



COVID-19: KEEPING UP WITH A MOVING TARGET

Aug 26, 2020 UPDATE



Paul Auwaerter, MD, MBA, FIDSA
Clinical Director, Division of Infectious Diseases
Sherrilyn and Ken Fisher Professor of Medicine
Fisher Center for Environmental Infectious Diseases
Johns Hopkins University School of Medicine



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Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	Scientific Advisor: DiaSorin, Shionogi Inc. JNJ: Ownership equity

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials. These include COVID-19 convalescent plasma.

All activity, content, and materials have been developed solely by the activity directors, planning committee members, and faculty presenters, and are free of influence from a commercial entity.





CME Information

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Learning Objectives

- Discuss the current CDC guidance of COVID-19 testing in asymptomatic people
- Describe the limitations of the currently available data concerning convalescent plasma





Thank You

This activity is supported by an educational grant from Pfizer, Inc. and in-kind support by DKBmed, LLC.

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Please see **COVID19.DKBmed.com** for additional resources and educational activities

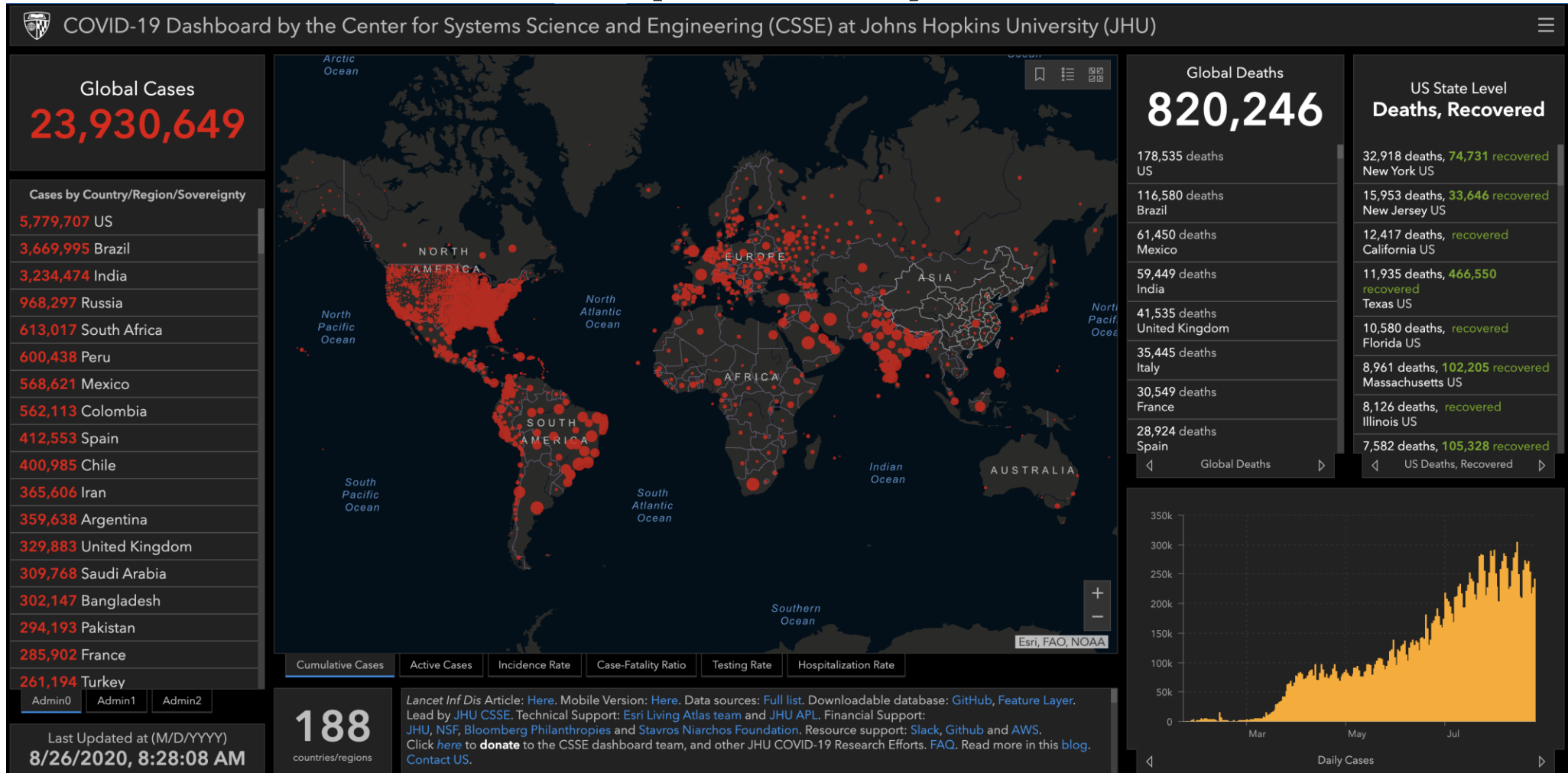




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Total Global Cases (8/26/20)

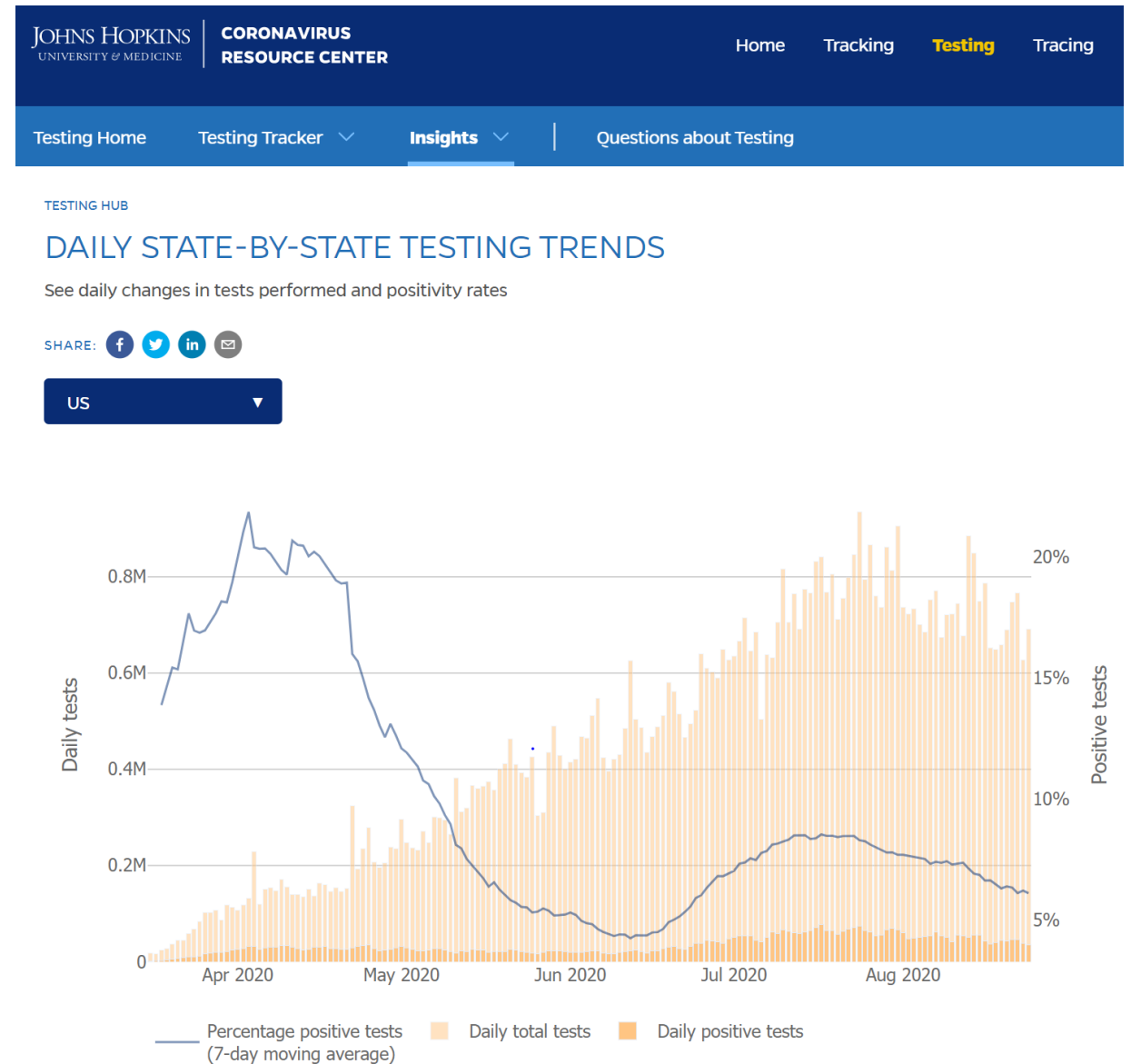


coronavirus.jhu.edu/map.html



COVID Trends, US

- Improving trends in many states/locales
- Still insufficient testing capabilities
- Number of tests lower than desired (3-4M/day estimate needed)



<https://coronavirus.jhu.edu/testing/individual-states> Accessed 8/25/20





Diagnostics: CDC – no Testing if no Symptoms

HEALTHCARE WORKERS

Overview of Testing for SARS-CoV-2 (COVID-19)

Updated Aug. 24, 2020

[Print](#)



Note: This document is intended to provide guidance on the appropriate use of testing for SARS-CoV-2 (COVID-19) and does not address decisions regarding payment for or insurance coverage of such testing.

Summary of Changes

Revisions made on August 24, 2020

- Diagnostic testing categories have been edited to focus on testing considerations and actions to be taken by individuals undergoing testing

- If you do not have COVID-19 symptoms and have not been in close contact with someone known to have a COVID-19 infection:
 - You do not need a test.
 - A negative test does not mean you will not contract an infection at a later time.
 - If **you** decide to be tested, you should self-isolate at home until your test results are known, and then adhere to your health care provider's advice. This does not apply to routine screening or surveillance testing at work, school, or similar situations.
- If you are in a high COVID-19 transmission area and have attended a public or private gathering of more than 10 people (without widespread mask wearing or physical distancing):
 - You do not necessarily need a test unless you are a vulnerable individual or your health care provider or State or local public health officials recommend you take one.
 - A negative test does not mean you will not develop an infection from the gathering or contract an infection at a later time.
 - You should monitor yourself for symptoms. If you develop symptoms, you should evaluate yourself under the considerations set forth above.
 - You should strictly adhere to CDC mitigation protocols, especially if you are interacting with a [vulnerable individual](#). You should adhere to CDC guidelines to protect vulnerable individuals with whom you [live](#).
 - If you are tested, you should self-isolate at home until your test results are known, and then adhere to your health care provider's advice.

<https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html>

Laboratory Developed Tests: FDA

Coronavirus

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Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests

The Trump Administration is committed to combating COVID-19, to ensuring that the American people are protected against future pandemics, and to keeping duplicative regulations and unnecessary policies from interfering with those efforts. Consistent with the President's direction in Executive Orders 13771 (Executive Order on Reducing Regulation and Controlling Regulatory Costs) and 13924 (Executive Order on Regulatory Relief to Support Economic Recovery), and as part of HHS's ongoing department-wide review of regulatory flexibilities enacted since the start of COVID-19, the department has determined that the Food and Drug Administration ("FDA") will not require premarket review of laboratory developed tests ("LDT") absent notice-and-comment rulemaking, as opposed to through guidance documents, compliance manuals, website statements, or other informal issuances. Those seeking approval or clearance of, or an emergency use authorization ("EUA") for an LDT may nonetheless voluntarily submit a premarket approval application, premarket notification or an EUA request, respectively, but are not required to do so, and FDA will adjudicate those submissions. Those opting to use LDTs in their laboratories without FDA premarket review or authorization may do so with the understanding that they would not be eligible for PREP Act coverage absent approval, clearance or authorization and would remain subject to regulation by the Centers for Medicare & Medicaid Services under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. § 263a, and its implementing regulations at 42 C.F.R. pt. 493. Those with an active EUA to use an LDT to detect the virus causing COVID-19 or its antibodies are unaffected by this announcement.

Content created by Assistant Secretary for Public Affairs (ASPA)
Content last reviewed on August 19, 2020

<https://www.hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html>





Treatment





FDA Authorizes EUA for Convalescent Plasma

- Uproar over information presented by FDA EUA
 - Fact sheet for Healthcare providers misleading
(8/23: www.fda.gov/media/141478/download)
 - “Analysis of over 35,000 transfused patients in the EAP study found a dose-response between antibody level and reduction in mortality”
- 35% mortality reduction for COVID-19 touted, misleading
 - President
 - HHS
 - FDA
- EUA appears to be a rapid reversal?





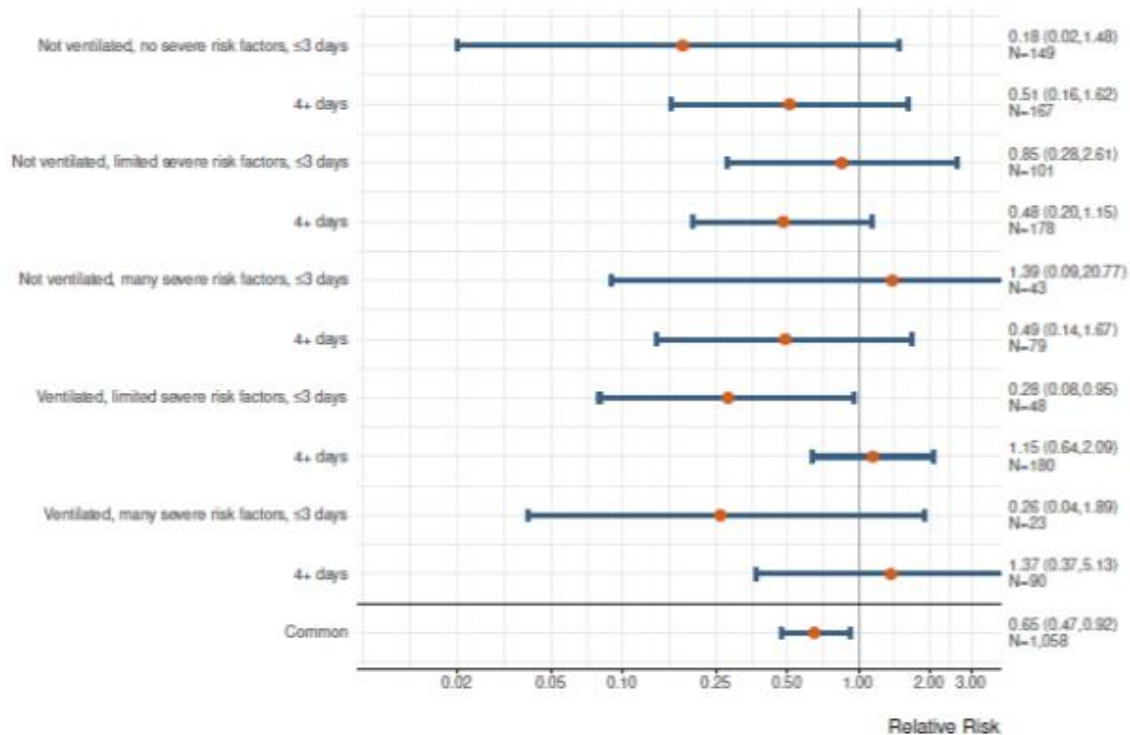
FDA Authorizes EUA for Convalescent Plasma

- Preprint data “facts”: www.medrxiv.org/content/10.1101/2020.08.12.20169359v1
 - Dose-response analysis, subset of 3082
 - 7 & 30d mortality outcomes overlap for entire group
 - Subset of this data:
 - “Significant association if antibody levels stratified by time to transfusion.”
 - < 3d hospitalization if received high titer (compared to low titer), 35% mortality reduction, relative risk
 - ❖ < 80 years
 - ❖ Not on a ventilator
 - No placebo component, “low antibody titers” compared to high titer recipients—medium titer units not included.

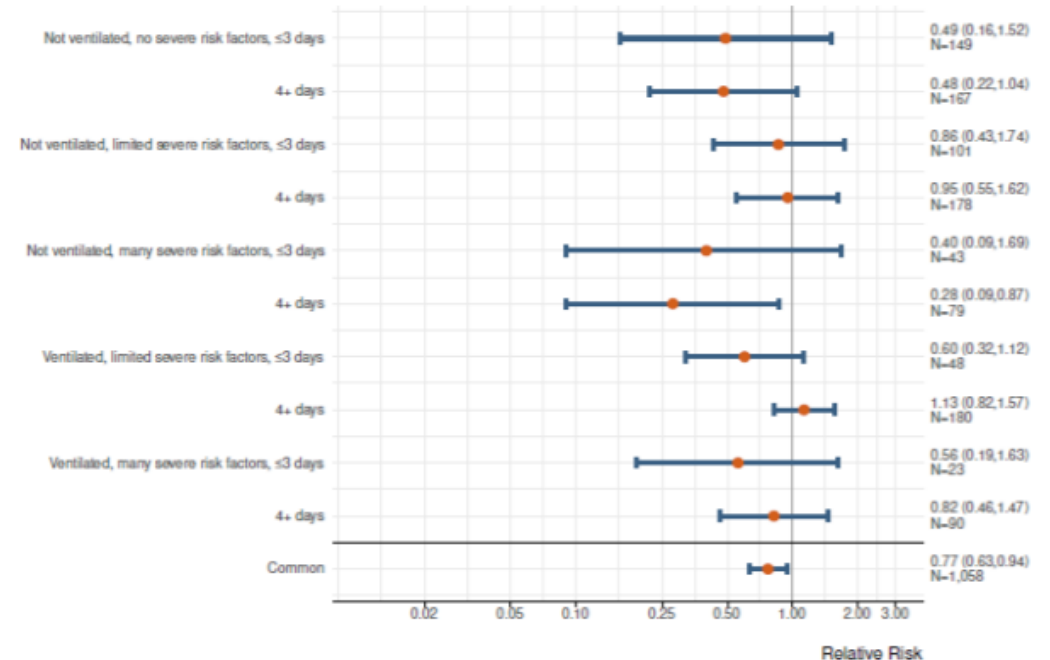


Convalescent Plasma – Mortality Risk

A. 7-Day Mortality



B. 30-Day Mortality



Pooled relative risk of mortality\ compared to low antibody level plasma units:

High antibody level plasma units 0.65 [0.47-0.92] at 7 days

0.77 [0.63-0.94] at 30 days

www.medrxiv.org/content/10.1101/2020.08.12.20169359v1





Problems

- Relative risk between treatment groups
 - May obscure the magnitude of the effect of an intervention
 - Tend to overestimate the effect when it is presented in relative terms
- Absolute risk= difference between two groups
 - Exposed and not exposed
 - Best estimates, can lead to number need to treat
- Study could not look at absolute risk, all received plasma





Other issues per EUA

- **SARS-CoV-2 neutralizing antibody titers, if available**
 - **Neutralizing antibody titers of at least 1:160. A titer of 1:80 may be considered acceptable if an alternative matched unit is not available.**
 - Per EUA: Ortho VITROS SARS-CoV-2 IgG test
 - Signal-to-cutoff (S/C) value of ≥ 12
 - **When measurement of neutralizing antibody titers is not available, consider storing a retention sample from the convalescent plasma donation for determining antibody titers at a later date.**
 - IDSA recommendations
 - MINIMUM titer of $>1:320$
- EUA includes high titer units, and also low titer if deemed acceptable by clinician





Other Issues per EUA

- EUA says its not standard of care—which was implied in the Remdesivir EUA.
 - Status a help for clinical trials?
- How to procure?
 - Only existing eIND, single patient pathway?





Convalescent Plasma

- Appears mostly safe
- Benefits not proven
 - Who
 - When
- Scarce resource
- If beneficial, best given early in disease course





To submit your own question, please email QA@dkbmed.com





Are there any updates in the literature on COVID-19 and pregnancy? Does pregnancy put a woman at higher risk of infection or severe infection? Are there risks to the fetus?





What does the current evidence say about a correlation, if any, between vitamin D and COVID-19?





Can you please comment on the accuracy of a rapid test vs a PCR sent out to a lab?





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- Upon registering and successfully completing the activity evaluation, you will have immediate access to your certificate.

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To ask your own question, email: QA@dkbmed.com

