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HIV and Hepatitis C – An Update for Primary Care Physicians

SIPPA – Orientation
June 8, 2016

Dr. Alexander Wong, MD, FRCPC.
Internal Medicine & Infectious Diseases
Regina Qu'Appelle Health Region

Disclosures – AW

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- **I have received consulting fees and honoraria from the following companies:** Merck, Gilead Sciences, Bristol Myers Squibb, Pfizer, Janssen, Boehringer-Ingelheim, Abbvie.

- **I have received funding for regional and provincial programming from the following companies:** Merck, Gilead Sciences, Bristol Myers Squibb, ViiV, Janssen, Abbvie.

- **I currently participate in clinical trials with the following companies:** Gilead Sciences, ViiV, Merck, Abbvie, Bristol Myers Squibb.

- If you detect **any** commercial bias, please tell me ASAP! Email: *alexander.wong@usask.ca*

Contacting Us…

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- For any questions, criticisms, patient care issues, or clarifications in southern Saskatchewan:
  - **Email:** alexander.wong@usask.ca
  - **Pager:** Call RGH switchboard at 306-766-4444 and ask for myself, ID physician on-call, or infectious diseases clinic.
  - **Clinic:** Call 306-766-3915 to speak with our clinic nurses for help with patient issues or referrals. Fax referrals to 306-766-3995.
  - **WWW:** *http://www.rqhealth.ca/specialized-ambulatory-care/rqhr-infectious-diseases-clinic*

- For referrals in central/northern Saskatchewan, contact the Positive Living Program based at RUH:
  - **Clinic:** Call 306-655-1783, Fax 306-655-0614
  - **Web:** *https://www.saskatoonhealthregion.ca/locations_services/Services/Positive-Living/Pages/Home.aspx*

- "You test, we'll do the rest."

HIV – The Basics

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- **Epidemiology**
  - **September 2013:** ~35.3 million worldwide with HIV infection, > 35 million dead since the beginning of epidemic.
  - ~25 million living in sub-Saharan Africa, where overall prevalence is ~4.7% of adult population.
  - 71,300 individuals with HIV in Canada as of 2011.

- **Pathophysiology**
  - HIV attacks and depletes CD4 T-cells, which form significant component of adaptive immune system.
  - **CD4 count** represents “strength” of immunity.
  - **HIV viral load** represents amount of virus in plasma.
  - Over time, as the CD4 count drops lower, patients become at risk for infection, malignancy, wasting, etc.

HIV – The Basics

- **HIV vs. AIDS?**
  - **AIDS** represents untreated / suboptimally treated HIV infection, characterized by AIDS-defining conditions and/or CD4 count <= 200 (normal >= 500)
  - **HIV infection ≠ AIDS.**
  - Goal is to link individuals to treatment so that they STAY HEALTHY and do not progress to AIDS.

HIV – The Basics

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- **Treatment**
  - No cure exists, promising studies and work done with aggressive treatment of early / acute infection.
  - Antiretroviral medications highly effective, minimal toxicity, simple to take (once-daily, often 1 pill/day).
  - Viral load ↓ & CD4 ↑, even advanced disease.
  - Patients stay healthy and live normal healthy lives.

- **Prognosis**
  - Lifespan of HIV-infected individuals on HAART nearing that non-infected age matched cohorts.
  - **HIV is not a death sentence.**

HEALTH

'Africa on the Prairies'

How does an area in one of the world's richest nations end up with Third-World rates of HIV infection?

BY KEN MACQUEEN · Sometimes, when Dr. Alex Wong wants to draw the attention of government policy-makers to the HIV epidemic in his home province of Saskatchewan, he entitles his statistical presentation "Africa on the Prairies." Here in Vancouver, at the biennial conference of the International AIDS Society, he took a more scholarly tone: "The Developing World in Our Own Backyard: Concentrated HIV Epidemics in High-Income Settings." He was sharing the stage with doctors from the hard-hit American regions of Appalachia and the southeastern U.S., but the point was made. That regions of two of the world's wealthiest countries are dealing with Third World levels of HIV infection rates reflects, in his view, a sad failure of policy, planning and political will.

At its peak, five years ago, the infection rate in Saskatchewan was more than 19 people per 100,000, two and a half times the national average—by far the highest rate in Canada. While that has since fallen to about twice the national average, those numbers don't address the racial disparity and a potential looming disaster, says Wong, a clinical director of the HIV provincial leadership team.

Turnaround: *Initiatives like Insite in B.C. helped slow that province's AIDS epidemic*

The infection rate for Saskatchewan's non-Aboriginal population is below the national average. Yet while First Nations and Metis account for about 16 per cent of Saskatchewan's population, they represented about 80 per cent of all new cases of HIV diagnosed in 2011, Wong told a conference workshop. "The incidence rate in our Aboriginal population is about 88 per 100,000, which is 14 times the national average, on par with various African countries."

The primary cause of the HIV outbreak is an epidemic of injection-drug use in the urban centres like Regina and Saskatoon, and of injected prescription drugs in rural regions and isolated reserves.

But blame also falls on the legacy of colonialism, residential schools and discrimination, as Margaret Poitras, a Cree and CEO of the All Nations Hope AIDS Network, told the panel. In 2012, Poitras's network collaborated with the Public Health Agency of Canada and the Regina Qu'Appelle Health Region to survey a representative sample of more than 1,000 members of Regina's Aboriginal population. More than half reported being removed as children from their families by child welfare agencies, churches or governments. Some 43 per cent were placed in foster care, 58 per cent reported having spent time in a youth or adult correctional facility and 50 per cent reported having used injection drugs.

That social chaos translated into troubling levels of disease. More than 1,000 of those surveyed submitted anonymous blood samples. About one in 20 samples was infected with HIV, and almost half those people were unaware they carried the disease. Overall, 42 per cent of respondents carried hepatitis C antibodies. "So two in five Indigenous individuals walking the streets of Regina were hepatitis C-positive," says Wong. "Those numbers, to me, are absurd."

Appalachia and the southeastern U.S. are also reeling from an epidemic of HIV and hepatitis C, with striking similarities, including a plague of injection-drug use. Like infected populations in Saskatchewan, many live in rural areas of high unemployment with poor access to health care.

In the U.S., state laws prohibiting needle exchanges and syringe possession without prescriptions led to increased transmission of infections, said John Brooks of the Centers for Disease Control and Prevention in Atlanta. In Saskatchewan, Wong is frustrated by inadequate harm-reduction strategies and gaps in care that are contributing to the epidemic. While health care is primarily a provincial responsibility, reserve and status Indians are largely a federal responsibility. "You've got health regions that don't want to touch it, saying it's federal," Wong says. "Then you have the province saying, 'Well, the health regions are responsible for this.' Nobody is really taking ownership. But when push comes to shove, what's happening on these reserves falls to the feds."

Federal Health Minister Rona Ambrose didn't attend the conference, but a spokesman said the government has committed $600 million since 2010 to its AIDS initiative and $300 million since 2006 for related research. And Health Canada spokeswoman Maryse Durette said, in an emailed response, "HIV testing and treatment fall under the jurisdiction of the provinces and territories, and are most appropriately based on each jurisdiction's unique epidemiology and context."

Wong sees sad parallels between Saskatchewan today and the British Columbia of 25 years ago, when it was the Canadian epicentre of the HIV/AIDS epidemic. It took the declaration of a medical emergency, community activism, a massive infusion of provincial funds and, in the case of Vancouver's supervised injection site, the challenging of federal drug laws to turn B.C. into a world-leading success story.

Mental health services and food and housing security also have to be part of the solution if people are going to stay on their life-saving medications, says Wong. "That's what we're trying to deal with in the province right now: Opening our politicians' eyes and saying, 'You know, we just have to be pragmatic about this. It's either going to cost us now or it's going to cost us 10 times more down the road.'" ♣

DARRYL DYCK/CP

The SK HIV Epidemic

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- **The Epidemic is Unique.**
  - **Worldwide:** heterosexual > MTCT > MSM > IVDU
  - **NA/Europe/Australia:** MSM > heterosexual > IVDU > MTCT
  - **Saskatchewan:** IVDU > heterosexual > MSM > MTCT

- **Background**
  - Epidemic of injection drug usage, predominantly in urban cores and rural/remote reserve communities.
  - Disproportionately affected populations in these communities, namely First Nations / Aboriginal / Metis populations.
  - **Urban:** IV cocaine (similar to early years in BC), now meth.
  - **Rural:** injection of prescription drugs (benzos, stimulants, opiates).
  - **IV cocaine/meth** → frequent usage, higher relative chaos compared to opiate usage, no available substitution therapy.

Saskatchewan - Overview

SK Ministry of Health, 2016

Food For Thought.

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- **Aboriginal vs. Non-Aboriginal Populations**
  - In 2011, national rate of HIV infection = 6.4 / 100K.
  - SK rate of HIV infection = 17.2 / 100K.
  - ~80% of HIV diagnoses in 2011 in Aboriginal / FN population, comprising 15.6% of SK population (Statistics Canada).
  - Therefore, rate of infection in Aboriginal population = 88 / 100K (14x national average, ~ Nigeria).
  - Non-Aboriginal infection rate = 4.1 / 100K, 36% below national average.
- **An "Epidemic of Injection Drug Use"**
  - SK has the highest reported rates of co-infection with hepatitis C and HIV in the world (77%). In parts of SK, co-infection rates > 80%.
  - In RQHR, ~60% of HIV+ individuals are positive for anti-HCV.

Overview of A-Track

- **Pilot Point Prevalence Survey in Regina, SK.**
  - Collaboration between community and public health partners.
  - December 5/11 – June 15/12.
  - 1045 individuals provided blood samples for HIV testing: **54 (5.2%)** were HIV positive, **24 (2.3%)** were unaware of HIV-positive status.
  - 1044 individuals provided blood samples for HCV testing: **41.6%** had previous exposure to hepatitis C.
- **Injection Drug Use & HIV**
  - 50% of participants reported some previous use of injection drugs; males >> females.
  - In participants with self-reported history of injection drug use, 9.5% were HIV-positive.

http://www.phac-aspc.gc.ca/aids-sida/publication/reports/a-track/index-eng.php, accessed June 15, 2015

Relevant Questions

- What tests do you order?
- What do you do when your HIV / hepatitis C “screening test” comes back positive?
- What do you tell the patient?
- Who can you refer to in southern / central / northern Saskatchewan for specialized care?
- Are there extra precautions that I need to take around people who have HIV and/or hepatitis C?
- What constitutes a meaningful “accidental exposure” to either HIV or hepatitis C, and what do we do about it?

Diagnosis of HIV Infection

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- **Why is it important to test for HIV?**
  - There are individual-level benefits for the patient and societal benefits for testing for HIV infection.
  - Early identification allows for prompt initiation of antiretroviral therapy (ART), which improves life expectancies for HIV-positive individuals to that of the general population.
  - Knowledge of one's HIV status modifies risk behaviours.
  - Treatment with ART reduces an individual's HIV viral load, which in turns reduces their risk of transmission significantly.
- **What are the consequences of NOT testing for HIV?**
  - Many individuals remain unaware that they are HIV-positive. In the United States and Canada, it is estimated that ~20% of individuals who are HIV-positive are unaware of their status.
  - In Canada, 75,500 individuals are living with HIV, and an estimated 16,020 are unaware of their diagnosis.
  - Many patients who are HIV-positive have numerous encounters with the health care system (e.g. family physician, emergency department) but are not tested.

Diagnosis of HIV Infection

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- **Who do I test for HIV infection?**
  - Voluntary confidential HIV testing and counseling should be considered **at least once every five years in all adults**, and can be considered more frequently based on risk factors.
  - Target groups include:
    - **All patients between ages of 13 and 70 unaware of their HIV status.**
    - All persons sexually active with multiple / successive partners who have not had HIV testing in the last year.
    - All patients who request HIV testing.
    - All pregnant women.
    - All patients assessed for a sexually-transmitted infection, hepatitis B, or hepatitis C.
    - All persons with a current or previous history of illicit drug use.
    - All persons from endemic countries.
    - All patients with active or latent tuberculosis.
    - All patients with signs/symptoms consistent with HIV-related disease.

Diagnosis of HIV Infection

- **How do I counsel patients prior to testing for HIV?**
  - HIV testing requires the consent of the individual being offered testing. Consent must be voluntary, informed, and documented.
  - **Verbal informed consent** is all that is required for HIV testing, as opposed to written / signed consent.
  - When you obtain verbal informed consent, document this clearly on the patient record: *Verbal consent obtained for HIV testing.*
  - It is important to **normalize testing** for HIV and other blood-borne infections and to adopt an inclusive testing strategy rather than one focused on identification of risk, no different than checking for dyslipidemia or diabetes.

Diagnosis of HIV Infection

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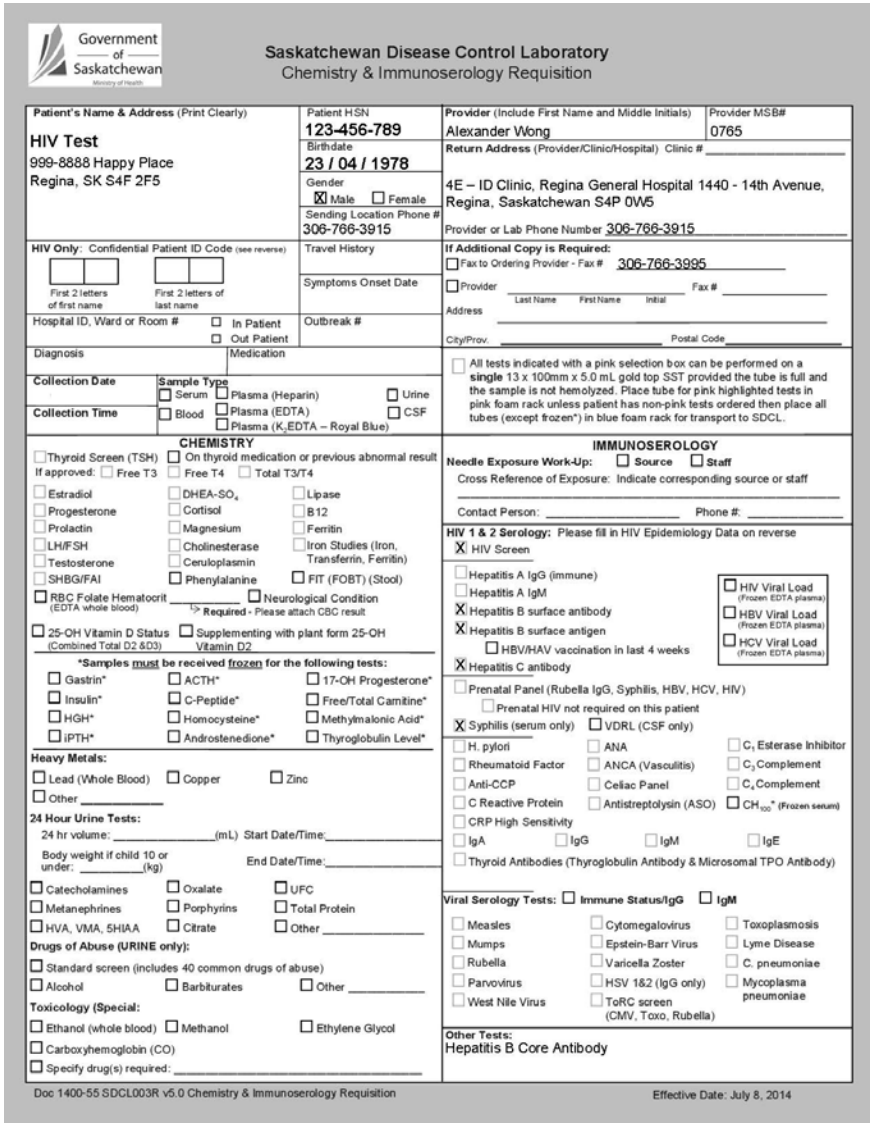
- **What tests do I order for a patient that I want to test for HIV infection?**
  - Order an ***HIV Screen*** on the SDCL Immunoserology requisition.
  - Consider screening for other blood-borne infections and sexually transmitted infections, including but not limited to:
    - Urine NAT for chlamydia / gonorrhea
    - Syphilis serology.
    - Hepatitis C antibody.
    - Hepatitis B surface antibody, surface antigen, and core antibody.
  - **SDCL Immunoserology Requisition:** HIV screen, hepatitis C antibody, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody (written), syphilis (serum only).
  - **SDCL Microbiology Requisition:** Chlamydia & Gonorrhoea Screen (Urine)

SDCL Immunoserology



Government of Saskatchewan

Saskatchewan Disease Control Laboratory
Chemistry & Immunoserology Requisition

Patient's Name & Address (Print Clearly)
HIV Test
999-8888 Happy Place
Regina, SK S4F 2F5

Patient HSN: 123-456-789
Birthdate: 23 / 04 / 1978
Gender: ☒ Male ☐ Female
Sending Location Phone #: 306-766-3915

Provider (Include First Name and Middle Initials): Alexander Wong
Provider MSB#: 0765
Return Address (Provider/Clinic/Hospital) Clinic #:
4E – ID Clinic, Regina General Hospital 1440 - 14th Avenue, Regina, Saskatchewan S4P 0W5
Provider or Lab Phone Number: 306-766-3915

HIV Only: Confidential Patient ID Code (see reverse)
First 2 letters of first name | First 2 letters of last name
Travel History
Symptoms Onset Date
Hospital ID, Ward or Room # ☐ In Patient ☐ Out Patient
Outbreak #

If Additional Copy is Required:
☐ Fax to Ordering Provider - Fax # 306-766-3995
☐ Provider (Last Name, First Name, Initial) Fax #
Address
City/Prov. Postal Code

Diagnosis
Medication

All tests indicated with a pink selection box can be performed on a **single** 13 x 100mm x 5.0 mL gold top SST provided the tube is full and the sample is not hemolyzed. Place tube for pink highlighted tests in pink foam rack unless patient has non-pink tests ordered then place all tubes (except frozen*) in blue foam rack for transport to SDCL.

Collection Date
Collection Time
Sample Type
☐ Serum ☐ Blood ☐ Plasma (Heparin) ☐ Plasma (EDTA) ☐ Plasma (K_2EDTA – Royal Blue) ☐ Urine ☐ CSF

CHEMISTRY

☐ Thyroid Screen (TSH) ☐ On thyroid medication or previous abnormal result
If approved: ☐ Free T3 ☐ Free T4 ☐ Total T3/T4

☐ Estradiol
☐ Progesterone
☐ Prolactin
☐ LH/FSH
☐ Testosterone
☐ SHBG/FAI
☐ DHEA-SO_4
☐ Cortisol
☐ Magnesium
☐ Cholinesterase
☐ Ceruloplasmin
☐ Phenylalanine
☐ Lipase
☐ B12
☐ Ferritin
☐ Iron Studies (Iron, Transferrin, Ferritin)
☐ FIT (FOBT) (Stool)

☐ RBC Folate Hematocrit _____ (EDTA whole blood) ☐ Neurological Condition
↳ Required - Please attach CBC result

☐ 25-OH Vitamin D Status (Combined Total D2 &D3) ☐ Supplementing with plant form 25-OH Vitamin D2

*Samples must be received frozen for the following tests:

☐ Gastrin* ☐ ACTH* ☐ 17-OH Progesterone*
☐ Insulin* ☐ C-Peptide* ☐ Free/Total Carnitine*
☐ HGH* ☐ Homocysteine* ☐ Methylmalonic Acid*
☐ iPTH* ☐ Androstenedione* ☐ Thyroglobulin Level*

Heavy Metals:
☐ Lead (Whole Blood) ☐ Copper ☐ Zinc
☐ Other _____

24 Hour Urine Tests:
24 hr volume: _____(mL) Start Date/Time:_____
Body weight if child 10 or under: _____(kg) End Date/Time:_____

☐ Catecholamines ☐ Oxalate ☐ UFC
☐ Metanephrines ☐ Porphyrins ☐ Total Protein
☐ HVA, VMA, 5HIAA ☐ Citrate ☐ Other _____

Drugs of Abuse (URINE only):
☐ Standard screen (includes 40 common drugs of abuse)
☐ Alcohol ☐ Barbiturates ☐ Other _____

Toxicology (Special:
☐ Ethanol (whole blood) ☐ Methanol ☐ Ethylene Glycol
☐ Carboxyhemoglobin (CO)
☐ Specify drug(s) required: _____

IMMUNOSEROLOGY

Needle Exposure Work-Up: ☐ Source ☐ Staff
Cross Reference of Exposure: Indicate corresponding source or staff
Contact Person: _____ Phone #: _____

HIV 1 & 2 Serology: Please fill in HIV Epidemiology Data on reverse
☒ HIV Screen
☐ Hepatitis A IgG (immune)
☐ Hepatitis A IgM
☒ Hepatitis B surface antibody
☒ Hepatitis B surface antigen
☐ HBV/HAV vaccination in last 4 weeks
☒ Hepatitis C antibody

☐ HIV Viral Load (Frozen EDTA plasma)
☐ HBV Viral Load (Frozen EDTA plasma)
☐ HCV Viral Load (Frozen EDTA plasma)

☐ Prenatal Panel (Rubella IgG, Syphilis, HBV, HCV, HIV)
☐ Prenatal HIV not required on this patient
☒ Syphilis (serum only) ☐ VDRL (CSF only)

☐ H. pylori
☐ Rheumatoid Factor
☐ Anti-CCP
☐ C Reactive Protein
☐ CRP High Sensitivity
☐ ANA
☐ ANCA (Vasculitis)
☐ Celiac Panel
☐ Antistreptolysin (ASO)
☐ C_1 Esterase Inhibitor
☐ C_3 Complement
☐ C_4 Complement
☐ CH_{100}* (Frozen serum)

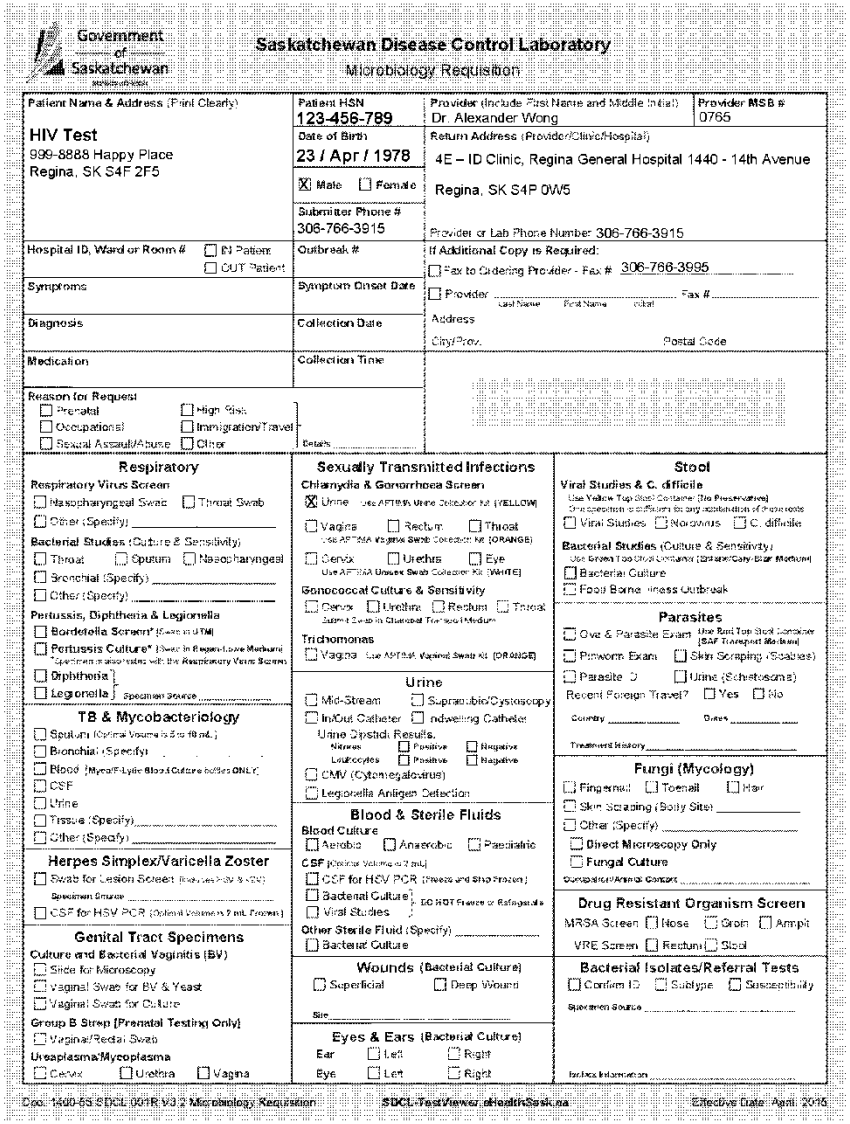
☐ IgA ☐ IgG ☐ IgM ☐ IgE
☐ Thyroid Antibodies (Thyroglobulin Antibody & Microsomal TPO Antibody)

Viral Serology Tests: ☐ Immune Status/IgG ☐ IgM
☐ Measles
☐ Mumps
☐ Rubella
☐ Parvovirus
☐ West Nile Virus
☐ Cytomegalovirus
☐ Epstein-Barr Virus
☐ Varicella Zoster
☐ HSV 1&2 (IgG only)
☐ ToRC screen (CMV, Toxo, Rubella)
☐ Toxoplasmosis
☐ Lyme Disease
☐ C. pneumoniae
☐ Mycoplasma pneumoniae

Other Tests:
Hepatitis B Core Antibody

Doc 1400-55 SDCL003R v5.0 Chemistry & Immunoserology Requisition
Effective Date: July 8, 2014

SDCL Microbiology



Government of Saskatchewan

Saskatchewan Disease Control Laboratory

Microbiology Requisition

Patient Name & Address (Print Clearly)
HIV Test
999-8888 Happy Place
Regina, SK S4F 2F5

Patient HSN: 123-456-789
Date of Birth: 23 / Apr / 1978
☒ Male ☐ Female
Submitter Phone #: 306-766-3915

Provider (Include First Name and Middle Initial): Dr. Alexander Wong
Provider MSB #: 0765
Return Address (Provider/Clinic/Hospital): 4E – ID Clinic, Regina General Hospital 1440 - 14th Avenue
Regina, SK S4P 0W5
Provider or Lab Phone Number: 306-766-3915

Hospital ID, Ward or Room # ☐ IN Patient ☐ OUT Patient
Outbreak #
If Additional Copy is Required:
☐ Fax to Ordering Provider - Fax # 306-766-3995
☐ Provider ____ Fax # ____
Last Name First Name Initial
Address
City/Prov. Postal Code

Symptoms
Symptom Onset Date
Diagnosis
Collection Date
Medication
Collection Time

Reason for Request
☐ Prenatal ☐ High Risk
☐ Occupational ☐ Immigration/Travel
☐ Sexual Assault/Abuse ☐ Other
Details

Respiratory
Respiratory Virus Screen
☐ Nasopharyngeal Swab ☐ Throat Swab
☐ Other (Specify)
Bacterial Studies (Culture & Sensitivity)
☐ Throat ☐ Sputum ☐ Nasopharyngeal
☐ Bronchial (Specify)
☐ Other (Specify)
Pertussis, Diphtheria & Legionella
☐ Bordetella Screen* (Swab in UTM)
☐ Pertussis Culture* (Swab in Regan-Lowe Medium)
*Specimen also tests with the Respiratory Virus Screen
☐ Diphtheria
☐ Legionella Specimen Source

TB & Mycobacteriology
☐ Sputum (Optimal Volume is 5 to 10 mL)
☐ Bronchial (Specify)
☐ Blood (Myco/F-Lytic Blood Culture bottles ONLY)
☐ CSF
☐ Urine
☐ Tissue (Specify)
☐ Other (Specify)

Herpes Simplex/Varicella Zoster
☐ Swab for Lesion Screen (Swab in UTM or VSP)
Specimen Source
☐ CSF for HSV PCR (Optimal Volume is 2 mL Frozen)

Genital Tract Specimens
Culture and Bacterial Vaginitis (BV)
☐ Slide for Microscopy
☐ Vaginal Swab for BV & Yeast
☐ Vaginal Swab for Culture
Group B Strep (Prenatal Testing Only)
☐ Vaginal/Rectal Swab
Ureaplasma/Mycoplasma
☐ Cervix ☐ Urethra ☐ Vagina

Sexually Transmitted Infections
Chlamydia & Gonorrhoea Screen
☒ Urine Use APTIMA Urine Collection Kit (YELLOW)
☐ Vagina ☐ Rectum ☐ Throat
Use APTIMA Vaginal Swab Collection Kit (ORANGE)
☐ Cervix ☐ Urethra ☐ Eye
Use APTIMA Unisex Swab Collection Kit (WHITE)
Gonococcal Culture & Sensitivity
☐ Cervix ☐ Urethra ☐ Rectum ☐ Throat
Submit Swab in Charcoal Transport Medium
Trichomonas
☐ Vaginal Use APTIMA Vaginal Swab Kit (ORANGE)

Urine
☐ Mid-Stream ☐ Suprapubic/Cystoscopy
☐ In/Out Catheter ☐ Indwelling Catheter
Urine Dipstick Results
Nitrites ☐ Positive ☐ Negative
Leukocytes ☐ Positive ☐ Negative
☐ CMV (Cytomegalovirus)
☐ Legionella Antigen Detection

Blood & Sterile Fluids
Blood Culture
☐ Aerobic ☐ Anaerobic ☐ Paediatric
CSF (Optimal Volume is 2 mL)
☐ CSF for HSV PCR (Freeze and Ship Frozen)
☐ Bacterial Culture } DO NOT Freeze or Refrigerate
☐ Viral Studies
Other Sterile Fluid (Specify)
☐ Bacterial Culture

Wounds (Bacterial Culture)
☐ Superficial ☐ Deep Wound
Site

Eyes & Ears (Bacterial Culture)
Ear ☐ Left ☐ Right
Eye ☐ Left ☐ Right

Stool
Viral Studies & C. difficile
Use Yellow Top Stool Container (No Preservative)
One specimen is sufficient for any combination of these tests
☐ Viral Studies ☐ Norovirus ☐ C. difficile
Bacterial Studies (Culture & Sensitivity)
Use Green Top Stool Container (Cary-Blair Medium)
☐ Bacterial Culture
☐ Food Borne Illness Outbreak

Parasites
☐ Ova & Parasite Exam Use Red Top Stool Container (SAF Transport Medium)
☐ Pinworm Exam ☐ Skin Scraping (Scabies)
☐ Parasite ID ☐ Urine (Schistosoma)
Recent Foreign Travel? ☐ Yes ☐ No
Country Dates
Treatment History

Fungi (Mycology)
☐ Fingernail ☐ Toenail ☐ Hair
☐ Skin Scraping (Body Site)
☐ Other (Specify)
☐ Direct Microscopy Only
☐ Fungal Culture
Occupation/Animal Contact

Drug Resistant Organism Screen
MRSA Screen ☐ Nose ☐ Groin ☐ Armpit
VRE Screen ☐ Rectum ☐ Stool

Bacterial Isolates/Referral Tests
☐ Confirm ID ☐ Subtype ☐ Susceptibility
Specimen Source
Isolate Information

Doc. 1400-65 SDCL 001R V3.2 Microbiology Requisition | SDCL-TestViewer.eHealthSask.ca | Effective Date: April, 2015

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Diagnosis of HIV Infection

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- **What constitutes a positive result for HIV, and what do I tell a patient who has a positive result for HIV?**
  - SDCL currently uses a 4th-generation combined HIV antigen / antibody test, whose sensitivity in chronic HIV infection is near 100%, although sensitivity in acute HIV infection is variable.
  - Confirmatory Western Blot testing is performed on all positive HIV screens to ensure that the result is not a false positive.
  - **Only** when Western Blot is confirmed positive is the result reported to the provider, who is responsible for informing the patient.
  - Public Health can assist providers who cannot reach individuals who are diagnosed HIV positive.
  - *"Unfortunately, your testing for HIV was positive. We need to order some more tests, and have you see a specialist who provides HIV care. HIV is not a death sentence, and with medication the lifespan of someone with HIV is nearly identical to that of someone who does not have HIV."*

Diagnosis of HIV Infection

- **What do I do next when a patient is newly diagnosed with HIV?**
  - Counsel the patient regarding the diagnosis.
    - *"HIV is not a death sentence, and with excellent medication the lifespan of someone with HIV is nearly equivalent to someone without HIV."*
    - Public Health will be contacting for purposes of contact tracing.
    - A referral will be made immediately to a multidisciplinary care team for further assessment.
  - Refer the patient immediately to the appropriate care facility.
  - **Saskatoon – Westside Clinic:** 1528-20th Street W, phone 306-664-4310, fax 306-934-2506
  - **Saskatoon – Positive Living Program / Royal University Hospital:** 103 Hospital Drive, phone 306-655-1783, fax 306-655-0614
  - **Regina Infectious Diseases Clinic:** 4E – Regina General Hospital, phone 306-766-3915, fax 306-766-3995.
  - **Prince Albert / Access Place:** 101 15th Street East, phone 306-765-6541.

What Happens Next?

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- **If the patient is referred to the RQHR IDC…**
  - One of our nurses will be in contact with them, ideally within 1-5 business days, to set up an appointment.
  - At their first appointment in the clinic, they will be seen by the nurse, pharmacist, and social worker. Baseline laboratory investigations are ordered, and then depending on circumstances, they are seen by physician immediately or after labs return.
  - Numerous support mechanisms in place, including psychology referral and peer-to-peer programming. The clinic strives to be an environment built upon trust, safety, lack of judgement, and mutual respect.
  - Most patients, in the absence of contraindications, will be offered antiretroviral therapy shortly after diagnosis.

Hepatitis C – Basics

- Single-stranded linear RNA virus.
- In North America, most transmissions are secondary to injection drug use. Sexual transmission is very uncommon, but incidence higher in MSM with localized epidemics now well-reported.
- **Other modes of transmission:**
  - Blood transfusion. (Risk now 1 in 1,000,000 per unit transfused.)
  - Organ transplantation.
  - Perinatal transmission. (~5% mono-infected, ~10% co-infected)
  - Percutaneous exposures.
  - Household transmissions (rare).

Hepatitis C – Basics

- **Canada:** ~300,000 infected, 1% prevalence, ~25% unaware of diagnosis, but data may be inaccurate.
- **USA:** Prevalence ~1.6%, but 3.6% in “baby boomer” cohort (born b/w 1945-1965, ages 50-70).
- Canadian screening guidelines have historically emphasized risk-factor based screening:
  - Patients who engage in risk behaviours.
  - Patients with clinical signs / symptoms suggestive of HCV.
- **Problem:** Risk factor based screening is ineffective.
  - Many providers unaware of risk factors for HCV.
  - No time or inadequate knowledge to provide counselling.

HCV – Natural History

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- Infection with hepatitis C virus causes acute hepatitis C and **MAY** cause chronic hepatitis C.
- **Acute Hepatitis C**
  - ~25% will experience clinical symptoms, remainder have mild course or asymptomatic (anti-HCV+, HCV RNA+)
  - 75-80% will progress to chronic infection (anti-HCV+, HCV RNA-), 20-25% will clear spontaneously (anti-HCV+, HCV RNA-)
- **Chronic Hepatitis C**
  - 60-80% of patients will develop chronically elevated liver enzymes, and if untreated, ~50% will progress to cirrhosis over 10-20 years.
  - Proportion may develop end-stage liver disease or hepatocellular carcinoma; clinical outcomes include transplantation, resection / ablation, or death.

HCV – Natural History

- Most patients with chronic infection are asymptomatic or have mild, non-specific symptoms such as fatigue. Presence or absence of symptoms is not reflective of degree of underlying disease activity.
- Various risk factors predict increasing risk of fibrosis:
  - **Age:** older at time of acquisition = increased risk of progression
  - **Ethnicity:** progression slower in blacks.
  - **Gender:** males progress quicker than females.
  - **HIV Co-Infection:** accelerated fibrosis in co-infected patients.
  - **Obesity:** increased risk of hepatic steatosis and progression.
  - **Behavioural:** alcohol intake, marijuana usage (hepatitis steatosis and subsequent progression of fibrosis).

Hepatitis C – Genotypes

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- Highly heterogeneous virus with 11 distinct genotypes, many subtypes. Most common genotypes = 1 through 6.
- Genotypes 1-3 have worldwide distribution.
  - **Genotype 1:** North America & Northern Europe.
  - **Genotype 2:** Far less common in NA & Europe.
  - **Genotype 3:** Endemic in SE Asia, less so elsewhere.
  - **Genotype 4:** Middle East, central Africa, Egypt.
  - **Genotype 5:** South Africa.
  - **Genotype 6:** Asia.
- Genotypes matter because they determine response to various forms of antiviral treatment.
- **RQHR: 61% G1**, 4% G2, **31% G3**, 5% mixed.

Hepatitis C – Screening

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- **Why screen?**
  - Many individuals are unaware that they are infected.
  - Prevalence is increased in high-risk populations and baby boomers.
  - Chronic hepatitis C infection is curable.
  - Patients whose infection is eradicated before development of cirrhosis have a life expectancy similar to those of uninfected age-matched cohorts.

- **Why NOT screen?**
  - Stigmatization with diagnosis or “feeling targeted”.
  - False positive results.
  - Lack of capacity to treat volume of newly diagnosed cases.
  - **All can be mitigated by appropriate pre-test counseling and expansion of systems to treat newly-diagnosed individuals.**

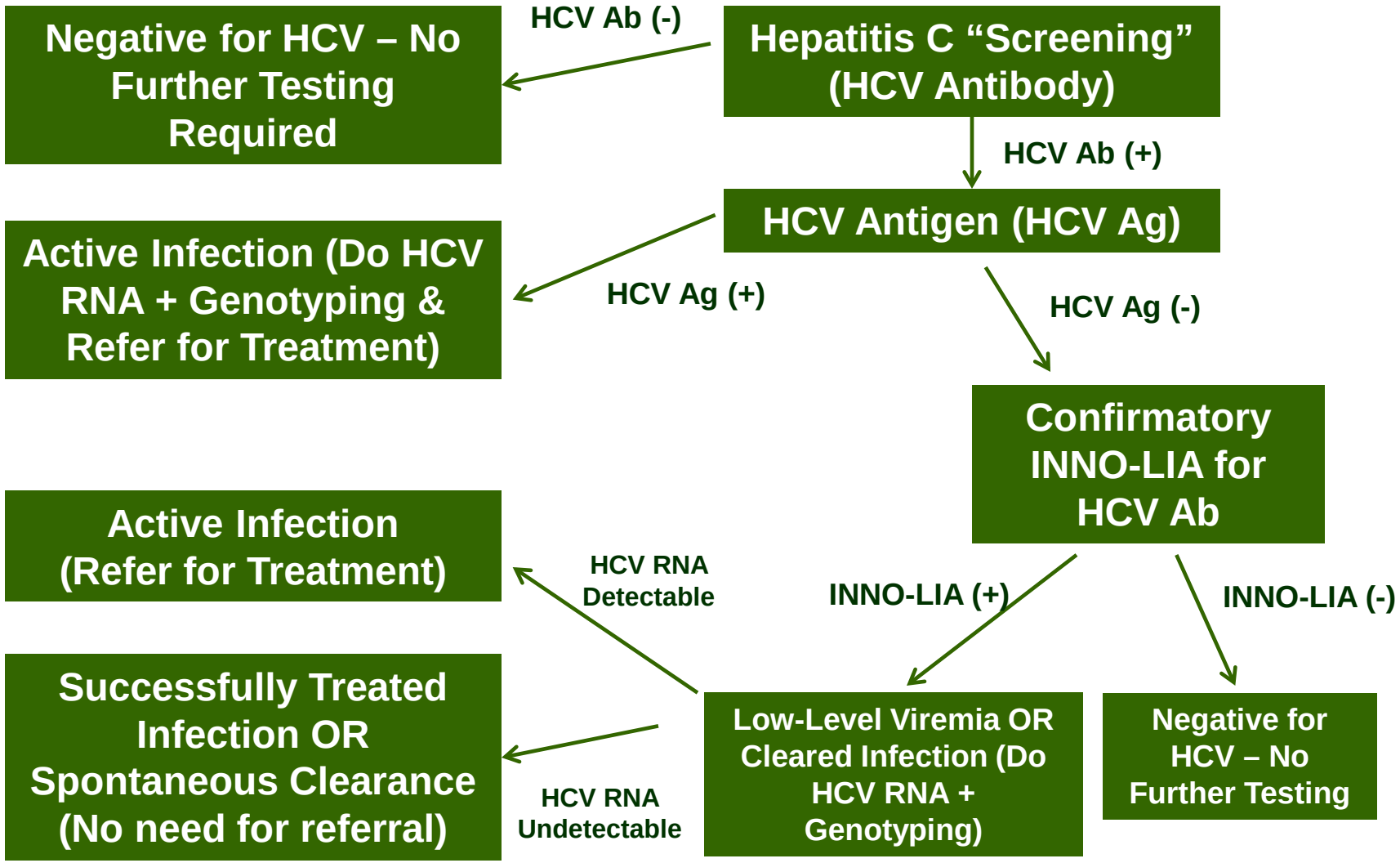
Hepatitis C – Screening

- **Who should be screened?**
  - Anyone who has ever injected drugs, even once.
  - Anyone born in Canada b/w 1945-1975 (~ ages 40-70).
  - Anyone who received a blood transfusion, blood products, or organ transplant in Canada before 1992.
  - Those with evidence of liver disease (high ALT).
  - Anyone who has ever been on chronic hemodialysis.
  - Anyone infected with HIV.
  - All incarcerated individuals.
- **What do you screen with?**
  - Screen with standard 3rd generation HCV antibody test. High sensitivity (97.2-100%) and specificity (> 99%).
- **How often do you screen?**
  - If no ongoing risk, one-time screen is enough.
  - If ongoing risk, frequency of screening unclear, at least annual.

Hepatitis C – Diagnostics

- **Hepatitis C Antibody (HCV Ab):**
  - Marker of previous exposure to virus.
  - Not necessarily marker of active viremia as patients can clear viremia either spontaneously or with successful therapy.
- **Hepatitis C Antigen (HCV Ag):**
  - Marker of viremia – a positive HCV Ag confirms viremia and active infection.
  - If negative, not necessarily indicator that viremia has completely cleared as assay is not sensitive for low-level viremia (<= 10,000 IU/mL).
- **Hepatitis C Viral Load / RNA:**
  - Presence of viremia signals active infection.
  - Low-level viremia is possible, but can also represent potential spontaneous clearance of viremia.
- **Hepatitis C Genotyping:**
  - Determination of genotyping, mainly for treatment purposes.

HCV – SDCL Algorithm



Hepatitis C – Diagnosis

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- **Potential Pitfalls of Diagnostics**
  - **Immunocompromised Individuals:** Higher rates of false negative tests than immunocompetent patients.
  - **Acute Infection:** “Window period” for positive antibody test.

- **General Rules of Thumb**
  - Positive antibody and antigen confirms the diagnosis of chronic hepatitis C, unless the possibility of acute infection exists.
  - Those who have a positive antibody +/- antigen still require a hepatitis C viral load and genotype to be performed.
  - A positive antibody combined with a negative antigen test does not mean with 100% certainty that the patient has cleared their viremia spontaneously, given limitations of antigen testing. Viral load testing is still required.
  - Refer patients with confirmed viremia only, and counsel patients carefully if they have spontaneously cleared.

Hepatitis C – A Timeline

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- **1989:** Hepatitis C described in *Science* as the cause of “non-A non-B hepatitis”.
- **1990s:** Epidemiology and transmission risks clearly described, as well as recognition of genotypes. Natural history described, including associated with cirrhosis, ESLD, hepatocellular carcinoma.
- **1990s:** Original studies for interferon (IFN) monotherapy re-examined, determined that response differed by genotype.
- **1994:** Addition of guanosine nucleoside ribavirin to IFN for therapy reported, shown to be far superior to IFN monotherapy in 1998, becomes new standard of care.

Courtesy: Dr. S. Shafran

Hepatitis C – A Timeline

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- **2001:** IFN replaced by pegylated-IFN, modest improvement in SVR for genotype 1, no change in SVR for genotypes 2 or 3. Therapy more convenient.
- **2001-2010:** Many advances in peg-IFN + RBV (PR) therapy for 24-48 weeks of therapy.
  - Peg-IFN and ribavirin still poorly tolerated, many adverse effects including hematologic, flu-like symptoms, and neuropsychiatric.
  - Still difficult to administer to many patients with relative contraindications (i.e. life chaos, mental illness).

Courtesy: Dr. S. Shafran

Hepatitis C – A Timeline

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Genotype	Weeks of Rx	SVR Rate (%)
1	48	45
2	24	80
3	24	70
4	48	60

Courtesy: Dr. S. Shafran

Hepatitis C – A Timeline

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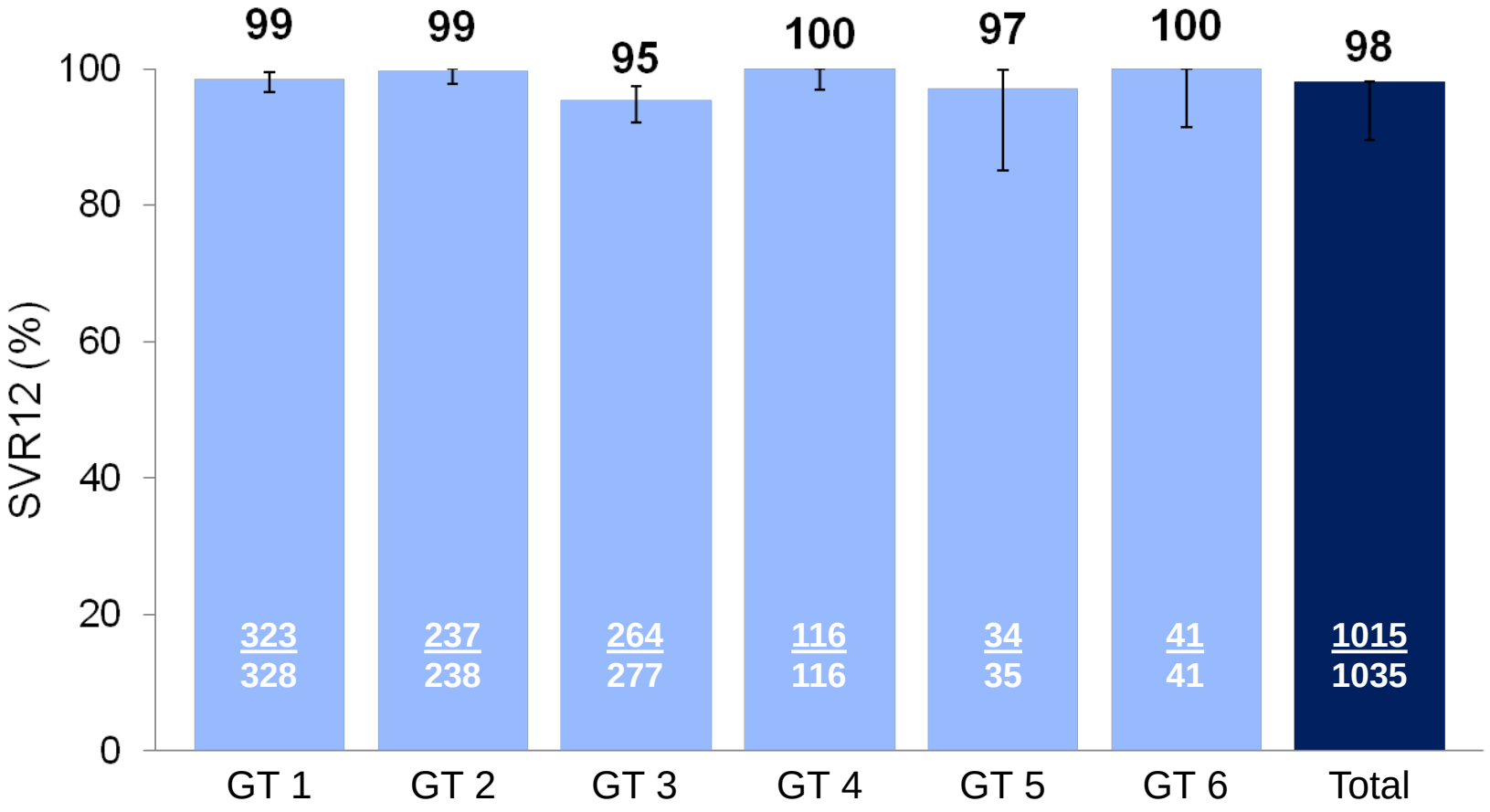
- **2003:** First proof-of-concept study for HCV therapy against NS3 target with PI monotherapy published.
- **2011:** First DAAs (boceprevir and telaprevir) approved for GT1 in USA (May) and Canada (July).
  - First IFN-free SVRs in GT1 reported with daclatasvir + asunaprevir x 24 weeks (EASL, April 2011).
  - First IFN-free SVRs reported in GT2 / GT3 with sofosbuvir & ribavirin x 12 weeks. (AASLD, November 2011).
  - Four validated classes of DAAs now widely available:
    - NS3 PIs
    - NS5A inhibitors
    - NS5B non-nucleoside inhibitors
    - NS5B nucleoside/nucleotide inhibitors.

Courtesy: Dr. S. Shafran

Hepatitis C – The Future…

- **Genotype 1 Virus (97-100% SVR12)**
  - Harvoni™ (LDV/SOF) x 8-12 weeks.
  - Holkira™ (3 DAA +/- RBV) x 12 weeks.
  - Zepatier™ (GZR/EBR) x 12 weeks
- **Genotype 2 Virus (86-97% SVR12)**
  - Sofosbuvir + ribavirin x 12 weeks.
- **Genotype 3 Virus (79-97% SVR12)**
  - Daclatasvir + Sofosbuvir x 12 weeks.
  - Sofobuvir + Ribavirin x 24 weeks.
- **End of 2016:** Sofosbuvir / Velpatasvir x 12 weeks → 98-100% for all GT 1/2/4/5/6/, 95% for GT3.

SOF/VEL STR for 12 Weeks



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Hepatitis C – $$$

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- **So What's The Catch?**
  - New medications for hepatitis C are **very very expensive**.
  - List price for 12 weeks of LDV/SOF = $65,000 CDN.
  - List price for 24 weeks of peg-IFN + RBV = $10,000 CDN.

- **Who Can Currently Access Treatment in SK?**
  - People who have $40-65K to spend on medication.
  - **GT1:** F2 fibrosis or worse on Fibroscan.
  - **GT2/GT3:** F2 fibrosis or worse, and either intolerant of peg-IFN (depression, anxiety, other mental illness), or failed / intolerant of previous peg-IFN therapy.
  - Hope is access improves as new molecules come to market.
  - *"There is treatment for hepatitis C, but we have to do more tests, and then we can discuss further whether you are eligible."*

What is “Fibroscan”?

- Ultrasound-based transient elastography is alternative to liver biopsy for assessment of hepatic fibrosis.
  - Non-invasive, simple, no risk of complications.
  - Determines degree of liver “stiffness”, usually most affected by hepatic fibrosis though other factors can play role including heart failure / central venous pressure / eating.
  - Shear waves are transmitted from transducer through liver parenchyma, and pulse-echo U/S acquisition follows propagation of shear waves and measures average speed. Results expressed in kPa.
- RQHR has two units – Pasqua GI Unit & RQHR IDC.

Summary – Hepatitis C

- **Screening & Diagnosis**
  - Lower your threshold to screen for hepatitis C and serially screen those with identified risk. Early identification = less morbidity and mortality.
  - Access eHealth Portal and don't mindlessly repeat what has been done before – order the right tests!
  - Population-based screening for all b/w ages 45-75 with one-time testing is appropriate.
  - Follow anti-HCV / HCV antigen with HCV RNA & genotyping.
- **Treatment**
  - New treatments paradigm is sea change from previous paradigm. Treatment is effective, simple, and well-tolerated. Problem remains accessibility due to high costs.