
When World War II began in September 1939, Zuckerman fled to Soviet-occupied eastern Poland, where he organized Zionist youth groups. In April 1940 he returned to German-occupied Poland to encourage underground activities. At that time, he also met and fell in love with fellow underground leader, Zivia Lubetkin. The couple later married.

When the Germans launched mass deportations from Warsaw during the summer of 1942, Zuckerman called for armed resistance against the Germans. On July 28 he and other youth movement leaders established the ZOB, an underground resistance organization. That December, Zuckerman was sent by the ZOB to Cracow to meet with resistance fighters. During that mission, Zuckerman was wounded in the leg, and barely made it back.

When the Nazis initiated a second wave of deportations in January 1943, Zuckerman led a group of fighters in armed battle with the Germans. The ZOB spent the next three months preparing for a revolt. Zuckerman became commander of one of the three main areas of the ghetto. However, as it got closer to the uprising, the ZOB ordered Zuckerman to cross over to the Polish side of Warsaw to represent the organization there. During the Warsaw Ghetto Uprising, Zuckerman tried to supply his comrades with arms, and in the revolt's final leg, Zuckerman and others set up a rescue team that saved fighters by leading them through the sewer system.

After the uprising, Zuckerman joined the Jewish National Committee (Zydowski Komitet Narodowy), an organization which provided aid for Jews. He wrote a summary report about the ZOB that he sent to London. He also commanded a group of Jewish fighters in the Warsaw Polish Uprising.

After the war, Zuckerman and his wife got involved in the Beriha movement, helping Jews reach Palestine. They immigrated to Palestine themselves in 1947, where Zuckerman helped found the Ghetto Fighters' Kibbutz and the
Ghetto Fighters’ House. (see also Jewish Fighting Organization, Warsaw and Resistance, Jewish.)