatory authorities in LMICs.

CURRENT UCAB PROJECTS

UCAB focusses on the development of biotherapeutics that have the greatest impact on public health in LMICs, which are preferably included in the *WHO Model Essential Medicine List (EML)*[6] or the Neglected Tropical Disease portfolio of the WHO. The projects are selected in close collaboration with the WHO.

PALIVIZUMAB PROJECT

The first project started by UCAB is the development of a palivizumab biosimilar for the prevention of respiratory syncytial virus (RSV) infections. RSV causes respiratory tract infections, most commonly in children under five years of age, and can be life threatening especially in premature infants.[7] Only one preventive treatment is available, palivizumab, which is an antiviral monoclonal antibody marketed under the brand name Synagis®. Palivizumab is indicated for children who are at high risk of severe RSV infections and is administered by intramuscular injection once every month during the RSV season (generally five months/year). This prophylactic treatment reduces the RSV-related hospitalisations in pre-term infants by about 80%. But palivizumab treatment is expensive (US$ 9,600/season in the USA, €5,000/season in Europe), which makes this product unaffordable for use in children in LMICs, the areas where the virus is most prevalent and mortality rates are highest. Although the patent for Synagis® has expired, no biosimilar products are available yet. In collaboration with a biosimilar manufacturer, UCAB developed a collaborative model to facilitate development, manufacturing, validation, and registration of palivizumab in LMICs.

BEVACIZUMAB PROJECT

Bevacizumab, a humanized monoclonal antibody that inhibits the vascular endothelial growth factor (VEGF) is approved for the treatment of several forms of cancer. VEGF has been proven to play a major role in the pathogenesis of neovascular age-related macular degeneration (nAMD), and bevacizumab is widely used off-label as an intravitreal

injection for the treatment of this disorder.[8] Since 2013, bevacizumab has been on the EML of the WHO for the treatment of nAMD. Over ten years of clinical use has demonstrated bevacizumab to be an affordable and safe alternative for ranibizumab (brand name Lucentis®), the only licensed but expensive product for this indication. However, there is no pharmaceutical form of bevacizumab yet available on the market in prefilled syringes as is the case for Lucentis®. For the ophthalmic indication, bevacizumab, which is provided in vials for intravenous injection, needs to be prepared for intravitreal administration under aseptic conditions and kept sterile until use. This process carries the risk of contamination and puts the patient at risk of infections. Moreover, the bevacizumab vials are manufactured for intravenous injection, and the formulation (particle size and excipients) may not always be suitable for intravitreal injection. To prevent the safety risks associated with the dispensing of bevacizumab and to improve the ease of the injection procedures, UCAB is exploring the possibilities for developing a pharmaceutical presentation of a bevacizumab biosimilar in a prefilled syringe, designed and authorised for intravitreal injections in LMICs.

INSULIN PROJECT

Even though insulin has been on the market for hundred years and has been on the WHO EML since 1977, availability and especially affordability in LMICs is still poor. For this project, UCAB is currently exploring different strategies. One of them is to acquire bulk insulin from one of the current insulin manufacturers for compounding and distribution by local manufacturers. Providing insulin to LMICs is only one element in the treatment of diabetes. Many other factors, such as blood sugar monitoring and patient education, play a significant role. Therefore, in this project it is important to work closely with international and national diabetes associations to make sure that the provision of insulin fits within the local diabetes treatment programmes.

Many organisations advocate for better access to medicines across the world. UCAB is one of the very few who strive to improve affordability and access to biologicals in LMICs by actively stimulating development and lower-cost production through international consortia of local manufacturers and tech transfer. We are open to exploring new project opportunities for biosimilar development that address urgent public health needs in LMICs.

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* Biological medicines (also called biologicals or biotherapeutics) are biotechnology-based medicines and are comprised of proteins such as hormones (growth hormones, insulins), enzymes that are naturally produced in the human body, monoclonal antibodies, sera, vaccines, allergens, and advanced technology products such as gene and cell therapy products. Like all medicines, biological medicines work by interacting with the body to produce a therapeutic outcome, but the mechanisms by which they do this may vary from product to product and across indications.

** A biosimilar is a biological medicine which is highly similar to an approved biological. Biosimilars can only be marketed once the patent of the original biological has expired.

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High tech in rural dermatology

HISTORICAL PERSPECTIVE

Dermatology was often considered a medical specialty that, by inspection alone, deduced and diagnosed the mechanisms that occurred under the skin. It did not use fancy equipment, maybe just a magnifying glass. For teaching and follow-up there used to be watercolour drawings ('aquarelles') (Figure 1) and wax mouldings of common conditions, and later analogue photography, which became more useful for the dermatologist when colour photography was introduced. At this stage, a consultation could be as simple as sending photos or negatives by post.

Figure 1. Watercolour drawing (aquarelle). A case for diagnosis in 1937 (NTvG 1937: 3504). In 1953 diagnosed as ulerythema ophryogenes as described (NTvG 1953; 3150 and 3153). Now generally diagnosed as keratosis pilaris atrophicans faciei.

THE NEGLECT OF PATIENTS WITH SKIN DISEASES

Like neglected tropical diseases (NTDs), dermatology seemed like a neglected medical specialty, especially in low- and middle-income countries (LMICs). Skin diseases account for approximately a third of the burden of disease in LMICs (in high-income countries only fifteen percent), and they are among the top five causes of morbidity. They are responsible for at least fifteen percent of all peripheral health care clinic visits. [1] About ninety percent of the patients with dermatological conditions are seen by primary health care workers or traditional healers with little or no dermatological training, while for more than eighty percent of the patients hardly any specialised knowledge for diagnosis is needed.[1] Most skin diseases are preventable and curable with simple, inexpensive, and effective medications, but must be diagnosed for proper treatment and care. And here help is needed.

The few dermatology specialists present in LMICs almost all resided in the urban areas with little or no contact with rural communities or underprivileged people in slums. As a result, health workers working in these areas were left alone with their patients' skin problems. Occasionally, they were visited by leprosy health workers from the leprosy/tuberculosis programme, who knew more about the skin, but who were still not likely to be familiar with other dermatological conditions. Moreover, funding for leprosy became limited since the World Health Organization (WHO) stated in 2005 that leprosy was no longer a public health problem. Later, primary health care workers in general were likely to know more about more acute and highly prevalent illnesses like HIV/AIDS and tuberculosis that would have been a larger aspect of their training. Only recently has interest in dermatology increased as donors and the WHO have put more focus on NTDs with dermatological symptoms, the so-called skin NTDs.

NEW DEVELOPMENTS – FOCUS ON TEACHING

Alternative strategies were developed through combining efforts. By the 1980s, Zimbabwe and other countries showed the positive effect of combining leprosy control clinics with general skin health care. It was the first country to control endemic leprosy with multiple drug treatment (MDT), good follow-up, and early detection of infected people. At the same time, the International League of Dermatological Societies (ILDS) established a training centre – the Regional Dermatology Training Centre (RDTC) for 'community dermatologists' – in Moshi, Tanzania: a two-year in-service training in general dermatology, which trained health officers and senior nurses who worked on sexually transmitted diseases (STDs) and leprosy care. To date, 240 senior clinical officers from thirteen different countries have been trained who provide most of the dermatological care in Zambia, Uganda, Tanzania, Kenya, Eswatini, Lesotho and Malawi. In other LMICs, similar training centres were established, usually with a shorter training period. However, these professionals with limited training needed the option of consultations with fully trained dermatologists, which were done by post and enclosed photographs.

Figure 2. Screen of a mobile phone showing prurigo nodularis.

TELEDERMATOLOGY GOES ON LINE

When the internet became available, photos could be sent by e-mail. This greatly speeded up consultations, which were previously done by post, and greatly improved efficiency. This made teledermatology much more feasible and efficient. This great opportunity for low-resource settings was dramatically improved when affordable digital cameras became available that could take excellent pictures. Nowadays, many people have a smartphone, and internet

coverage is continuously improving in rural areas, making direct contact between the community dermatologist/primary health care worker and the dermatology specialist in a town possible. Fortunately, this is changing as more dermatologists are being trained in LMICs or intend to work there.

Figure 3. Different dermatoscopes (courtesy Dr Salvatore Noto).

Clearly, teledermatology helps in making a likely diagnosis with advice for treatment. This increasingly benefits patients who no longer need to travel to see a dermatology specialist, saving them time and money. It is of benefit for the primary health care worker who learns from the consultation by telemedicine, and equally for the dermatology specialist who may earn an income in town and still serve his country. This approach has proven successful, but its sustainability depends on motivated and experienced dermatology specialists who are willing to participate. Teledermatology forums (a panel of dermatology specialists where the one who has time answers first, after which the others add to the discussion) appear to be a possible solution, and some are already operational. For the Dutch reader, the best known example is organised by TROIE: dermatoloog@troie.nl. Over time, telemedicine coverage may increase as more primary health care workers, including community dermatologists, experience the benefit of this service.

SMART APPLICATIONS FOR SKIN HEALTH

The use of smartphones and digital health technologies is becoming common practice. Applications for dermatology in the field have become increasingly available. However, most technologies are based on the dermatology of the light skin in HICs. The recently launched mobile Netherlands Leprosy Relief (NLR) SkinApp, for example, could be a great support in identifying common NTD- and HIV-related skin diseases, including presentation in the dark skin at the peripheral health care level.[2] The NLR SkinApp can be used during the patient consultation as a source of information about signs and symptoms as well as about the therapy of common skin diseases. It contains pictures to be compared with the lesions of the patient or with pictures taken and stored on the mobile phone. It runs an algorithm that recognises signs and symptoms on the affected body parts and provides peripheral health workers knowledge on less common skin diseases by offering an easy-to-use database of skin diseases as a training tool, including signs and symptoms, pictures, and treatment options. This application can be consulted even in offline settings. While usage is still limited, the ILDS is actively promoting this tool. It is continually under review to improve its performance. It does not completely replace books focused on the common skin diseases in the area. Face-to-face supervision remains necessary, and algorithms need validation, including in HICs.

OTHER NEW DEVELOPMENTS COMING INTO USE IN REMOTE AREAS

The traditional magnifying glass is becoming more commonly accompanied by the dermatoscope. Dermatoscopy is the examination of skin lesions by means of the dermatoscope (Figure 3). It is also known as dermoscopy or epiluminescence microscopy. It enables inspection of skin lesions to better interpret what is underneath the epidermis (Figure 4). The dermatoscope consists of a focusable magnifying lens, a light source (LED

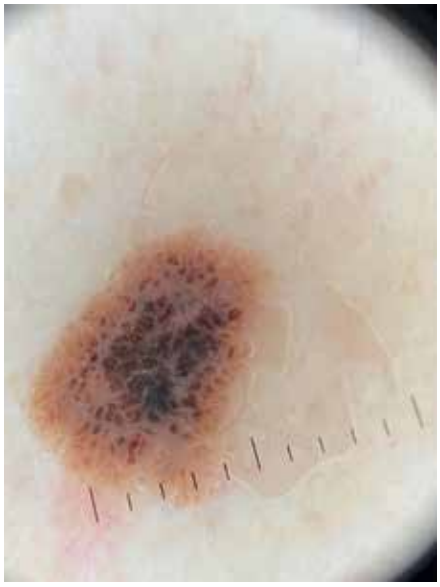

Figure 4. A dermatoscopic picture: seborrhoeic keratosis (courtesy Dr Paola Pini).

illumination), a flat transparent plate that is in contact with the skin, and sometimes a liquid medium between the instrument and the skin. The new dermatoscopes can digitise the information obtained and send it to experts by mobile phone. Algorithms have been developed to interpret those pictures but are not quite reliable yet and are mostly focused on diagnosing melanoma. For dark skin, extra expertise is needed. This will become available as the dermatoscope is now present in most dermatology training centres in LMICs. For the diagnosis of scabies, it has proven to be extremely handy.

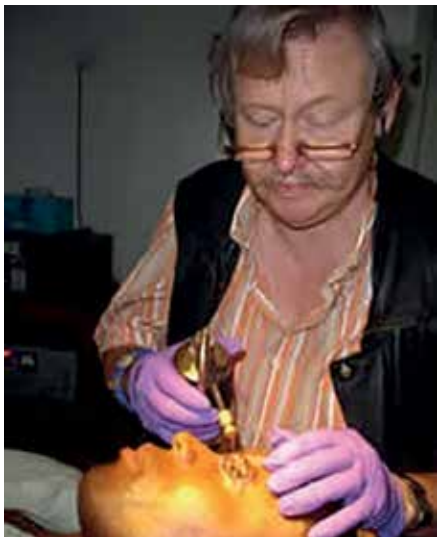

Figure 5. Treatment of Kaposi's sarcoma using the cryogun.

Point-of-care tests in dermatology at ground level overlap with those available for NTDs and STDs; a discussion of this is beyond the scope of this paper. Treatment options that are well established in HICs are becoming increasingly available in LMICs, including laser therapy, treatment with UV light (A and B), and radiotherapy, but are not yet available in rural areas. However, the cryogun is now increasingly replacing the liquid nitrogen containing cottonwool swab for cryotherapy of skin malignancies, especially in people suffering from albinism or xeroderma pigmentosum (Figure 5). Common warts and condyloma acuminata can also be treated in this way, even in immunocompromised people. Newer, innovative treatments, for example with biologicals, are beyond the capacity of LMICs and first need research on their safety and efficacy.

CONCLUSION

The care of skin diseases in LMICs is slowly improving thanks to an increasing number of community dermatologists and the use of new technologies such as the smartphone that facilitate teledermatology, including clinical images and the use of digitised images from the dermatoscope. The introduction of (new) treatment options that are well established in HICs is slow. While some of these tools have been introduced in LMICs some years ago, a systematic evaluation of their impact on patient management in rural areas is eagerly awaited.

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Digital health is our past, present and future

Digital health was introduced a long time ago. In 1878 *The Lancet* published an article about the radio doctor, implementing the telephone in the health care practice to prevent home visits in the United Kingdom. A few decades later there was discussion about the telecardiogram in 1906, for which Willem Einthoven won the Nobel Prize in Medicine in 1924. In the 60's and 90's of the last century, respectively, teleradiology and teledermatology were introduced. It was only at the start of the new millennium that digital health took off significantly, mainly due to the development of internet (e-health) and the mobile phone (m-health).

The relatively new terminology of digital health covers the above-mentioned developments. The Healthcare Information and Management Systems Society (HIMSS), an American not-for-profit organisation dedicated to improving health care quality, has launched the often used definition of digital health as: "Digital health connects and empowers people and populations to manage health and wellness, augmented by accessible and supportive provider teams working within flexible, integrated, interoperable, and digitally-enabled care environments that strategically leverage digital tools, technologies and services to transform care delivery."[1]

This definition partly includes the 'why' of digital health. Like traditional medicine, digital health focuses on four goals: enhancing patient experience, improving population health, reducing costs, and improving the wellbeing of the health care provider.[2] In addition to these specific targets, it is often the lack of health care providers in low-and middle-income settings that makes digital health solutions even more beneficial here.

IT WAS ONLY AT THE START OF THE NEW MILLENNIUM THAT DIGITAL HEALTH TOOK OFF SIGNIFICANTLY

The rise of technology and especially the increased usage of mobile phones induced a spectacular growth of digital health. In 2018 close to 5 billion people worldwide used a mobile phone, and almost half of them used a smartphone.[3] Mainly through the mobile phone, in 2017 already more than 325,000 health apps were available, accounting for 3.7 billion downloads worldwide, which is a growth of 700% between 2013 and 2018. However, the quantity of apps and digital healthcare does not necessarily say something about the quality.

There are multiple elements of digital health. Telemedicine is one of the first and still one of the main elements of digital health. This includes: (i) health education via websites

with patient information, like the British NHS.uk or the Dutch website Thuisarts.nl,[4] (ii) interventions to measure and manage blood pressure at home,[5] (iii) remote diagnostics and treatment advice through tele-dermatology,[6] and (iv) online treatment and care of depression.[7]

Other important elements of digital health are the medical devices which range from weighing scales which send measurements to digital platforms[8] to devices to control blood glucose in diabetics,[9] often increasingly linked to artificial intelligence components and electronic health records.

Digital health is rapidly increasing in almost all areas of medicine, like the previously mentioned dermatology, radiology and cardiovascular prevention, with mental health in the lead. The application of mental digital health is partly due to the increased burden of mental health worldwide, combined with the relatively limited number of trained health care workers, and possibly a lower need for direct physical examination compared to other fields of medicine. Both in high- and in low-income countries there is a strong need for digital components to cover mental support and care, and to both literally and figuratively close the distance between the patient and the caregiver.[10] Current digital interventions in mental health cover almost the complete range from prevention and diagnostics of mental health disorders to online standardised and validated questionnaires and apps as well as chatbots and online therapists for treatment and medication.

Digital health however faces barriers and challenges. Electronic devices and a digital network are dependent on the reliability of the electricity supply, network and devices. Next to these technical requirements, the level of digital literacy and privacy issues play a pivotal role as well as the costs involved, from developing to implementing a reliable digital health care intervention system including programming and marketing input.A major challenge of digital health is how to include the most vulnerable and marginalised. Although there is an enormous growth in the usage of digital health, there is a risk that this mostly benefits those who already know how to find their way in the health system. Due to practical and commercial reasons, several digital health interventions are aimed at the so called 'worried well', a relatively healthy and wealthy subpopulation who would like to spend large amounts of money and time to continuously optimise their wellbeing although the overall impact on their health is limited.[11] On the other hand, unfortunately there still are specific groups getting less access to digital health interventions than others.[12] The Covid-19 pandemic demonstrated once again the further increase in health care inequality, partly due to the fact that the most marginalised groups, such as the elderly and less educated people, had difficulties in continuing their care online.[13]

THE COVID-19 PANDEMIC DEMONSTRATES AGAIN THAT THE HEALTH INEQUALITY IS FURTHER INCREASED

There are several inspiring examples of how digital healthcare is functioning already in several LMICs, ranging from a digital health ID in Benin or online pharmacy in Bangladesh to an innovative genetic testing programme in Nigeria and a digital platform to connect with dietitians, nutritionists or health coaches in Egypt.[14] Digital health is our past, present and future. It has been woven into medical practice since the 19th century, is now a much greater part of our daily practice, and will definitely increase the access of present and future generations to more efficient, effective and equitable healthcare.

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Amniotic band syndrome

SETTING

This case is from Lolwa, a rural village in the Ituri rainforest located in the Democratic Republic of the Congo. A local Congolese medical officer and a medical doctor in global health and tropical medicine (MD GHTM) are running the hospital, which consists of 55 beds. The nearest option for advanced general surgery is a three-hour drive, but due to safety reasons patients are often not willing to travel.

CASE

A healthy woman, gravida 3, para 1 (one spontaneous abortion) gave birth to a term neonate. She had three antenatal consultations during pregnancy, all of these without complications. She did not undergo any ultrasound examination during pregnancy. There was no evident history of abdominal trauma, although she reported occasional falls during her work on the fields. The family history consists of congenital clubfoot in the father's family. During labour the membranes were artificially ruptured at 8 cm dilatation to improve the progression of labour. The amniotic fluid was red-brownish coloured and looked like old blood. There seemed to be more amniotic fluid than normal. After birth, the medical doctor was informed that the left arm was found amputated at the site of the proximal humerus, and the arm had been delivered after the head of the baby was born. At inspection, the amputated arm was oedematous and the hand looked smaller than the intact right hand of the neonate. At inspection of the neonate, the residual stump of the humerus was not completely covered with any tissue. There was also a bilateral clubfoot (Figures 1-4)*. The medical doctor in charge thought of an amniotic band syndrome and consulted the Consult Online panel for therapeutic advice on the residual stump and asked if antibiotic prophylaxis was indicated.

SPECIALIST ADVICE

The diagnosis was confirmed by the specialists. They advised shortening the humerus until it was covered by soft tissue. But if the humerus does not or barely extends past the wound, healing per secundam (e.g. without surgical intervention) was suggested because of the lower risk of infection and to retain a maximum length of the stump. Antibiotic prophylaxis was recommended.

AMNIOTIC BAND SYNDROME

Amniotic band syndrome or sequence (ABS) is a congenital disorder of foetal anomalies associated with foetal-placental fibrous bands. The aetiology is still unknown and considered to be multifactorial.[1,2] Different theories exist, suggesting either an intrinsic or an extrinsic cause. An intrinsic cause suggests that anomalies of the foetus result from the formation of amniotic bands due to a disturbance of the developing embryonic disk. An extrinsic cause suggests foetal entanglement occurs by mesodermal bands after disruption of the amnion.[2] The impact of ABS ranges from minor

Figure 1. The newborn with the site at which the arm was amputated in utero. There is a bilateral clubfoot.

Figure 2. A close-up of the site of amputation; the distal part of the humerus is not covered with tissue.

Figure 3. The amputated arm after delivery.

Figure 4. The situation after surgical correction of the stump.

deformity to miscarriage or stillbirth. The incidence varies from 1:12,000 to 1:15,000 live births.[2]

The diagnosis of ABS can be made antenatally or, as in this case, peripartum. An antenatal diagnosis is suspected in the presence of amnion loose in the cavity, digital amputations, asymmetric limbs, or random anomalies during an ultrasound examination.[1,2] One should scan for amnion bands and see if movement of the foetus is restricted due to fixation. A foetal structural assessment is indicated in case of an amnion band. Clearly, all these findings are highly dependent on the quality of the ultrasound machine and the skills of the radiographer or radiologist. After antenatal diagnosis, timely intervention is recommended to release the amniotic bands via foetal surgery by fetoscopy to recover the perfusion of the affected area. Postnatal therapy consists of immediate surgical release of the bands or repair of the affected body part. Recurrence is rare, but some familial cases have been described. Club feet are associated with ABS, as is seen in this case.[3] To date, ABS is considered a sporadic event with no commonly accepted risk factors.

FOLLOW-UP

The neonate was admitted and the stump was covered with salinised compresses. The next day, the humerus was slightly shortened and covered with subcutaneous tissue and skin, using local anaesthesia and antibiotic prophylaxis. Wound healing was uncomplicated and shoulder movement intact. The correction of both club feet was done successfully using the Ponseti method.

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* Figures 1-4 published with the permission of the child's mother.

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Ethical considerations in using high tech solutions in low-resource settings

One does not have to watch the news extensively to see evidence of the incredible strain that today's challenges are putting on health systems globally. Amidst the devastating Covid pandemic that relentlessly pushes on into its second year, there are conflicts crippling whole regions, incalculable numbers of refugees and displaced persons stuck in camps, and a full sheet of infectious and non-communicable diseases continuing to devastate communities with sub-optimal access to healthcare. In many of the low- and middle-income countries (LMICs) most affected, these stories highlight a truth that pertains to far more than just these events: that the health systems themselves are often inadequate for many of the people whom they are supposed to be serving, and more advanced solutions are needed beyond the ones currently being offered.
Rapidly improving technologies offer promise in every sector of health in both low- and high-resource settings. High tech interventions in some LMICs range from medication delivery by drone to remote hospitals, medical imaging that can be done through mobile phones, diagnostic algorithms that reduce the requirements of clinical oversight, and mobile health technologies that can facilitate transition to electronic health recording, to name just a few. While these technologies are badly needed in many areas, there are important ethical factors

regarding their appropriate delivery that should be considered when they are implemented in new locations.

SUSTAINABILITY AND HEALTH SYSTEM STRENGTHENING

While some emerging technologies are being used for short-term solutions, such as disaster relief and aberrant outbreaks of infectious diseases, the gold standard for global health interventions is to enable them to integrate sustainably within local health systems. Technology that is implemented and only used for short periods of time not only fails to address issues in the long term, but will actually leave gaps in health care delivery system once it stops working. This means that high tech solutions that are introduced into new systems should have the capacity for long-term use and in many cases should include the potential for scaling up to cover larger areas and populations. They must be capable of being used autonomously and being repaired, maintained, and sometimes even produced locally. If not, the introduction of the technologies will deepen the cycles of dependence that local health systems will have on foreign institutions or the technologies may end up being completely neglected, resulting in wasted resources in desperate areas. It is not uncommon, for example, for tropical medicine doctors working in LMICs to report seeing unused medical equipment such as ECG machines or even extremely expensive neonatal resuscitation tables left in an ignored corner of the hospital. Such tools, which have already proven to be lifesaving, still struggle with implementation in certain areas. This underlines the fact that the success of these interventions is due as much to the strategy of implementation and subsequent training as it is to the efficacy of the tool.

To improve the sustainability of new tools, capacity building should be an essential focus where such technologies are implemented. Involvement by members of local health organisations at every level of a programme can not only seek to increase the likelihood of the programmatic success and sustainability of such interventions, but can also improve the technological capability of local health workers. This can be done by ensuring adequate provision of training programmes for local workers and managers when introducing new interventions that involve technological components. Additionally, there should be an infrastructure in place to promote good practice for standardised and optimal use of new interventions, such as standard operating procedure guides (SOP) guides, instructional manuals, and support groups for community health workers and others who may be trialling the interventions in the field, such as via WhatsApp.

LOCAL CONTEXT AND COMMUNITY CONSIDERATIONS

It is essential that researchers and proponents of new technologies from high-income countries (HICs) who plan to implement interventions in LMICs have a comprehensive understanding of local contextual challenges and the true limitations of resources in the field. Foreign implementers need to perform a considerable amount of formative research alongside local partners in areas where interventions are to be implemented. When introduced, technologies should also be streamlined to support the way in which local health staff work, in as user-friendly a manner as possible, improving the likelihood of their feasibility and success.

In light of the numerous challenges and risks that can come with the introduction of new technological tools in health systems, it is vital that these technologies are introduced through a needs-driven approach. That is to say, just because high tech tools are available does not mean that they should be introduced unless it is clear that there is a need for what the technology offers in that region and that the potential benefits outweigh the associated risks. When introduced with plans for scaling up, the intervention should also be proven to be cost-effective and not duplicating efforts that existing services are already covering. This reinforces the importance of a comprehensive understanding of local circumstances that is best obtained through local partnerships and extensive research.

Additionally, programmes should, whenever possible, try to incorporate feedback from the beneficiaries, including patients receiving care, community health workers, and members of the ministry of health, to aid in an objective and local needs assessment.

As new technologies can, particularly in remote settings, be a source of apprehension, sensitisation to products and materials is integral both to improving local understanding and eliminating cycles of mistrust. Involving local leaders can be fundamental to a programme's success and may offer a way to mitigate such mistrust, particularly in remote areas where such technologies may not be well understood by local community members. They can also help to ensure that programme delivery is more equitable and targets hard to reach populations, a huge benefit particularly when targeting communicable diseases.[1]

Finally, as m-health interventions and other technologies become more accessible in low-resource settings, the security risks to local users must also be considered. The proliferation of digital data entry and data sharing means that more local workers will have to be trained in good data practices to avoid potential exposure of protected personal data. Once digital data networks are established, they become vulnerable to ransomware attacks and hacking. Implementing institutions for such interventions should also take responsibility for improving local data security and ensuring that they do not give populations any reason for mistrust.

TRIALS AND RESEARCH FOR HIGH TECH SOLUTIONS

Research and control trials in LMICs working to examine the efficacy and feasibility of high tech solutions are a vital part of the scientific process. They should be strictly scrutinised – both at the project's inception and during publication through the peer review process – to maintain the highest standards of research integrity. Recent movements calling to decolonise global health have helped to spotlight an issue that global health research

has historically overlooked, research fairness. This term refers specifically to a systematically unfair ecosystem in which local institutions in LMICs have a significant disadvantage in their competitiveness for research funding and for creating subsequent publications. As grants for high tech solutions in particular will likely favour the wealthy and well-equipped institutions, it is all the more important that they make efforts to promote research fairness in the areas where they work. This can be done in part through the formation of local partnerships, promotion of local institutions, promoting authorship in publications of local researchers from LMICs, and subsequent inclusion in the presentation of results.

Beyond research fairness, partnerships should further aim to empower researchers from the global South to also develop innovative technologies. High tech solutions in the global South, created in the country where they were implemented, have in many cases shown better odds of success and scalability than ones that were developed in HICs and then trialled locally.[2] These 'local' innovations come with a number of advantages such as involving health ministries as stakeholders (advantageous in both maintaining sustainability and strengthening the existing health system), potentially gaining faster regulatory approval and therefore being more readily available for use, and using lower-cost goods that are available through existing supply chains. Such successes in locally conceived and produced innovations have even resulted in global health experts like Madhukar Pai advocating for a change in the way in which global health technologies are introduced, saying that we should move away from models where everything is developed in the global North and expected to function accordingly in LMICs.

CONCLUSION

High tech solutions can be an incredible asset in improving health outcomes in low-resource settings in the future. With vast threats to human health at an exceptional moment in history, finding new and effective solutions will be vital to solving the immense challenges that interrupt adequate delivery of health care globally. The global health community would be remiss if it were to ignore these solutions. However, like everything else in the field, we must closely examine and scrutinise every intervention to ensure that it upholds appropriate ethical standards.

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