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Seroprevalence of Hepatitis B Surface Antigen Among Voluntary Blood Donors Over a Five-Year Period

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ABSTRACT

Hepatitis B surface antigen (HBsAg) is the oldest and most widely used marker for keeping infectious units out of the blood supply, and the proportion of donors who test positive is often quoted as a measure of how safe a blood service is. This narrative review asks what such a figure can and cannot tell a reader. It draws on published work on the virus and its natural history, on the global pattern of infection and its link to age at infection, on donor selection and screening strategies, and on the performance of HBsAg assays, and it reports no donor data of its own. HBsAg positivity among donors reflects the community the donors come from, the way they are recruited and deferred, the assay used and the point in infection at which they happen to give blood. Window-period and occult infections are invisible to HBsAg testing, so a low figure is not proof that the supply is free of risk, and a high one does not by itself identify which donors or settings are to blame. Comparisons between services are weakened by differences in donor type, first-time and repeat donation, and reporting. The review concludes that donor HBsAg figures are best read as a description of screening yield in one setting and period, and it sets out what a transparent report of such figures should contain.

Keywords: Hepatitis B; HBsAg; Blood donors; Transfusion safety; Seroprevalence; Occult hepatitis B; Donor screening; Narrative review

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Article Class: Narrative Review

1. Introduction

Blood services have tested donations for hepatitis B surface antigen (HBsAg) for several decades, and the share of donors who test positive has become one of the numbers most often quoted about transfusion safety. A single percentage is

easy to print and easy to compare, which is exactly why it deserves some suspicion. The surface antigen was first noticed in a study of serum proteins (1), and the long road from that observation to a routine screening test is told well in a recent historical account (2).



Hepatitis B remains a major public health problem. A large share of the world's population has been exposed, and a substantial number carry the virus for life (3, 4). For anyone receiving blood the question is practical: how likely is it that a unit declared negative still carries the virus, and how much does the donor HBsAg figure reveal about that chance? The two questions overlap, but they are not the same.

The title topic, HBsAg seroprevalence among voluntary blood donors over a five-year period, is a question about local data, but no donor records, laboratory results or counts from any blood centre are reported here, and nothing in the article should be read as local data. Instead, the review looks at what the published literature says about the biology behind the test, the way donor figures arise, and the reasons they are so hard to compare. The aim is to separate what is firmly established from what is merely repeated.

The article proceeds from the virus to the donor. Section 2 reviews the biology, natural history and epidemiology of infection and the screening strategies in use. Section 3 describes how the review was assembled, Section 4 sets out what the literature shows about reading donor figures, and Section 5 discusses limits and gaps.

2. Literature Review

2.1 The Virus and Its Surface Antigen

Hepatitis B virus is a small enveloped virus with a partly double-stranded DNA genome, and it replicates through an RNA intermediate, a feature that makes it unusual among DNA viruses (5). Liver cells are its main target, and the sodium taurocholate cotransporting polypeptide has been identified as a functional entry receptor (6). The envelope carries the surface antigen, which is the protein the

standard screening test looks for.

HBsAg is made in great excess. Infected cells release not only complete virions but also large numbers of empty particles that carry the antigen and no genome (2, 5). This is convenient for diagnosis, because the antigen is far more plentiful than the virus itself. It also means that a positive HBsAg result says a person is infected, but says little about how much virus is circulating, which is why other markers are used to judge infectivity and disease activity in clinical care (7, 8).

The virus is not uniform. Eight main genotypes, lettered A to H, are recognised, and they differ in geographic distribution and in some clinical features (9, 10). Variation matters for screening because assays are built around the antigen's structure, and a changed surface protein can be recognised less well by some tests (11). Table 1 lists the markers a blood service meets and what each one tells it.

Table 1. Hepatitis B serological and molecular markers and what each tells a blood service.

Marker	What it indicates	Role in donor screening
HBsAg	Viral envelope protein in blood; current infection	Core screening test worldwide (12, 13)
Anti-HBc	Past or present exposure to the virus	Extra screen in some services; discards many resolved infections (14, 15)
Anti-HBs	Immunity after recovery or vaccination	Used to judge reactive anti-HBc donors (16)
HBV DNA	Virus genome in blood; can precede HBsAg	Detected by nucleic acid testing (17, 18)
HBeAg	Marker of high replication in many carriers	Not used for donor screening (7)

Note: Qualitative summary. Timing and detectability vary with the assay, the viral genotype and the individual.



2.2 Natural History and Why Age Matters

Most adults who meet the virus clear it, and the surface antigen disappears from the blood as antibodies appear. The typical pattern of markers is shown in [Figure 1](#) and should be read as a general outline rather than a timetable ([13](#), [19](#)). In a minority of adults and in a much larger share of infants and young children, infection persists and the person becomes a chronic carrier ([20](#), [21](#)).

That age gradient has a plain consequence for populations. Where the virus is passed from mother to infant or among young children, many carriers are created early and stay positive into adulthood, so the adult population carries a high background of infection. Where transmission happens mostly in adulthood, fewer people become carriers. A blood donor pool drawn from adults inherits whichever pattern the community has ([21](#), [22](#)).

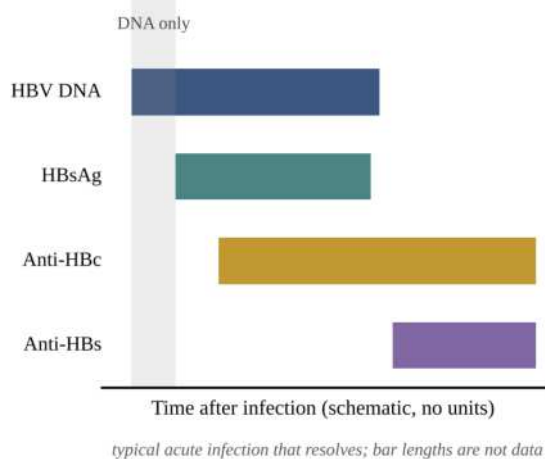


Figure 1. Order in which hepatitis B markers usually appear after infection (schematic of a typical pattern, not data).

Chronic carriage is not benign in the long run. Prospective work in Taiwan linked carriage of the surface antigen to a sharply raised risk of liver cancer ([23](#)), and later cohort work showed that the risk rises with the level of virus in the blood ([24](#)). Reviews of chronic hepatitis B describe

how some carriers remain well for decades while others develop cirrhosis or cancer ([7](#), [12](#)). A donor who is found to be HBsAg positive is therefore also a person with a diagnosis that needs follow-up, a point blood services sometimes treat as secondary.

2.3 The Global Pattern

Estimates of the proportion of people with a positive surface antigen test vary enormously from region to region. Systematic compilations group countries as high, intermediate or low in endemicity, with the highest levels in parts of Africa and East Asia and low levels in much of western Europe and North America ([3](#), [4](#)). India is commonly described as intermediate overall, though a national label hides large differences between states, communities and age groups ([25](#), [26](#)).

Vaccination has changed the picture where programmes reached infants. The Taiwanese experience is the best known: after universal infant immunisation began, the incidence of liver cancer in children fell ([27](#)). Broader reviews describe the same direction of travel wherever coverage became high ([28](#), [29](#)). Yet cohorts born before vaccination keep their carriers, so donor figures in a country that vaccinates its infants today will not fall evenly across age groups.

2.4 Blood Donors and Transfusion Risk

Donors are not a random sample of the community. They are people who chose, or were asked, to give blood, and who passed a health check and a questionnaire. Voluntary non-remunerated donors are generally regarded as the safest group, family or replacement donors less so, and paid donors the least, a ranking built partly on early evidence that commercial donors carried more post-transfusion hepatitis ([30](#)). The ranking is a tendency, not a law,



and local studies do not always follow it.

First-time donors are another source of difference. Large North American series found that markers of hepatitis B were more common among first-time than repeat donors, and that rates in the donor population fell over the 1990s as selection and screening improved (31, 32). Any donor figure that mixes the two groups without saying so is hard to interpret. A rise or fall over a few years may reflect a change in who is donating rather than a change in the community (33).

Estimates of transfusion risk usually concentrate on the window period, when an infected donor can give blood that tests negative. Published estimates of the risk of hepatitis B from a screened unit are model-based, and they rest on assumptions about incidence among repeat donors and on the length of the window (34, 35). Modern accounts of transfusion-transmitted hepatitis B emphasise that the window period is the principal gap, along with occult infection (16). These points hold for any transfusion-transmissible infection, not only hepatitis B.

2.5 Screening Strategies and Their Limits

The basic strategy is selection followed by laboratory testing. Selection removes some people whose history suggests exposure, and testing then removes donations carrying detectable antigen. Table 2 summarises the main options. HBsAg immunoassays are inexpensive and well established, but their sensitivity is not identical across brands, and performance differs against particular genotypes and against variants with altered antigen (36, 37). Figure 2 sketches where infectious units can slip through the pathway. The sketch is deliberately simple; real services vary in the order and number of steps, and some skip stages entirely.

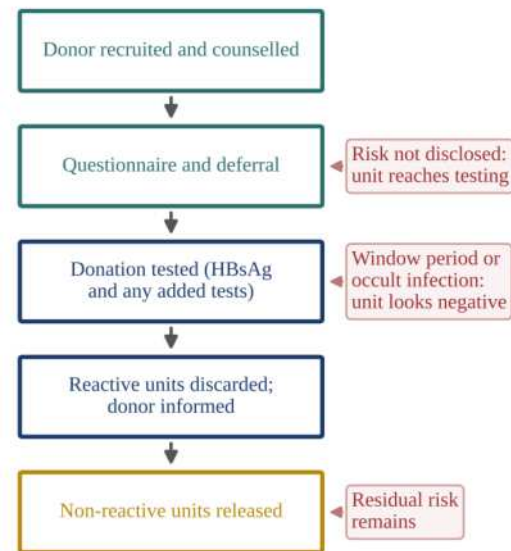


Figure 2. Stages of donor screening and the points where infectious units can pass through (schematic, not data).

Adding a test for antibody to the core antigen (anti-HBc) catches some donors who carry the virus at a level below the reach of the antigen test, and German work suggested that combining it with nucleic acid testing improved safety (14, 18). The price is a larger number of donors who are excluded although they have recovered from infection. Where exposure is common, as in several South Asian settings, that price is steep, and Indian and Pakistani authors have described the dilemma openly (15, 38).

Nucleic acid testing for viral DNA shortens the window and detects some infections the antigen test misses (17). Experience from very large national programmes suggests that, for hepatitis B, the yield of such testing is small relative to the volume tested, though not nil (40). Even in a high-endemicity country with individual-donation testing, transmissions by transfusion were still documented (41). No single strategy removes risk; each one trades cost and donor loss against the infections it catches.

**Table 2.** Donor screening strategies for hepatitis B and their principal limits.

Strategy	Strength	Main limit
Donor selection and deferral	Lowers the chance of risk-exposed donors reaching the test stage (32, 34)	Relies on honest answers
HBsAg immunoassay	Cheap, established, high throughput (36)	Misses window and occult infection (39)
Add anti-HBc	Catches some HBsAg-negative infections (14, 18)	Many false alarms where exposure is common (15, 38)
Add HBV DNA testing	Shortens the window; finds occult infection (17, 40)	Cost and laboratory demands (41)
Rapid tests	Usable without a laboratory	Usually less sensitive than laboratory assays (36, 37)

Note: Strategies are often combined; the limits listed are those discussed in the cited literature.

3. Materials and Methods

3.1 Scope

The review asks one question in two parts: what does a donor HBsAg percentage actually measure, and what should a reader know before comparing it with another? The focus is on voluntary blood donors, but because the interpretation of the figure depends on virology, epidemiology and assay performance, the review ranges across those areas rather than confining itself to donor surveys.

3.2 Literature Assembly

Sources were chosen by the authors from the published literature available up to the end of 2013, with priority given to reviews, large donor series, guidelines and methodological studies. We did not run a formal systematic search and we do not claim one. The work is a narrative

synthesis, so some relevant studies will have been missed, and the selection reflects the authors' judgement of which sources best illustrate each point.

3.3 Appraisal Framework

To judge how far a donor figure can be trusted, we used four questions. Who was counted, in terms of donor type and first-time or repeat status? Which assay and which confirmation steps produced the result? What did pre-donation selection remove before testing? And in what community, and over what period, was the study set? These questions are used throughout the next section, and Table 3 lists the sources of variation we found most often discussed. None of these steps is difficult, but each one is easy to skip.

4. Results

4.1 What an HBsAg Figure Measures

Read narrowly, a donor HBsAg percentage is the proportion of donations, or of donors, that gave a reactive result with the assay in use, usually after confirmation. It is a measure of screening yield. It is not the proportion of donors with hepatitis B, because infected donors can be negative, and it is not the proportion of the community with hepatitis B, because donors are selected. That is a modest claim, but it is the one the literature currently supports.

A figure can also be expressed per donation or per donor, and these are not interchangeable. Repeat donors contribute many donations, so a per-donation figure leans toward the habits of regular donors. A per-donor figure leans toward whoever came forward in the period. Reports that do not say which they used leave the reader to guess. A reader looking at a prevalence figure should ask a plain question: who was counted, and when?



4.2 What HBsAg Testing Misses

Two kinds of infection pass an HBsAg test. The first is the window period, early in infection, when the virus is present but the antigen has not yet reached a detectable level. A donor tested at the wrong moment tells the service very little about the next unit. The second is occult infection, defined at an expert meeting as the presence of viral DNA in a person who is negative for the surface antigen, usually at low levels (42). Occult infection may follow resolution of an earlier episode or reflect variants that the assay fails to recognise (39).

Figure 3 sets out, qualitatively, what each marker can be expected to detect at each stage. The point of the matrix is not precision but contrast: no single marker covers every state. A low antigen figure among donors therefore cannot be converted into a statement that the blood supply carries little hepatitis B.

	Window period	Acute	Chronic carrier	Occult	Past, resolved
HBsAg	misses	detects	detects	misses	misses
Anti-HBc	may detect	detects	detects	often detects	detects
HBV DNA	detects	detects	detects	often detects	misses

qualitative expectation, not measured data

Figure 3. Qualitative matrix of what each test is expected to detect at each infection state (schematic, not data).

4.3 Why Figures Differ Between Services

Several sources of variation operate at once (Table 3). The first is the community itself, since donors reflect the background level of infection in the population they come from (3, 26). The second is donor

type and selection: a service that relies on paid or replacement donors, or that screens poorly at the questionnaire stage, will see more infection than one that does not (30). Differences like these look small one donation at a time and add up across a blood service.

The third is the assay. An evaluation of dozens of HBsAg tests on a diverse panel found that analytical sensitivity differed appreciably between products and between viral types (36), and studies of mutant surface antigens tell a similar story (11, 37). Two services using different kits in different decades may be counting subtly different things. This is why the same assay can look excellent in one evaluation and unremarkable in the next.

Table 3. Why donor HBsAg figures from different services are hard to compare.

Source of variation	Effect on the figure	Useful report
Donor type	Paid, family and voluntary donors differ in risk (30)	Give donor types separately
First-time and repeat donors	First-time donors usually show more markers (31, 32)	Report both groups
Assay and confirmation	Sensitivity differs by assay (11, 36)	Name assay; state confirmation
Pre-test deferral	Fewer risk donors reach testing	Describe donor selection
Background infection	Reflects the community (3, 26)	Give local context

Note: The list is drawn from the cited methodological and epidemiological literature and is not exhaustive.

The fourth source is time. Donor figures can move quickly in a region when recruitment drifts, when testing changes or when an outbreak occurs, and a short series makes it difficult to say which of these happened (33). A five-year window is long enough to show a trend only if the donor mix stays steady, which is rarely



documented.

4.4 Reading and Reporting Donor Figures

From these observations a short set of reporting expectations follows. A good report gives the number of donors and donations tested, separates first-time from repeat donors, names the assay and the confirmation algorithm, describes the pre-donation selection, and places the result in the context of the surrounding community. It states whether anti-HBc or nucleic acid testing was used, because those change what a negative result means. It is a habit worth keeping even when the answer seems obvious.

A reader meeting a figure with none of these details can still make use of it, but only as a local indicator. It should not be used to compare one service with another, or to claim that a supply has become safer, without data on incidence among repeat donors and on residual risk estimates. Where such estimates exist, they depend on explicit assumptions about the length of the window period and the incidence of new infection (34, 35). The point is not that a study is poor, only that its result travels less far than its headline suggests.

5. Discussion

5.1 Interpretation

The main conclusion of this review is a conditional one. A donor HBsAg figure is informative about screening yield in a given setting and period, and much less informative about the safety of the units released. It sits at the end of a chain of choices about whom to recruit, whom to defer, which kit to use and which additional tests to run. Each choice leaves a mark on the number.

This does not make donor figures useless. They help a blood service see whether its donors are changing, whether deferral is

working and whether confirmation is catching errors. They help public health planners spot pockets of infection, though donors are an imperfect sentinel. The warning is only against stretching them past what they can carry.

5.2 Limitations

This is a narrative review, and it has the limitations of the form. The selection of sources was not systematic, and the choice of studies may have favoured those that made a point neatly. Large parts of the literature are from North America and Europe, while the settings in which donor HBsAg figures are most debated are often elsewhere.

The review also draws on work about different populations and on technology that has since moved on, so some conclusions about assays and nucleic acid testing may already be dated. Few of the cited studies were designed to answer the question of how donor HBsAg figures should be compared, and the appraisal questions used here are the authors' own, not a validated tool. Reviews of this kind are more useful when they say where the evidence stops than when they smooth it over.

5.3 Directions for Future Work

Three needs stand out. The first is a standard minimum dataset for reporting donor serology, so that figures from different services can be set side by side. The second is more work on the combination of donor type, first-time status and age, because those factors interact and are usually reported one at a time. The third is better evidence on the cost and donor loss of adding anti-HBc or nucleic acid testing in settings where hepatitis B is common. A saving that vanishes once every cost is counted is not a saving a blood service would ever feel.



6. Conclusion

Donor HBsAg positivity is a useful number that is easily over-read. It reflects the community, the donors who are recruited and deferred, the assay and the timing of donation, and it cannot see window-period or occult infection. A low figure is not proof of a safe supply, and a high one does not by itself identify where the problem lies.

The practical message is modest. Report donor figures with their context, compare them only where the context is similar, and treat them as a description of screening yield rather than a verdict on transfusion safety. Supplementing HBsAg with other tests can narrow the gap, but only at a price that each service has to weigh for itself.

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9. Conflict of Interest

The authors declare no conflict of interest.

10. Author Contributions

C.G. conceived the review and wrote the sections on virology and natural history. R.K. wrote the sections on epidemiology and donor selection. L.K. wrote the sections on transfusion risk and screening strategy. All authors revised the manuscript and approved the final version.

11. Ethics Statement

This is a review of published literature. No human participants, donor records or samples were used, and no ethical approval was required.

12. Data Availability

No new data were generated. All sources are cited in the reference list.

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