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Title: Effects of tobacco smoke and poly IC, alone and in combination, on mouse lung pathology

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Body: Tobacco smoke (TS) exposure for 4d induced lung inflammation in mice which was exaggerated by the viral mimetic poly IC (pIC). The effects of each agent, alone and in combination, on lung pathology were examined. Methods Mice were exposed to air or TS for 4d. Saline or pIC was administered intra-nasally and mice killed 4-72hrs after the last exposure. Lungs were lavaged prior to inflation and fixed for histopathological assessment. Results No findings were seen in air-exposed mice. Dosing of pIC gave a time-dependent change in incidence/severity of lesions (mononuclear cell accumulation, diffuse alveolitis and pneumonitis) which was maximal at 4hr, falling by 48hr. TS-exposure gave a different histological phenotype, with acute cell influx and reactive damage the major features seen at 24hr, declining in severity by 48hr. Combination of pIC and TS gave an increased incidence and severity of lung pathology compared to the phenotype seen which each alone. At 4hr, diffuse mononuclear cell infiltration was apparent which increased in disposition and severity by 24hr, with an associated expansion of lymphoid tissue. At 48hr, inflammatory cell infiltration was very pronounced with reactive pneumonitis, initiation of reactive changes in the bronchioles and more pronounced vasculature damage. At 72hr the pathology was still verpronounced with reactive changes, notably in the bronchiolar mucosa and the epithelium of the transitional zone. Initiation of alveolar wall damage was evident. Conclusion As well as an exaggerated steroid sensitive BAL inflammation, the combination of pIC and TS provoked a more severe/persistent tissue inflammation with alveolar wall damage evident within 3 days.