Transmission of hepatitis B, hepatitis C and human immunodeficiency viruses through unsafe injections in the developing world: model-based regional estimates

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Thousands of millions of injections are delivered every year in developing countries, many of them unsafe, and the transmission of certain bloodborne pathogens via this route is thought to be a major public health problem. In this article we report global and regional estimates of the number of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections that may occur from unsafe injections in the developing world. The estimates were determined using quantitative data on unsafe injection practices, transmission efficiency and disease burden of HBV, HCV and HIV and the prevalence of injection use obtained from a review of the literature.

A simple mass-action model was used consisting of a generalized linear equation with variables accounting for the prevalence of a pathogen in a population, susceptibility of a population, transmission efficiency of the pathogen, proportion of injections that are unsafe, and the number of injections received. The model was applied to world census data to generate conservative estimates of incidence of transmission of bloodborne pathogens that may be attributable to unsafe injections. The model suggests that approximately 8–16 million HBV, 2.3–4.7 million HCV and 80 000–160 000 HIV infections may result every year from unsafe injections. The estimated range for HBV infections is in accordance with several epidemiological studies that attributed at least 20% of all new HBV infections to unsafe injections in developing countries. Our results suggest that unsafe injections may lead to a high number of infections with bloodborne pathogens. A major initiative is therefore needed to improve injection safety and decrease injection overuse in many countries.

Keywords: hepatitis B; hepatitis C; HIV infections, injections; linear models; risk factors.

Introduction

Transmission of bloodborne pathogens through contaminated needles and syringes has long been recognized (1). However, the extent of this problem in developing countries has been poorly quantified. Increased rates of bloodborne infections in exposed groups, such as health care workers and injecting drug users, have been well described in the industrialized world (2–5). This has resulted in routine immunization against viral hepatitis B and measures to prevent needle-stick injuries in health care workers (6). Before widespread hepatitis B immunization, it was estimated that approximately 8700 cases of viral hepatitis B from percutaneous exposures, mostly needle-sticks, occurred every year in the USA (7). Supplies of free needles and bleach disinfection kits have been distributed in many cities to control disease transmission among injecting drug users (8, 9). However, the transmission of disease to health care workers and between injecting drug users in industrialized countries is only a small fraction of the total transmission from contaminated needles and syringes worldwide.

Thousands of millions of injections, many of them unsafe, are given each year in developing countries. WHO defines a safe injection as one that does not harm the recipient, the health care worker or the community. For the purpose of this paper, we defined an unsafe injection as reuse of a syringe or needle from patient to patient without sterilization. The high prevalence of bloodborne pathogens, the popularity and overuse of injections, and the high proportion of injections that are unsafe have generated concern (10–13). Although the spread of human immunodeficiency virus (HIV) among injecting drug users has been modelled (8), no global estimates for nosocomial patient-to-patient transmis-

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sion of hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV have been published.

We have developed a simple modelling approach that permits quantification of the risk of cross-infection due to unsafe injections, and which considers variables such as susceptibility of the patient, transmission efficiency of a virus, prevalence of a virus, proportion of injections that are unsafe and number of injections received. The model is similar to that used by Aylward (14) and Allard (15). Elsewhere in this issue we have reviewed and compiled from the literature all available data on quantitative aspects of unsafe injection practices in developing countries (16) and estimated the proportion of injections that may be unsafe. The number of injections received per capita per year was also estimated, based on Expanded Programme on Immunization (EPI) country reports, as well as data in the published literature. For this study, we used median parameter values from the review (16) to generate an estimate of the number of HBV, HCV and HIV infections that occur from unsafe injections in various geographical regions in the developing world.

Method

The model approach

We created a model consisting of a simple generalized linear equation for calculating the probability that an average individual in a particular geographical region will acquire the infectious agent of interest each year. This probability was then multiplied by population size for each world region to give an estimate of the incidence of transmission of bloodborne pathogens per year.

The equation used to estimate the individual risk of becoming infected is as follows:

$$P(I) = 1 - (1 - P(s) \cdot P(t) \cdot P(e))^{n},$$

where $P(I)$ is the probability of an individual becoming infected each year, $P(s)$ is the probability that the individual is susceptible to the organism, $P(t)$ is the probability that the organism will be transmitted given the injection equipment is contaminated with infectious blood, $P(e)$ is the probability that the individual is exposed to injection equipment contaminated with infectious blood, and n is the number of injections that an individual receives in a one-year period.

$P(e)$ is a function of the prevalence of an organism, $P(v)$, and the proportion of injections that are unsafe, $P(u)$. $P(e)$ was calculated using the following equation:

$$P(e) = P(v) \cdot P(u).$$

Susceptibility to HBV is a function of the prevalence of active infection with hepatitis B surface antigen (HBsAg) and the prevalence of immunity, defined as possession of surface antibody (anti-HBs) such that:

$$P(s) = 1 - [\text{Prevalence(HBsAg-positive)} + \text{Prevalence(anti-HBs-positive)}]$$

For modelling HCV and HIV transmission, we assumed that susceptibility was a function of the prevalence of HIV and HCV in the particular population, such that for HIV:

$$P(s) = 1 - \text{Prevalence(HIV-positive individuals)}.$$

The following assumptions are implicit in this model:
– everyone in a population (i.e. sick and not sick) receives the same number of injections;
– all members of a population are equally at risk of becoming infected from an unsafe injection.

Results

Parameter values

For the model, the variables that have been well documented in the literature include the prevalence and transmissibility of particular diseases, and the probability that an individual, in a specific population or population subgroup, would be susceptible to the pathogen. The variables that have not previously been established in the literature, and which were therefore estimated for the model, include the proportion of injections that are unsafe and the number of injections received.

The parameters used for modelling were median values generated from the data compiled and analysed in our literature review (16).

The transmission efficiency, $P(t)$, of an infectious agent was assumed to be the same as for needle-stick injuries in health care workers. Median values of $P(t)$ were 0.3% for HIV, 30% for hepatitis B carriers, and 6% for HCV carriers (16). The hepatitis B transmission was taken to be 30% because many infected people are e-antigen-positive in the developing world. The actual transmissibility of these organisms through an unsafe medical injection may be higher than for a needle-stick injury owing to possible contamination of the syringe, although the quantity of blood found at needle-stick and injection sites has been found to be similar (17).

Prevalence of injections

Approximately 25 billion (25 thousand million) syringes are used globally each year, at least half of them for injections (Becton Dickinson, personal communication, 1999). This number is consistent with EPI country reports, that about a thousand million injections per year are given for immunization purposes, and that 8–12 curative injections are given for each immunization injection (18). Thus, we assume that 8–12 billion injections are given worldwide each year in the health sector, roughly 1.5–2 injections per person per year. The literature review (16) reports an average incidence of 1.5 injections per person per year, with a range of 0.9–7.5. Therefore, for the purposes of

the model, we allowed the number of yearly injections per person (*n*) to range from 1 to 2.

Prevalence of bloodborne pathogens

The prevalences of HIV, HBV and HCV infections by world region are presented in Table 1 (*19–21*).

Prevalence of unsafe injections

The most critical variable is the proportion of injections that are unsafe, *P*(u). From the quantitative data reviewed (*16*), estimates for *P*(u) were made (Table 2).

The WHO regional classifications do not distinguish industrialized versus developing countries. Therefore, for the model, countries were grouped by the standard World Bank regional classifications, as follows:

– Established market economies;
– Latin America and the Caribbean;
– Sub-Saharan Africa;
– Former Socialist Economies of Europe
– India;
– China;
– Middle Eastern crescent;
– Other Asian and Pacific islands.

At least 50% of injections were unsafe in 14 of 19 countries (representing five world regions) for which data were available. Since the precise proportion of injections that are unsafe is not known, and as this parameter is the most controversial, we chose for the model the median value (50%) for regions in Asia and sub-Saharan Africa. The lowest levels of safety were assumed to occur in sub-Saharan Africa and in Asia, where at least 50% of injections were unsafe in all but three countries for which data were available (*16*). For the Middle Eastern crescent and the former socialist economies of Europe, the proportion of injections that are unsafe has not been addressed in many studies, but is assumed to be lower than in Africa or Asia. In two wealthy countries in the Middle Eastern crescent, injection safety was reported to be excellent, but in other countries, such as Pakistan, more than 80% of injections were unsafe (*16*). Because economic diversity and quality of health services are highly variable, we conservatively estimated that a median of 15% of injections were unsafe in these regions. For Latin America, data on unsafe injection practices were only available for one small country, and therefore model-based estimates of viral transmission in this region were not made.

Model results

According to our model (Table 2), the highest numbers of infections from unsafe injections occur in Asia and sub-Saharan Africa, where the prevalence of the pathogens is highest and injection safety poorest. The model calculates that approximately 8–16 million HBV, 2.3–4.7 million HCV and 80 000–160 000 HIV infections may occur annually due to

Table 1. Population and prevalence of hepatitis B carriers, hepatitis C virus (HCV), and human immunodeficiency virus (HIV), by region

Region	Population (x 1000)	Hepatitis B carriers	HCV prevalence	HIV prevalence[a]
Established market economies	669 606	0.005	0.020	0
Latin America and the Caribbean	456 963	0.001	0.020	0.00340
Former Socialist Economies of Europe	413 443	0.040	0.020	0.04000
Middle Eastern crescent	481 752	0.040	0.020	0.00034
India	871 158	0.040	0.019	0.00200
China	1 155 795	0.120	0.041	0.00010
Sub-Saharan Africa	520 425	0.100	0.020	0.04100
Other Asian countries and Pacific islands	837 373	0.100	0.020	0.00620

[a] HIV prevalence for the total population. Note: these prevalence rates differ from figures provided by UNAIDS, where prevalence rates are based on the sexually active population only (i.e. those aged 15–49 years).

unsafe injections. The ranges were generated considering that between 1 and 2 injections are received per person per year on average.

If a sterile needle and syringe are used for each injection, the number of resulting infections is zero. As the sensitivity analyses demonstrate (Fig.1), for many realistic parameter values an essentially linear relationship exists between the proportion of injections that are unsafe and the number of HIV, HBV and HCV infections that could occur. Thus, reducing the proportion of injections that are unsafe by one half reduces the number of infections by one half. The HIV estimates demonstrate that, for a disease with a relatively low transmissibility and prevalence, unsafe injections can result in substantial transmission in situations where susceptibility is high.

Discussion

Unsafe injections are a major public health problem in many areas of the developing world for the following reasons: the high prevalence of certain bloodborne diseases (*1*); the enormous popularity and overuse of injectable therapy (*10*); and the high proportion of these injections that are unsafe (*16*). Considering that 8–12 billion injections are given yearly, and that 50% of these are unsafe in most of the countries in the developing world, we estimate, using a simple linear mass-action model, that this situation results in approximately 8–16 million HBV infections, 2.3–4.7 million HCV infections and 80 000–160 000 HIV infections per year. Enormous numbers of additional injections are given outside the health sector, in markets, by traditional and unlicensed practitioners, with the "family syringe", and by dentists. Other parenteral exposures, such as scarification, skin-piercing, circumcision, tattooing and acupuncture also carry high risk of transmission of bloodborne pathogens, and are not included in these estimates.

Table 2. **Estimated proportion of unsafe injections and estimated number of hepatitis B (HBV), hepatitis C (HCV), and human immunodeficiency virus (HIV) infections, by region**

Region	Proportion of unsafe injections, P(u)	Estimated no. of infections[a]					
		HBV		HCV		HIV	
		$n = 1$	$n = 2$	$n = 1$	$n = 2$	$n = 1$	$n = 2$
Established market economies	0	0	0	0	0	0	0
Latin America and the Caribbean	NA	NA	NA	NA	NA	NA	NA
Former Socialist Economies of Europe	0.15	446 278	892 555	60 772	121 543	11 907	23 814
Middle Eastern crescent	0.15	520 011	1 040 022	70 813	141 625	122	243
India	0.50	3 130 524	6 261 047	405 430	810 859	4 312	8 624
China	0.50	2 078 559	4 157 117	1 136 743	2 273 485	286	572
Sub-Saharan Africa	0.50	780 052	1 560 104	254 946	509 892	51 208	102 415
Other Asian countries and Pacific islands	0.50	1 255 118	2 510 235	410 212	820 424	12 850	25 699
Total		**8 210 541**	**16 421 081**	**2 338 915**	**4 677 829**	**80 684**	**161 367**

[a] n = No. of injections received per person per year; NA = not available.

As part of a new injection safety initiative at WHO, we have performed a literature review gathering quantifiable data from all available studies on unsafe injection practices, popularity of injections, and studies linking unsafe injections to transmission of bloodborne pathogens (16). Unfortunately, the status of injection safety has been addressed by relatively few studies, and many countries are poorly represented or simply lacking in any appropriate data at all. The accuracy of our estimates depends on how generalizable the available data are, and how our simple mass-action model would compare with more complex, stratified models. Our model estimates for hepatitis B transmission via unsafe injections were in agreement with several epidemiological studies that attributed at least 20% of new hepatitis B infections to unsafe injections (16). WHO estimates that approximately 67 million new hepatitis B infections occur yearly (22). The global contribution of unsafe injections to the transmission of HCV and HIV remains unclear. In certain cases, however, the essential contribution of unsafe injections has been clearly demonstrated for outbreaks of these diseases, most notably the HIV outbreak in orphanages in Romania (23), and HCV transmission in Egypt (24, 25).

Previous models of cross-infection risk (14, 15) took into account the possibility that contaminated injection equipment could place more than just the next susceptible recipient at risk. These models included an additional variable, which allowed either variance in the number of times a needle is reused (14), or in the number of subsequent susceptible recipients at risk of infection once equipment has been contaminated (15). The authors stressed that there is a nonlinear relationship between the number of infections in a population and the number of times

a needle is reused. The risk to a population rises rapidly with the first few reuses of a needle; the number of estimated cases of injection-associated HBV is only marginally higher when each needle is reused nine times compared to four times (14). Our model does not include such a variable, instead we simply introduced P(u) as the probability that an injection is unsafe, and considered each injection individually. This allowed us to make our final estimates based on the proportion of injections that are unsafe, a parameter that we can support with data from the literature review (16).

The model we have described here is a mass-action model, which assumes that everyone in a population is put at equal risk from unsafe injections. In fact, there are high-risk and low-risk groups depending on a number of factors. The prevalence of pathogens, the susceptibility to infection and the number of injections received vary considerably by country, by region, and by age group. More realistic models would therefore require stratification and data on all these parameters.

Some other considerations are too complex to be included in our simple mass-action model, but are important in any realistic understanding of the risk of unsafe injections for infants and children. Infants in developing countries normally receive approximately five immunization injections in the first year of life, in addition to any curative injections. Although immunization injections are considered safer in general than curative injections, the high number of injections received by this susceptible group merits concern. Many infants acquire HIV and HBV via the maternal route, and may be highly infectious. HIV is transmitted to more than one-third of infants of infected mothers, and HIV-infected infants have very high blood titres of the virus, presumably

resulting in higher infectivity of their blood. For hepatitis B, the outcome of the disease differs depending on the age of acquisition; children under 5 years of age have a relatively high chance of becoming chronic carriers and subsequently developing liver disease, while children over 5 years and adults have a relatively low chance. A further consideration is that infants and children with certain diseases tend to be over-represented in hospitals and clinics, and therefore the prevalence of infected blood in contaminated injection equipment may be higher than the background population prevalence. One study found that 50% of children in a ward in sub-Saharan Africa were HIV positive (26).

There are many reasons why unsafe injections are given in developing countries, the main logistic reasons being as follows: lack of sufficient quantities of syringes and needles; lack of operational sterilization equipment or fuel to operate such equipment; and high patient demand for injections. In many regions, there is also a lack of understanding on many levels in the health sector — by administrators, health workers and patients — of the real risk of unsafe injections, or even of what comprises an unsafe injection. A common misconception is that it is safe to reuse the syringe between patients if the needle is changed.

The transmission of hepatitis B, hepatitis C, and HIV are by no means the only risks involved in unsafe injections; besides abscesses caused by bacterial contamination, many outbreaks involving other pathogens have been linked to unsafe injections (16). Further investigation of the prevalence of unsafe injection practices, the contribution of unsafe injections to the transmission of hepatitis viruses and HIV in specific areas, the reasons for the lack of adequate sterilization practices, and the feasibility of various strategies for improving injection safety are urgently needed. Although the extent of unsafe injection practices is still poorly documented in many regions (e.g. Latin America), this model provides an estimate of the incidence of infection with bloodborne pathogens that may be expected from various estimated proportions of unsafe injections. ■

Acknowledgements

Fig. 1. **Sensitivity analysis varying proportion of unsafe injections for 1 or 2 injections per person per year: a) No. of viral hepatitis B infections per year in India. b) No. of viral hepatitis C infections per year in other Asian and Pacific islands. c) No. of human immunodeficiency virus infections per year in sub-Saharan Africa**
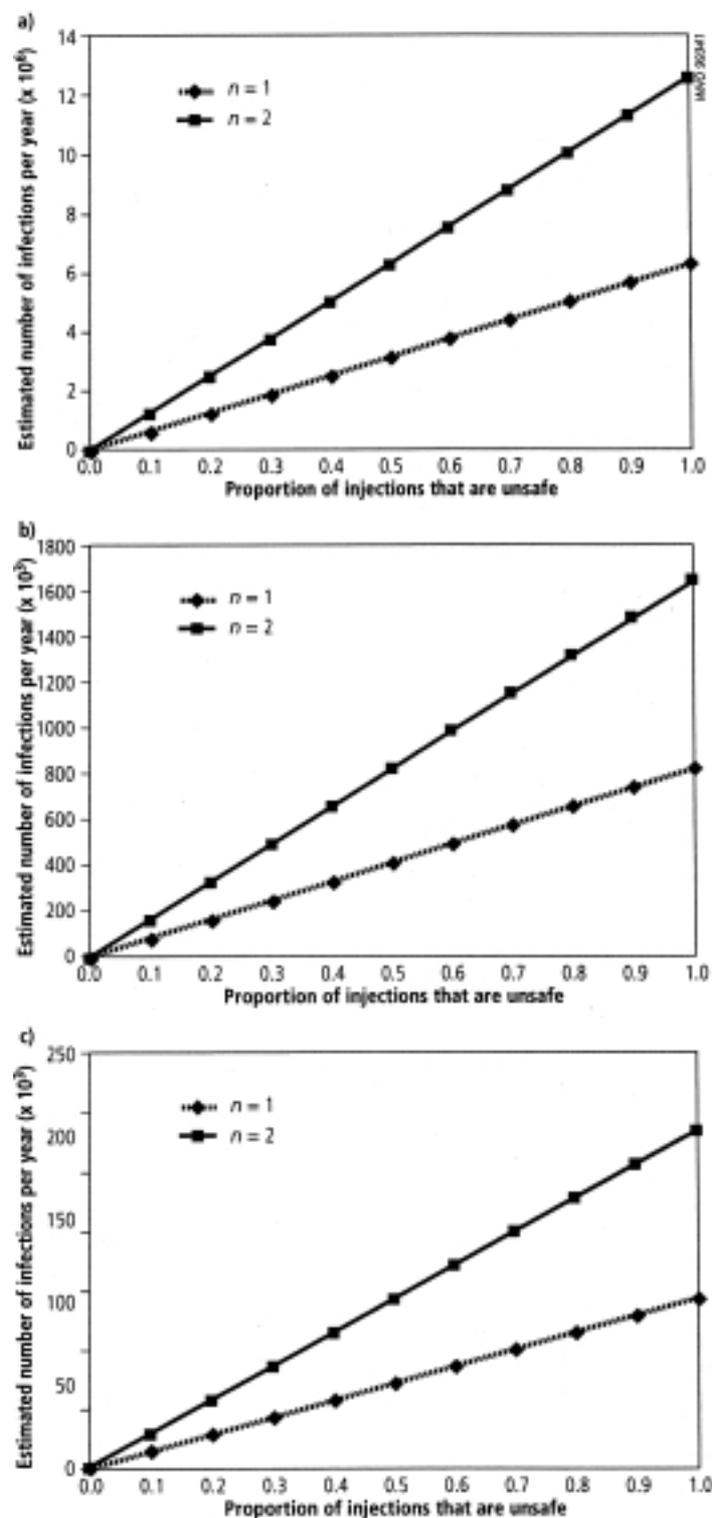
Résumé

Transmission du VHB, du VHC et du VIH par des injections pratiquées dans de mauvaises conditions d'hygiène

Des milliards d'injections sont administrées chaque année dans les pays en développement, souvent dans de mauvaises conditions d'hygiène, et la transmission par le sang de certains agents pathogènes apparaît comme un problème de santé publique majeur. Nous publions dans cet article le nombre estimatif, pour le monde et les régions, des infections par le virus de l'hépatite B (VHB), par le virus de l'hépatite C (VHC) et par le virus de l'immunodéficience humaine (VIH) pouvant être imputées à des injections pratiquées dans de mauvaises conditions d'hygiène dans les pays en développement. Le calcul de ces estimations repose sur des données quantitatives relatives aux injections faites dans de mauvaises conditions d'hygiène, à l'efficacité de la transmission et à la charge de morbidité due au VHB, au VHC et au VIH, et sur la prévalence de l'utilisation d'injections telle qu'elle ressort d'un examen de la documentation sur ce domaine.

On a utilisé un modèle « mass-action » simple consistant en une équation linéaire généralisée dont les variables rendent compte de la prévalence d'un germe pathogène dans une population, de la sensibilité d'une population, de l'efficacité de la transmission du germe pathogène, de la proportion d'injections dangereuses et du nombre d'injections reçues. Le modèle a été appliqué aux données de recensement mondiales pour obtenir des estimations prudentes de l'incidence de la transmission.

Le modèle fait apparaître que les injections pratiquées dans de mauvaises conditions d'hygiène pourraient être responsables chaque année d'environ 8–16 millions d'infections dues au VHB, 2–4,5 millions d'infections dues au VHC et 75 000–150 000 infections à VIH. La fourchette estimative des infections dues au VHB correspondait aux estimations comparables basées sur plusieurs études du programme élargi de vaccination fondées sur la population qui attribuent au moins 20% des nouvelles infections dues au VHB à des injections pratiquées dans de mauvaises conditions d'hygiène.

Il ressort des résultats obtenus que les injections pratiquées dans de mauvaises conditions d'hygiène peuvent entraîner un grand nombre d'infections dues à des germes pathogènes transmis par voie sanguine. Une initiative majeure s'impose donc pour améliorer la sécurité des injections et réduire l'utilisation excessive d'injections dans de nombreux pays.

Resumen

Transmisión del VHB, el VHC y el VIH a través de inyecciones peligrosas

En los países en desarrollo se administran cada año miles de millones de inyecciones, muchas de ellas peligrosas, y se considera que la propagación de ciertos agentes patógenos de transmisión hematógena por esa vía constituye un importante problema de salud pública. En este artículo presentamos estimaciones mundiales y regionales del número de infecciones por los virus de la hepatitis B (VHB), la hepatitis C (VHC) y la inmunodeficiencia humana (VIH) atribuibles a inyecciones peligrosas en el mundo en desarrollo. Las estimaciones se efectuaron empleando datos cuantitativos sobre las prácticas peligrosas de inyección, la eficiencia de la transmisión y la carga de morbilidad por el VHB, el VHC y el VIH, y la prevalencia del uso de inyecciones determinada mediante una revisión de la literatura.

Se utilizó un modelo simple de acción de masas consistente en una ecuación lineal generalizada con variables que reflejaban la prevalencia de un agente patógeno en la población, la susceptibilidad de ésta, la eficiencia de transmisión del agente patógeno, la proporción de inyecciones peligrosas y el número de inyecciones recibidas. El modelo se aplicó a datos censales mundiales, para obtener estimaciones prudentes de la incidencia de transmisión.

El modelo indica que las inyecciones peligrosas pueden estar provocando cada año aproximadamente 8-16 millones de infecciones por el VHB, 2–4,5 millones por el VHC, y 75 000–150 000 por el VIH. El intervalo estimado para la hepatitis B coincide con estimaciones similares de varios estudios poblacionales del Programa Ampliado de Inmunización, que atribuyen al menos un 20% de las nuevas infecciones por el VHB a las inyecciones peligrosas.

Los resultados obtenidos indican que las inyecciones peligrosas pueden dar lugar a un elevado número de infecciones por agentes patógenos de transmisión hematógena. Se necesita por tanto una iniciativa de gran calibre para mejorar la seguridad de las inyecciones y reducir el abuso de las mismas en muchos países.

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