**Table S1.** Systematic Review of Reported Cases of Hypersensitivity to Acetaminophen

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| **Study** | **Country** | **Population** | **Type of Reaction** | **Number of Participants** | **Diagnosis** | **Management** | **Excluded or included in meta-analysis** |
| Ban et al. 2016[26] | Korea | Adult | Non-immediate reactions: SJS/TEN | 6 | History | Corticosteroids, IVIg | Excluded as less than 10 patients |
| Calvo Campoverde et al. 2016[27] | Spain | Pediatric | Non-immediate reactions: Other | 1 | Oral challenge | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Carsin et al. 2016[28] | France | Pediatric | Non-immediate reactions: Other | 1 | Oral challenge | Antihistamines | Excluded as less than 10 patients |
| Chadli et al. 2016[29] | Tunisia | Adult | Non-immediate reactions: Other | 1 | Skin test | - | Excluded as less than 10 patients |
| Choi et al. 2016[13] | Korea | Pediatric | Unknown | 12 | Oral challenge | Antihistamines, Inhaled beta-2 agonists | Included |
| Misirlioglu et al. 2016[30] | Turkey | Pediatric | Non-immediate reactions: Fixed drug eruption | 1 | Skin test | - | Excluded as less than 10 patients |
| Numata et al. 2016[31] | Japan | Adult | Immediate reaction (including anaphylaxis) | 1 | Skin test | - | Excluded as less than 10 patients |
| Pena et al. 2016[32] | Spain | Pediatric | Non-immediate reactions: SJS/TEN | 1 | History | IVIg | Excluded as less than 10 patients |
| Perez-Alzate et al. 2016[33] | Spain | Adult | Immediate reaction (including anaphylaxis) | 4 | Oral challenge | - | Excluded as less than 10 patients |
| Suwarsa et al. 2016[34] | Indonesia | Pediatric/Adult | Non-immediate reactions: SJS/TEN | 9 | History | Corticosteroids | Excluded as less than 10 patients |
| Topal et al. 2016[14] | Turkey | Pediatric | Immediate reaction (including anaphylaxis) | 28 | Skin test, Oral challenge | - | Included |
| Trautmann et al. 2016[35] | Germany | Adult | Immediate reaction (including anaphylaxis) | 4 | Oral challenge | Antihistamines | Excluded as less than 10 patients |
| Watanabe et al. 2016[36] | Japan | Adult | Non-immediate reactions: SJS/TEN | 1 | In vitro testing | Corticosteroids, IVIg | Excluded as less than 10 patients |
| Barbarroja-Escudero et al. 2015[37] | Spain | Adult | Non-immediate reactions: Fixed drug eruption | 1 | Oral challenge | - | Excluded as less than 10 patients |
| Boccaletti et al. 2015[38] | Italy | Pediatric | Non-immediate reactions: Other | 1 | History | - | Excluded as less than 10 patients |
| Gaspar et al. 2015[39] | Portugal | Pediatric | Immediate reaction (including anaphylaxis) | 1 | History | - | Excluded as less than 10 patients |
| Guvenir et al. 2015[15] | Turkey | Pediatric | Immediate reaction (including anaphylaxis)  Non-immediate reactions: Fixed drug eruption | 54  1 | History, Oral Challenge | Corticosteroids, Antihistamines | Included |
| Harimoto et al. 2015[40] | Japan | Adult | Non-immediate reactions: SJS/TEN | 1 | - | Corticosteroids, IVIg | Excluded as less than 10 patients |
| Jain et al. 2015[41] | Australia | Adult | Immediate reaction (including anaphylaxis) | 2 | Skin test | Corticosteroids, Epinephrine | Excluded as less than 10 patients |
| Loh et al. 2015[16] | Singapore | Pediatric | Immediate reaction (including anaphylaxis) | 24 | Oral challenge | Corticosteroids, Antihistamines | Included |
| Nanishi et al. 2015[42] | Japan | Pediatric | Non-immediate reactions: Other | 1 | In vitro testing | Antihistamines | Excluded as less than 10 patients |
| Park et al. 2015[43] | South Korea | - | Non-immediate reactions: SJS/TEN | 3 | History | Corticosteroids, IVIg | Excluded as less than 10 patients |
| Slim et al. 2015[44] | Tunisia | Adult | Non-immediate reactions: SJS/TEN | 1 | History | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Ariza et al. 2014[45] | Spain | Adult | Immediate reaction (including anaphylaxis)  Cross-intolerance reactions | 7  35 | History, Oral Challenge | - | Excluded as cross-reactivity was assessed and less than 10 patients for immediate reactions. |
| Asero et al. 2014[46] | Italy | Adult | Cross-intolerance reactions | 97 | History, Oral Challenge | - | Excluded as cross-reactivity was assessed. |
| Biswal et al. 2014[47] | India | Pediatric | Non-immediate reactions: SJS/TEN | 1 | History | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Corzo et al. 2014[48] | Spain | Pediatric | Unknown  Cross-intolerance reactions | 3  38 | Oral challenge | - | Excluded as cross-reactivity was assessed and less than 10 patients for unknown reactions. |
| Hotaling et al. 2014[49] | U.S.A | Pediatric | Non-immediate reactions: SJS/TEN | 1 | History | - | Excluded as less than 10 patients |
| Jung et al. 2014[50] | Korea | Pediatric/Adult | Non-immediate reactions: Fixed drug eruption | 9 | - | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Kim EJ et al. 2014[51] | Korea | Adult | Non-immediate reactions: SJS/TEN | 2 | History | Corticosteroids, IVIg | Excluded as less than 10 patients |
| Kim YJ et al. 2014[52] | Korea | - | Cross-intolerance reactions | 149 | Oral challenge | - | Excluded as patients reported NSAID hypersensitivity and cross-reactivity with acetaminophen was assessed. |
| Rojas-Perez-Ezquerra et al. 2014[17] | Spain | Pediatric/Adult | Immediate reaction (including anaphylaxis)  Non-immediate reactions: Fixed drug eruption  Non-immediate reaction: other | 10  2  1 | History, Oral Challenge | Antihistamines | Included |
| Gomez-Traseira et al. 2013[53] | Spain | Adult | Non-immediate reactions: Fixed drug eruption | 1 | Oral challenge | - | Excluded as less than 10 patients |
| Guerriero et al. 2013[54] | Italy | Pediatric | Non-immediate reactions: Other | 1 | History | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Liew et al. 2013[24] | Singapore | Pediatric | Immediate reaction (including anaphylaxis) | 5 | - | - | Excluded as less than 10 patients |
| Lugovic-Mihic et al. 2013[55] | Croatia | Adult | Non-immediate reactions: Other | 1 | History | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Padmavathi et al. 2013[56] | India | - | Unknown | Unknown | - | - | Excluded as unknown number of patients |
| Rahman et al. 2013[57] | Bangladesh | Pediatric/Adult | Non-immediate reactions: Fixed drug eruption | 5 | Oral challenge | - | Excluded as less than 10 patients |
| Raucci et al. 2013[58] | Italy | Pediatric | Non-immediate reactions: SJS/TEN | 11 | History | Corticosteroids | Excluded as no diagnostic testing was done |
| Renaudin et al. 2013[18] | France | Pediatric/Adult | Immediate reaction (including anaphylaxis) | 13 | Oral challenge, In vitro testing | Corticosteroids, Antihistamines, Epinephrine | Included |
| Takeo et al. 2013[59] | Japan | Adult | Non-immediate reactions: Other | 1 | In vitro testing | Corticosteroids | Excluded as less than 10 patients |
| Thalayasingam et al. 2013[19] | Singapore | Adult | Unknown | 13 | Oral challenge | - | Included |
| Turk et al. 2013[60] | Turkey | Pediatric/Adult | Unknown | 6 | - | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Yilmaz et al. 2013[25] | Turkey | Pediatric | Immediate reaction (including anaphylaxis)  Non-immediate reactions: Other | 1  8 | Skin test, Oral challenge | Antihistamines | Excluded as less than 10 patients |
| Yokose et al. 2013[61] | Japan | Adult | Non-immediate reactions: Other | 1 | Oral challenge | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Zambonino et al. 2013[62] | Spain | Pediatric | Non-immediate reactions: Other | 1 | Oral challenge | - | Excluded as less than 10 patients |
| Arora et al. 2012[63] | U.S.A | - | Non-immediate reactions: Other | 1 | Oral challenge | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Chaudhry et al. 2012[64] | Australia | Pediatric/Adult | Cross-intolerance reactions | 11 | - | - | Excluded as patients reported NSAID hypersensitivity and cross-reactivity with acetaminophen was assessed. |
| Couto et al. 2012[65] | Portugal | Pediatric | Immediate reaction (including anaphylaxis) | 1 | History | Corticosteroids, Antihistamines, Epinephrine | Excluded as less than 10 patients |
| Elm et al. 2012[66] | U.S.A | - | Non-immediate reactions: Fixed drug eruption | 1 | History | - | Excluded as less than 10 patients |
| Khawaja et al. 2012[67] | Pakistan | Adult | Non-immediate reactions: SJS/TEN | 1 | History | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Ognongo-Ibiaho et al. 2012[68] | Congo | - | Non-immediate reactions: Fixed drug eruption | 1 | - | - | Excluded as less than 10 patients |
| Rutkowski et al. 2012[3] | United Kingdom | Pediatric/Adult | Immediate reaction (including anaphylaxis)  Non-immediate reactions: Other | 3  29 | Skin test, Oral challenge | - | Included |
| Umayahara et al. 2012[69] | Japan | Pediatric | Non-immediate reactions: Other | 1 | In vitro testing | Corticosteroids | Excluded as less than 10 patients |
| Zhong et al. 2012[70] | China | - | Unknown | 44 | - | - | Excluded as no diagnostic testing was done |
| Abuaf et al. 2011[71] | France | - | Unknown  Cross-intolerance reactions | 5  20 | Oral challenge | - | Excluded as less than 10 patients  and as patients reported NSAID hypersensitivity and cross-reactivity with acetaminophen was assessed. |
| Andrade et al. 2011[72] | Portugal | Pediatric/Adult | Non-immediate reactions: Fixed drug eruption | 8 | Oral challenge | Corticosteroids | Excluded as less than 10 patients |
| Aun et al. 2011[73] | Brazil | - | Cross-intolerance reactions | 44 | Oral challenge | Antihistamines | Excluded as patients reported NSAID hypersensitivity and cross-reactivity with acetaminophen was assessed. |
| Chalabianloo et al. 2011[20] | Norway | Pediatric/Adult | Immediate reaction (including anaphylaxis)  Non-immediate reactions: Other | 10  20 | Oral challenge | - | Included |
| Cristallo et al. 2011[74] | Italy | Pediatric/Adult | Non-immediate reactions: SJS/TEN | 10 | - | - | Excluded as no diagnostic testing was done |
| Dona et al. 2011[75] | Spain | Pediatric/Adult | Cross-intolerance reactions | 52 | - | - | Excluded as patients reported NSAID hypersensitivity and cross-reactivity with acetaminophen was assessed. |
| Na et al. 2011[76] | Korea | Pediatric | Immediate reaction (including anaphylaxis)  Non-immediate reactions: Other | 1  6 | Oral challenge | Corticosteroids, Epinephrine | Excluded as less than 10 patients |
| Bremec et al. 2010[77] | Slovenia | Adult | Non-immediate reactions: Fixed drug eruption | 1 | Oral challenge | - | Excluded as less than 10 patients |
| Honma et al. 2010[78] | Japan | Adult | Non-immediate reactions: SJS/TEN | 1 | In vitro testing | Corticosteroids | Excluded as less than 10 patients |
| Trujillo et al. 2010[79] | Spain | Pediatric | Non-immediate reactions: SJS/TEN | 1 | Oral challenge | - | Excluded as less than 10 patients |
| Drummond et al. 2009[80] | Australia | Adult | Non-immediate reactions: Fixed drug eruption | 1 | Oral challenge | Corticosteroids | Excluded as less than 10 patients |
| Ho et al. 2009[81] | China | Pediatric | Immediate reaction (including anaphylaxis) | 1 | Oral challenge | Corticosteroids, Antihistamines, Epinephrine | Excluded as less than 10 patients |
| Levi et al. 2009[82] | France | Pediatric | Non-immediate reactions: SJS/TEN | 24 | - | - | Excluded as no diagnostic testing was done |
| Lopez Abad et al. 2009[83] | Spain | Adult | Non-immediate reactions: Fixed drug eruption | 1 | Oral challenge | - | Excluded as less than 10 patients |
| Sanchez-Borges et al. 2009[84] | Venezuela | Pediatric/Adult | Cross-intolerance reactions | 75 | Oral challenge | - | Excluded as patients reported NSAID hypersensitivity and cross-reactivity with acetaminophen was assessed. |
| Treudler et al. 2009[85] | Germany | Adult | Non-immediate reactions: Other | 1 | Skin test | Corticosteroids | Excluded as less than 10 patients |
| Ben-Ari et al. 2008[86] | Israel | Adult | Non-immediate reactions: Other | 1 | in vitro testing | Corticosteroids | Excluded as less than 10 patients |
| Hassani et al. 2008[21] | France | Pediatric | Immediate reaction (including anaphylaxis) | 43 | History, Oral Challenge | - | Included |
| Oshikoya et al. 2008[87] | Nigeria | Pediatric | Immediate reaction (including anaphylaxis) | 1 | History | - | Excluded as less than 10 patients |
| Panchabhai et al. 2008[88] | India | Pediatric | Immediate reaction (including anaphylaxis) | 1 | History | Corticosteroids, Antihistamines | Excluded as less than 10 patients |
| Rodriguez-Trabado et al. 2008(89) | Spain | Pediatric/Adult | Immediate reaction (including anaphylaxis) | 2 | History | - | Excluded as less than 10 patients |
| Dhingra et al. 2007[90] | India | Pediatric | Non-immediate reactions: Other | 1 | History | - | Excluded as less than 10 patients |
| Inomata et al. 2007[91] | Japan | Adult | Cross-intolerance reactions | 2 | Oral challenge | - | Excluded as less than 10 patients |
| Kang et al. 2007[92] | Singapore | Pediatric | Immediate reaction (including anaphylaxis) | 1 | History | - | Excluded as less than 10 patients |
| Kidon et al. 2007[9] | Singapore | Pediatric | Cross-intolerance reactions | 18 | Oral challenge | Corticosteroids, Inhaled beta-2 agonists | Excluded as patients reported NSAID hypersensitivity and cross-reactivity with acetaminophen was assessed. |
| Matsuno et al. 2007[93] | Japan | Adult | Non-immediate reactions: Other | 1 | In vitro testing | - | Excluded as less than 10 patients |
| Morais-Almeida et al. 2007[94] | Portugal | Adult | Immediate reaction (including anaphylaxis) | 2 | Oral challenge | Corticosteroids | Excluded as less than 10 patients |
| Sezer et al. 2007[95] | Turkey | Pediatric | Non-immediate reactions: Other | 1 | History | Corticosteroids | Excluded as less than 10 patients |
| Tsujino et al. 2007[96] | Japan | Adult | Immediate reaction (including anaphylaxis) | 1 | Oral challenge | Antihistamines | Excluded as less than 10 patients |
| Wohl et al. 2007[97] | Israel | Adult | Non-immediate reactions: Other | 1 | Oral challenge, In vitro testing | - | Excluded as less than 10 patients |