Interactions between immunotoxicants and parasite stress: implications for host health: Supplementary Information

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Additional Analysis

Stability Analysis around the DFE

We perform the stability analysis for the system under the assumption $Z = 0$ before $Y = 0$ (equation 3 in the main text).

Phase I $\quad 0 \leq Q < \frac{c}{h} = Q_0^*$

We analyse the system in the region $c - hQ > 0$ and $\lambda - rQ > 0$ (phase I). This ensures that X, Y, Z exist. The system describing the dynamics of the host under toxicant exposure

$$\frac{dX}{dt} = \lambda - \beta YX - dX - rQ \tag{1a}$$
$$\frac{dY}{dt} = \beta YX - aY - pYZ \tag{1b}$$
$$\frac{dZ}{dt} = c - bZ - hQ \tag{1c}$$

has equilibria

$$(X_B^{DFE}, Y_B^{DFE}, Z_B^{DFE}) = \Big(\frac{\lambda - rQ}{d}, 0, \frac{c - hQ}{b}\Big)$$

$$(X_B^{EE}, Y_B^{EE}, Z_B^{EE}) = \Big(\frac{ab + cp - hpQ}{\beta b}, \frac{-abd - cdp + dhpQ - bQr\beta + \beta b\lambda}{\beta ab + cp\beta - hpQ\beta}, \frac{c - hQ}{b}\Big)$$

The Jacobian matrix of the system is calculated as follows

$$J = \begin{pmatrix} -d - \beta Y & -\beta X & 0 \\ \beta Y & -a - pZ + \beta X & -pY \\ 0 & 0 & -b \end{pmatrix}$$

The Jacobian evaluated at the DFE is

$$J_{DFE} = \begin{pmatrix} -d & \beta(\frac{rQ-\lambda}{d}) & 0 \\ 0 & -a - p(\frac{c-hQ}{b}) + \beta(\frac{\lambda - rQ}{d}) & 0 \\ 0 & 0 & -b \end{pmatrix}$$

which has eigenvalues

$$-b$$

$$-d$$

$$-\frac{abd + cdp - dhpQ + bQr\beta - b\beta\lambda}{bd}$$

The system has a stable node at the DFE when all eigenvalues are real and negative. Clearly $-b < 0$ and $-d < 0$, so the DFE is a stable node when

$$Q < \frac{abd + cdp - b\beta\lambda}{dhp - br\beta}$$

and a saddle (at least one of the eigenvalues is positive) when

$$Q > \frac{abd + cdp - b\beta\lambda}{dhp - br\beta}$$

Therefore $\frac{abd+cdp-b\beta\lambda}{dhp-br\beta}$ gives us the threshold toxicant exposure value at which a small density of parasite will cause outbreak within the host. In the parameter space explored in the manuscript the DFE is unstable for any value of Q in the phase I region $0 \leq Q < \frac{c}{h}$.

Phase II $\quad Q_0^* = \frac{c}{h} \leq Q < \frac{\beta\lambda - ad}{r\beta} = Q_1^*$

In this region, the system becomes

$$\frac{dX}{dt} = \lambda - \beta YX - dX - rQ \tag{1a}$$

$$\frac{dY}{dt} = \beta YX - aY \tag{1b*}$$

with equilibria

$$(X_B^{DFE}, Y_B^{DFE}) = \left(\frac{\lambda - rQ}{d}, 0\right)$$

$$(X_B^{EE}, Y_B^{EE}) = \left(\frac{a}{\beta}, -\frac{ad + r\beta Q - \beta\lambda}{a\beta}\right)$$

The Jacobian matrix is calculated as follows

$$J = \begin{pmatrix} -d - \beta Y & -\beta X \\ \beta Y & -a + \beta X \end{pmatrix}$$

The Jacobian evaluated at the DFE is

$$J_{DFE} = \begin{pmatrix} -d & -\beta(\frac{\lambda - rQ}{d}) \\ 0 & -a + \beta(\frac{\lambda - rQ}{d}) \end{pmatrix}$$

which has eigenvalues

$$\begin{aligned} &-d \\ &-a + \beta(\frac{\lambda - rQ}{d}) \end{aligned}$$

The system has a stable node at the DFE when all eigenvalues are real and negative. Clearly $-d < 0$, so the DFE is a stable node when

$$Q > \frac{\beta\lambda - ad}{r\beta}$$

and (unstable) saddle if eigenvalues are real and of opposite signs which occurs when

$$Q < \frac{\beta\lambda - ad}{r\beta}$$

which corresponds to the definition for Phase II ($Q < \frac{\beta\lambda - ad}{r\beta} = Q_1^*$). After this threshold toxicant exposure, the DFE becomes stable and hence the parasite is removed from the host.

Phase III $\quad Q_1^* = \frac{\beta\lambda - ad}{r\beta} \leq Q < \frac{\lambda}{r}$

In this phase, the system becomes

$$\frac{dX}{dt} = \lambda - dX - rQ \tag{1a*}$$

with equilibria

$$X_B = \frac{\lambda - rQ}{d}$$

and corresponding eigenvalue $-d$ evaluated at the equilibrium. Since this is negative, the equilibruim is always stable for $d > 0$. At the point at which the equilibrium becomes 0, the host is dead and the equations are undefined for larger Q. This happens when the assumption $\lambda - rQ > 0$ is reversed.

To summarise, the EE equilibria is feasible until one of $c - hQ > 0$ and $\lambda - rQ > 0$ is broken. After phase I ($Q = \frac{c}{h} = Q_0^*$), then $Z = 0$, and the equilibria is expressed in terms of the two dimensional system X and Y. After which the EE equilibria is feasible until $Q = \frac{\beta\lambda - ad}{r\beta} = Q_1^*$, at which point $Y = 0$, so the system reverts to the one dimensional system of X, and a stable DFE. This equilbria is feasible until $Q^* = \frac{\lambda}{r}$ after which all state values are equal to 0.

Additional Figures

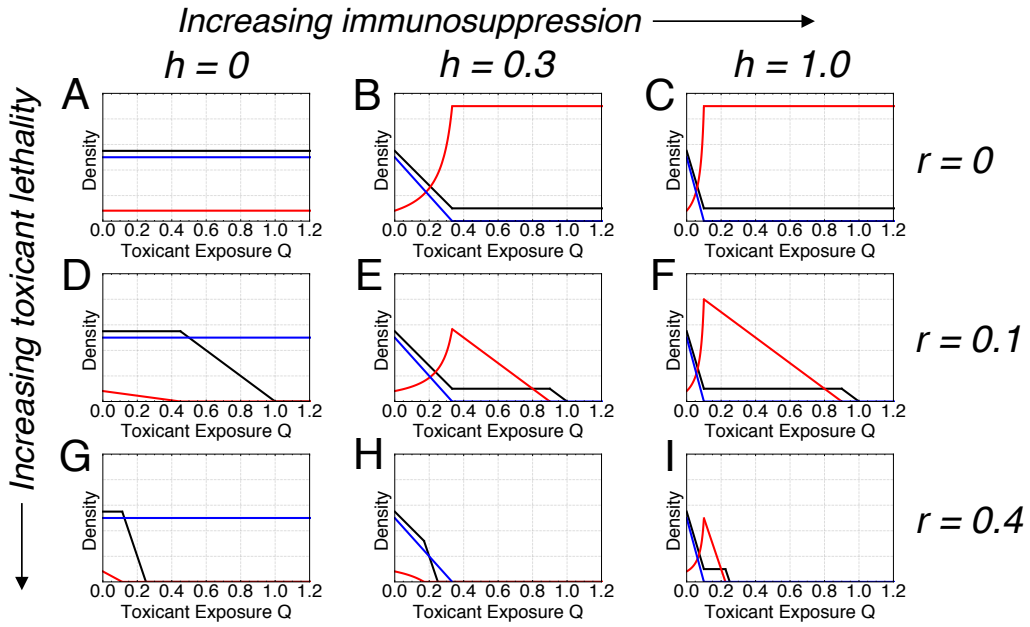


Figure S1a: The mechanism of parasite infection under increasing toxicant exposure, for a pairwise range of both immunosuppressive ($h = 0, 0.3, 1.0$) and lethal ($r = 0, 0.1, 0.4$) effects of toxicant with all parameters taken from Table 2. This shows the parameter dependence of immunity, parasite density and within-host cells at equilibrium within the dynamics of our model. The total densities of immune function (blue), parasite load (red) and within-host cells (black) change as an individual is subject to higher toxicant loads, according to the phases of the model.

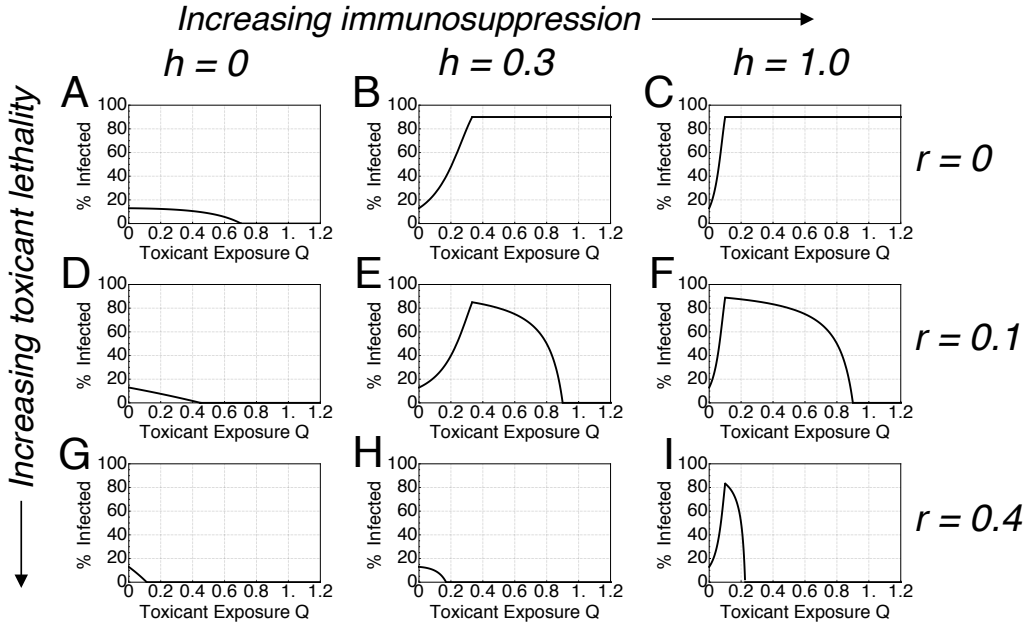


Figure S1b: The mechanism of parasite infection under increasing toxicant exposure, for a pairwise range of both immunosuppressive ($h = 0, 0.3, 1.0$) and lethal ($r = 0, 0.1, 0.4$) effects of toxicant with all parameters taken from Table 2. This shows how the total % parasite infection (black) changes depending upon the combination of both immunosuppressive and lethal effects.

Density dependent assumption

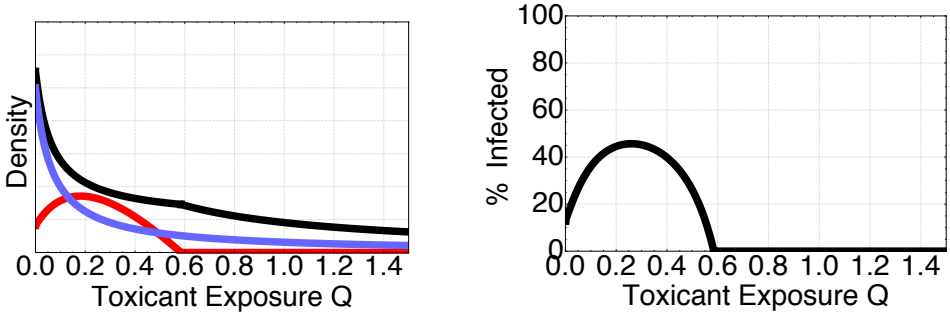
System (1) assumes that toxicant exposure reduces the sources of within-host cells λ and immunity c. In this supplementary analysis of the model we explore the alternative assumption that toxicant load reduces the within-host cells and immune function dependent upon the density of both, respectively. In this case, system (1) becomes

$$\frac{dX}{dt} = \lambda - \beta YX - dX - rQX \tag{4a}$$

$$\frac{dY}{dt} = \beta YX - aY - pYZ \tag{4b}$$

$$\frac{dZ}{dt} = c - bZ - hQZ \tag{4c}$$

We reproduce Figure 2 from the main text in order to examine the equilibria under this new assumption with the same parameter set. Figure 6 shows the dynamical behaviour of the model under this assumption. We show that parasite load is still maximised at an intermediate toxicant exposure, and the removal of the parasite at high toxicant exposure.



(a) (b)

Figure S2: The mechanism of parasite infection under increasing toxicant exposure for density-dependent assumption. This shows the parameter dependence of immunity, parasite density and within-host cells at equilibrium within the dynamics of our model. In (a) the total densities of immune function (blue), parasite load (red) and within-host cells (black) change as an individual is subject to higher toxicant loads. In (b) the total % parasite infection (black) changes as the toxicant load is increased. Parameters as in Table 2.