

Low Dose Interferon Alfa-2b (IFN) Delays the Onset of Symptoms in Experimental Rhinovirus (RV) colds. Meschievitz, C., and Turner, R., Schering, Kenilworth, NJ, USA and MUSC, Charleston, SC, USA.

Field trials have shown that 5 million units (MU) per day of intranasal IFN for seven days (35 MU) prevents rhinovirus colds. To determine the effectiveness of lower doses, 15 and 10.5 MU of IFN given over four days (6 MU on day one, followed by either 3 or 1.5 MU/day for the next three days) were compared to placebo in human volunteers. The volunteers were given IFN for two days prior to intranasal challenge with RV type 39. IFN in the doses used had no effect on RV shedding or the number of symptomatic colds. IFN did have an effect on the time to appearance of peak symptoms. Mean symptom severity (MSS) scores were highest on day 2 post-RV challenge (last day of treatment) in the placebo group compared to day 6 and 7 in the 10.5 and 15 MU-IFN treated groups respectively. The median day post-RV challenge to peak symptom score was day 2 for the placebo group compared to day 3.5 for the 10.5 MU and day 5 for the 15 MU treated groups. MSS scores were significantly lower ( $p < 0.05$ ) in both IFN treated groups on day 2 post-RV challenge when compared to placebo. Symptom pathogenesis in colds is unknown but host response to viral infection may be an important factor. While anti-viral effects were not seen at the doses used in this study, the dose response relationship in the delay in peak symptom onset suggests an IFN effect which may be related to IFN's immune modulatory activity.

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### MODULATION OF INTERFERON/ACYCLOVIR EFFECTS BY INDOMETHACIN IN CHRONIC HEPATITIS B.

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Antiviral therapy with alfa interferon ( $\alpha$ IFN) evokes flu-like symptoms and suppression of hepatitis B virus replication as well as display of HLA antigens. Since indomethacin (IMC) may prevent symptoms, we investigated the modulation by IMC of the effects of  $\alpha$ IFN with and without acyclovir (ACV) in chronic HBeAg (+) hepatitis. Patients received for 2 weeks either:  $\alpha$ IFN 12MU/day i.m. (group I, n=8),  $\alpha$ IFN 5MU/day s.c. (group II, n=10), ACV 30mg/kg/day i.v. (group III, n=11) or the combination ACV/- $\alpha$ IFN (group IV, n=5). Group I received also paracetamol 4 x 500 mg and group II and IV indomethacin 2 x 75 mg during day 0-3. Sera were tested for HBeAg, HBV-DNA polymerase activity (DNAP) and SGOT by standard methodology and, as measure of HLA turnover, for beta2 microglobulin (b2MG) by RIA before, 1 and 2 weeks after start of treatment. IMC in contrast to paracetamol completely prevented flu-like symptoms. There was a marked fall (54-97%) of DNAP after 1 and 2 weeks in all groups. No change was observed for serum HBeAg or SGOT levels. B2MG concentration showed a significant rise (44-64%) after 1 and 2 weeks in group I, II and IV ( $p < 0.05$ ), no rise was noticed in group III. The increment in serum B2MG levels was not due to cytolysis. The antiviral effect of  $\alpha$ IFN consists of selective depression of viral particle synthesis and enhancement of HLA antigen display. IMC prevents flu-like symptoms of  $\alpha$ IFN treatment, without a negative influence on  $\alpha$ IFN effects in DNAP or b2MG.