From Ritual Washing to Disease Control
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Thank you to Rabbi Fel, to Max Klein and especially to Terri Schwartz Russell for inviting me to talk today.

My 1973 *Bar Mitzvah Parashah* was *Hukkat - Parah* (the red heifer) & even then (in SWA/Namibia, 1000 miles from the nearest cities: Johannesburg and Cape Town in SA), I was intrigued at the idea that the ashes from the red heifer could be used for ritual washing and purification.

I was not focusing on the redness of the heifer, or the *Hukkat Hatorah* ritual (which is used to describe sections that "cannot be derived from human reasoning"), but instead, I was wondering about the scientific basis of these phrases:

14This is the law: if a man dies in a tent, anyone entering the tent and anything in the tent shall be unclean for seven days.	**יד**זֹאת הַתּוֹרָה אָדָם כִּי יָמוּת בְּאֹהֶל כָּל הַבָּא אֶל הָאֹהֶל וְכָל אֲשֶׁר בָּאֹהֶל יִטְמָא שִׁבְעַת יָמִים:
15Any open vessel which has no seal fastened around it becomes unclean.	**טו**וְכֹל כְּלִי פָתוּחַ אֲשֶׁר אֵין צָמִיד פָּתִיל עָלָיו טָמֵא הוּא:

14: I wondered: is this quarantine, and why did it last 7 days?

15: Is this to avoid airborne contamination of open vessels?

In other words: Were the *B'nei Yisrael*, traveling through the desert, essentially setting up clear rules of **hygiene, sanitation and**

quarantine thousands of years before 19th C. 'Germ theory of Disease (did this influence Ignaz Semmelweis – an Austrian Jewish physician (1847), then later Louis Pasteur). Would these ancient rules have prevented spread of Ebola?

Does this suggest that *B'nei Yisrael* were dealing with Infectious Diseases by preventing transmission amongst the **community**, rather than focusing solely on curing the **individual**? This is very sophisticated practice and resonates now. As you know, the discovery of penicillin in 1928 lead to the golden age of antibiotics, which focused on treatment of the sick individual. But with the rise of Multidrug Resistant (MDR) bacteria, e.g. MRSA, we need to look at ways to **control** disease, both by treating the individual **and** by **preventing** the spread through the population.

Treatment as a continuum not as piecemeal solutions:

In fact, I have a 2015 publication on my desk from the Obama White House setting up a **"National Action Plan for Combating Antibiotic-Resistant Bacteria."**

Goals:

1. Slow the emergence of resistant bacteria and prevent the spread of **resistant infections**

2. Strengthen National **<u>One-Health</u>** Surveillance efforts to combat resistance *(one health recognizes the health of people is connected to health of animals)*
3. Advance Development and Use of Rapid and Innovative **<u>Diagnostic</u>** Tests for identification and Characterization of Resistant Bacteria
4. Accelerate basic and applied research and development of New Antibiotics, Other Therapeutics and **<u>Vaccines</u>**
5. Improve International Collaboration and capacities for Antibiotic-resistance **<u>Prevention, Surveillance, Control</u>** and Antibiotic R&D.

<u>Fast forward from 1970 SWA to 1986 UK</u>

I did my Ph.D. at Great Ormond Street Hospital (GOSH) in London, studying a group of children who were unusually susceptible to bacterial and fungal infections, especially in the first 18 months of life. I showed that they were missing an ancient immune system protein that we later identified as mannose binding lectin (MBL). This protein binds to the sugars that coat the cell surface of pathogenic micro-organisms, but it does not bind to healthy human cells. The protein looks like a Bunch of tulips, where the "heads" bind to sugars on the microbe cell walls, while the "stalks" activate the immune system.

I found the children had a single point mutation that disrupts the collagen helix "stalks," the mutant protein could bind to the cell wall, but did not activate immune response amplification pathways.

I published this in the *Lancet*, and before I knew it, I was doing a post-doc at Harvard Medical School/Boston Children's Hospital, schlepping Ruth and our 18-month old daughter – Dinah.

Harvard did not sponsor green cards, so I went to industry, developing monoclonal antibodies for Cancer treatment at a small startup, which was acquired by larger and larger companies & taking me further and further away from my science. In 2009, they closed my department and let me go (the best decision they could have made for me.)

Back at Harvard, at the new Wyss Institute for Biologically Inspired Engineering. I engineered a new version of MBL – FcMBL, designed to bind a broad spectrum of different pathogens (this has only the MBL "tulip heads" [no stalks] & these are fused to antibody fragments for better expression & purification). Great timing, because DARPA sent out a Broad Area Announcement (BAA) looking for a broad-spectrum pathogen binding protein to use in dialysis-like treatment of sepsis.

1) FcMBL: Binds > 100 different pathogen species, fungi, Gram Negative Bacteria such as *E. coli, Pseudomonas, Klebsiella, A*.

baumani, Gram Positive Bacteria, e.g. MRSA, MTb, viruses, e.g. Ebola, HIV, parasites such as Malaria. Binds LIVE and DEAD pathogens, including Multidrug Resistant Bacteria.

2) Used in an infection diagnostic – 30 minute test with > 85% sensitivity & specificity, detects 86% of sepsis patients while blood culture (gold standard) only detected 18 % and in 5-7 days.
3) Used as a therapeutic – Dialysis-Like Therapy for treating Sepsis, with the companion diagnostic (hopefully going into the clinic this year.)
4) Used as a diagnostic in food industry – measure yeast and mold in yogurt – results in < 8 hr vs. the current 3-5 days.
5) Used for environmental monitoring – sterile surfaces in food prep, water filter.
6) Used as an infection vaccine - in combination with "artificial lymph node" technology developed with Glenn Dranoff (he used to be at Temple Emunah) capture dead pathogen material (even directly from an infected patient) and use this to make a "ring vaccine" that can protect caregivers against the index patient's disease. Strength of the technology – fast to make, safe, cheap, modular (military biothreat application.)
   a) Single vaccination (does not need boosting) in slow-release scaffolds
   b) Stable dry formulation at room temperature (does not need refrigeration)

c) Bacterial vaccine (most current vaccines are viral, childhood vaccines)
d) Applicable to veterinary and human disease, giving protective "herd immunity" against bacteria, virus, fungus, and parasite infection
e) Strong but safe immune response – using DEAD pathogen (almost as strong as live attenuated vaccines, but potentially safer)

To summarize, I am suggesting that in this week's *parashah*, there is a scientific explanation for the Talmudic rituals based on Disease control and in the future we should consider using this systematic approach of **hygiene, sanitation and quarantine,** as well as antimicrobial therapies to prevent the spread of multidrug resistant organisms.

And, who knows, with our modern technologies, could the passage "*Any open vessel which has no seal fastened around it becomes unclean"* instead read: "Check any open containers for contamination and discard any materials with pathogen load 3-fold over background!"

Shabbat Shalom and remember to wash your hands before *Hamotsi*.